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MEDICATION SAFETY PROFILE: A CASE REPORT OF FIRST TRIMESTER PREGNANCY PATIENTS WITH DEEP VEIN THROMBOSIS DIAGNOSIS ACCOMPANIED BY COMORBIDITY

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ABSTRACT

Pregnancy is a hypercoagulable state that elevates the risk of Deep Vein Thrombosis (DVT). The selection of pharmacological interventions for DVT during pregnancy necessitates rigorous consideration of both maternal and fetal safety. Management becomes increasingly complex when the condition is accompanied by comorbidities, which often lead to polypharmacy and a higher potential for drug-drug interactions. This case report discusses a 33-year-old pregnant woman in her first trimester diagnosed with DVT in the left lower extremity, complicated by secondary hypertension, type 2 diabetes mellitus, and fever. The therapeutic regimen comprised 13 medications, including anticoagulants, antibiotics, analgesic-antipyretics, antiemetics, antihypertensives, and antidiabetic agents. Medication safety profiles were evaluated based on FDA pregnancy categories and other peer-reviewed references. Potential drug interactions were analyzed using the UpToDate® Lexicomp™ database. The study identified two drugs in category A, five in categories B and C, respectively, and one agent for which data was unavailable. Four potential drug interactions were identified, ranging from moderate to minor severity. All prescribed drugs demonstrated an adequate safety profile supported by current clinical literature. This study emphasizes the critical importance of a thorough risk-benefit analysis. Stringent monitoring is essential to ensure both the safety and efficacy of the treatment.

Keywords: Deep Vein Thrombosis, Medication, Pregnancy, Safety

ABSTRAK

Kehamilan merupakan kondisi hiperkoagulasi yang meningkatkan risiko Deep Vein Thrombosis (DVT). Pemilihan medikasi DVT selama kehamilan memerlukan pertimbangan khusus terkait keamanan maternal dan fetal. Kondisi ini menjadi lebih kompleks apabila disertai dengan komorbiditas. Adanya komorbiditas tersebut meningkatkan jumlah obat yang digunakan, seiring dengan meningkatnya potensi interaksi obat. Laporan kasus ini membahas seorang wanita hamil berusia 33 tahun pada trimester pertama dengan diagnosis DVT pada ekstremitas kiri, yang disertai dengan hipertensi sekunder dan diabetes melitus tipe 2 dengan demam. Tata laksana terdiri dari 13 rejimen obat, termasuk antikoagulan, antibiotik, analgesik-antipiretik, antiemetik, antihipertensi, dan antidiabetik. Profil keamanan obat ditinjau berdasarkan kategori FDA dan referensi relevan lainnya. Potensi interaksi obat dianalisis menggunakan aplikasi UpToDate® Lexicomp™. Hasil studi menunjukkan dua obat dalam kategori A, lima obat dalam kategori B dan C, serta satu obat yang tidak memiliki data. Ditemukan empat potensi interaksi obat yang terdiri dari tingkat moderat dan minor. Seluruh obat menunjukkan profil

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keamanan yang memadai berdasarkan dukungan berbagai literatur. Studi ini menekankan pentingnya analisis risiko-manfaat. Pemantauan ketat diperlukan untuk memastikan keamanan dan efikasi pengobatan.
Kata Kunci: Deep Vein Thrombosis, Medikasi, Kehamilan, Keamanan

1. Introduction

Deep Vein Thrombosis (DVT) is defined as the formation of an abnormal mass within the deep venous system, derived from blood constituents [1]. Pregnant women exhibit up to a fivefold increased risk of developing DVT compared to non-pregnant individuals. Physiological adaptations during pregnancy trigger complex hemodynamic and hormonal alterations, which significantly elevate the risk of thromboembolic events [2]. Consequently, an accurate diagnosis is imperative to mitigate further morbidity and mortality [3]. The management of DVT in the obstetric population necessitates extreme caution; healthcare professionals must select anticoagulant therapies that are not only efficacious but also demonstrate a proven safety profile for both mother and fetus.

Furthermore, the presence of comorbidities presents a significant challenge in clinical management. Comorbid conditions often lead to polypharmacy, which subsequently increases the risk of drug-drug interactions. A high incidence of potential drug interactions in prescriptions for pregnant patients has been previously documented in an observational study in Brazil [4]. This case report aims to review the medication safety profile for a patient in the first trimester of pregnancy diagnosed with DVT and concurrent comorbidities. The safety assessment was conducted based on the Food and Drug Administration (FDA) pregnancy categories, and potential drug interactions were analyzed using the UpToDate® Lexicomp™ database. Additionally, corroborating data were synthesized from relevant peer-reviewed literature. This study is intended to contribute to more robust and rational clinical decision-making in comparable complex cases.

2. Case Presentation

A 33-year-old female patient, at 6 weeks of gestation (first trimester) with a body weight of 97 kg, was admitted to the hospital presenting with stabbing pain, edema, localized warmth, and erythema in the hallux and the dorsum of the left foot, which had persisted for two days prior to admission. The patient reported febrile episodes and fluctuating chills starting three days before admission, which showed transient improvement following the administration of antipyretics. Concomitant symptoms included headache, nausea without emesis, cough, dyspnea, and abdominal pain. Urinary and bowel functions were reported to be normal. The patient had no history of food allergies; however, a drug allergy to nifedipine was noted, manifesting as nausea and vomiting.

The patient's medical history was significant for hyperuricemia over the past ten years, with a recent uric acid level of 9.8 mg/dL and a peak level of 12 mg/dL within the last year. Additionally, the patient reported a five-year history of hyperglycemia and hypertension. There was also a clinical suspicion of Polycystic Ovary Syndrome (PCOS) based on a one-year history of amenorrhea and irregular menstrual cycles. The patient's pre-hospitalization medication regimen is summarized in Table 1.

Table 1. Patient's medication history before hospitalization

Timing	Medication	Dosage
before pregnancy	Lisinopril	unclear documentation
	Losartan	50 mg, once daily
	Bisoprolol	5 mg, once daily
	Metformin	850 mg, once daily
	Allopurinol	unclear documentation
during pregnancy	Methyldopa	250 mg, twice daily
	Metformin	850 mg, once daily

The diagnosis of DVT was confirmed via Doppler ultrasonography, which revealed a characteristic "smoky appearance" thrombus extending from the inguinal vein to the left popliteal vein, accompanied by diminished venous blood flow. Vital signs and laboratory parameters were monitored throughout the hospitalization, with a primary focus on blood pressure and glycemic control. Upon admission, the patient's blood pressure was 163/97 mmHg. Laboratory findings showed a fasting blood glucose level of 199 mg/dL, a

2-hour postprandial glucose level of 140 mg/dL, and an HbA1c of 8.4%. During the course of treatment, blood pressure showed a downward trend, reaching a minimum of 140/90 mmHg. Similarly, glycemic levels improved, decreasing to 108 mg/dL for fasting glucose and 106 mg/dL for 2-hour postprandial glucose.

The patient was diagnosed with DVT of the left lower extremity (sinistra), complicated by several comorbidities: secondary hypertension secondary to bilateral renal artery stenosis, obstetric febrile illness associated with a complicated urinary tract infection, uncontrolled type 2 diabetes mellitus with overweight, and emesis gravidarum. The pregnancy was at 6–7 weeks of gestation, classified as a high-risk pregnancy requiring intensive monitoring. During hospitalization, the patient received a pharmacological regimen tailored to the clinical indications and diagnoses, as detailed in Table 2.

Table 2. Patient's medication during hospitalization

Medication	Route	Day Start	Dosage and Frequency	Modification
Paracetamol	intravenous	D1	20 drops/minute PRN	-
Sodium Chloride 0.9%	intravenous	D1	20 drops/minute	
Insulin Glargine	subcutaneous	D3	10 IU QD	8 IU QD (modified on D8)
Ceftriaxone	intravenous	D4	2 g QD	Stop on D6
Heparin Injection	intravenous	D5	5000 IU QD	-
Metoclopramide	intravenous	D1	10 mg q8h	-
Paracetamol	oral	D2	1000 mg q12h	-
Methyldopa	oral	D2	250 mg q12h	50 mg q8h (modified on D5)
Metformin	oral	D2	850 mg QD	Stop on D2
Sucralfate	oral	D2	500 mg q8h	-
Methylprednisolone	oral	D2	4 mg QD	-
Folic acid	oral	D3	1 mg QD	-
Amoxicillin	oral	D6	500 mg q8h	

Abbreviations
D_: day of hospitalization.
PRN: *pro re nata;* as needed.
QD: *quaque die;* once daily.
q8h: *quaque 8 hora;* every eight hours.
q12h: *quaque 12 hora;* every twelve hours.

After 8 days of treatment, the patient was transferred to outpatient care with reduced complaints and good general condition of the mother and fetus.

3. Discussion

The risk of venous thromboembolism (VTE) during pregnancy is significantly elevated compared to non-pregnant women of childbearing age. Previous studies indicate that this risk increases up to fourfold during gestation, with an estimated DVT incidence of 1.1 per 1,000 births [5]. In this case, the patient presented with characteristic clinical manifestations of DVT, including pain, erythema, localized warmth, and edema in the left lower extremity. Laboratory evaluations revealed fibrinogen and D-dimer levels within normal limits. It is important to note that pregnancy can yield false-negative D-dimer results, complicating its diagnostic utility [6]. Consequently, definitive confirmation of DVT was established through Doppler ultrasonography. A meticulous diagnostic approach is essential, particularly when clinical symptoms and imaging findings are highly suggestive of DVT.

The patient received a multifaceted pharmacological regimen tailored to her clinical indications. Medication management during pregnancy necessitates a rigorous evaluation of both maternal and fetal safety, as drugs can cross the placental barrier and potentially induce congenital malformations or impair fetal growth and development [7]. To guide clinical decision-making, medication safety data are provided by the Food and Drug Administration (FDA) through its classification system (Categories A, B, C, D, and X) [8]. The safety profiles of the medications administered during the first trimester, categorized according to FDA standards, are summarized in Table 3.

Table 3. The FDA pregnancy category in the first trimester

Drugs	Pregnancy Category (FDA)*
Metoclopramide 10 mg	A
Folic acid 1 mg	A
Ceftriaxone	B
Methyldopa 250 mg	B
Metformin 850 mg	B
Sucralfate 500 mg	B
Amoxicillin 500 mg	B
Paracetamol	C
Sodium chloride 0.9%	C
Insulin glargine	C
Heparin injection	C
Methylprednisolone 4 mg	C
Domperidone 10 mg	*No Data* Prohibited in the United States

Definition
A: Adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy. B: Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women, or animal reproduction studies have shown adverse effects, but well-controlled studies in pregnant women have shown no adverse effects to the fetus. C: Animal reproduction studies have shown an adverse effect on the fetus, or there are no animal reproduction studies and no well-controlled studies in humans. D: Positive evidence of fetal risk, but benefits may outweigh risks. X: Positive evidence of fetal risk, and risks clearly outweigh any possible benefit.
*Based on the FDA pregnancy category accessed in May 2025

A total of 13 drugs were received during treatment. There are two drugs in category A and five each for categories B and C. The drug named domperidone does not have data and is prohibited in the United States.

Methyldopa, metformin, ceftriaxone, amoxicillin, and sucralfate are classified as Category B, indicating they are relatively safe for use during pregnancy. Ceftriaxone, methyldopa, metformin, and amoxicillin are known to cross the placental barrier [9][10][11][12]. Methyldopa remains the first-line pharmacotherapy for chronic hypertension in pregnancy, as it is not associated with fetal harm and contributes to improved neonatal outcomes [10]. Furthermore, untreated urinary tract infections during pregnancy are linked to adverse obstetric outcomes; thus, the administration of appropriate antibiotics is a critical therapeutic intervention [9]. No major congenital anomalies have been reported following the administration of amoxicillin or ceftriaxone [12].

In current clinical practice, agents other than metformin are generally recommended for managing diabetes mellitus during pregnancy. However, no increased risk of adverse fetal or neonatal outcomes has been observed with maternal metformin use, provided that optimal glycemic control is achieved [13]. If metformin therapy is maintained, discontinuation is typically advised by the end of the first trimester [11]. Conversely, sucralfate does not cross the placenta due to its negligible systemic absorption following oral administration. It does not appear to elevate the risk of adverse fetal events during the first trimester and is considered safe for use throughout pregnancy [14].

Heparin, paracetamol, 0.9% sodium chloride infusion, insulin glargine, and methylprednisolone are classified under pregnancy Category C. Anticoagulation is the cornerstone of DVT management. Oral anticoagulants, such as warfarin, are teratogenic and strictly contraindicated during pregnancy [5]. In contrast, heparin is the preferred agent as it does not cross the placenta and possesses a superior safety profile. While Unfractionated Heparin (UFH) is not routinely recommended as first-line thromboprophylaxis, Low Molecular Weight Heparin (LMWH) offers a more favorable safety profile, characterized by fewer bleeding episodes and a reduced risk of heparin-induced thrombocytopenia or osteoporosis [15].

Maternal pyrexia is associated with adverse fetal outcomes; therefore, the administration of antipyretics may mitigate these risks [16]. Paracetamol should be utilized at the lowest effective dose for the shortest possible duration [17]. Similarly, the use of methylprednisolone requires caution. Although corticosteroids are often essential for managing inflammatory conditions in pregnancy—such as rheumatoid

arthritis, systemic lupus erythematosus, or inflammatory bowel disease—current evidence suggests that first-trimester exposure may slightly increase the risk of oral clefts. However, data remain conflicting, and the extent to which the underlying maternal disease contributes to this risk remains unclear [18]. The American College of Rheumatology guidelines favor non-fluorinated corticosteroids, such as methylprednisolone, for musculoskeletal diseases, provided that chronic high doses are avoided [19].

Poorly controlled diabetes during pregnancy significantly increases the risk of adverse maternal and fetal outcomes [9]. Clinical targets for blood glucose in pregnancy are established at <95 mg/dL (fasting), <140 mg/dL (1-hour postprandial), and <120 mg/dL (2-hour postprandial). As metformin monotherapy often fails to achieve these glycemic targets, the addition of insulin is a viable strategy [11]. Despite its Category C classification, insulin glargine may be utilized, necessitating diligent monitoring and dose titration [20].

The FDA has expressed concerns regarding domperidone due to its association with severe adverse effects, including cardiac arrhythmias and sudden death. Data regarding domperidone outcomes in pregnancy are limited. Nevertheless, observational and healthcare database studies suggest that first-trimester use is not significantly linked to adverse fetal events [21]. Its use should be restricted to cases where it is clinically necessary and alternative therapies are unavailable. Lastly, a systematic analysis of potential drug-drug interactions (DDIs) using the UpToDate® Lexicomp™ database identified four drug combinations, as detailed in Table 4. These interactions were categorized as moderate to minor in severity, occurring through both pharmacodynamic and pharmacokinetic mechanisms [22].

Table 4. Potential drugs interactions

Potential Drug Interaction	Mechanism of Interaction	Severity level	Management
Metformin - Insulin glargine	Pharmacodynamic	Moderate	Monitoring blood sugar level
Methylprednisolone - Insulin glargine	Pharmacodynamic	Moderate	Monitoring blood sugar level
Methylprednisolone - Metformin	Pharmacodynamic	Moderate	Monitoring blood sugar level
Metoclopramide - Paracetamol	Pharmacokinetic (only applied to orally administered paracetamol)	Minor	No action needed

Management of these potential interactions requires monitoring of blood sugar levels. In cases where blood sugar targets have not been achieved, modification of therapy by increasing the dose may be necessary. Follow-up should be performed in an outpatient setting.

Based on this case study, the medications were prescribed in accordance with the patient's clinical indications, notwithstanding that several agents are classified under FDA Category C. While the FDA pregnancy categories serve as a foundational framework for drug selection, they should not be regarded as absolute determinants. Therapeutic management during pregnancy is inherently unique, requiring the healthcare team to simultaneously prioritize maternal health and ensure fetal safety and viability until delivery. Consequently, clinical decisions must be meticulously evaluated using the principle of the risk-benefit ratio. Corroborating literature underscores the necessity of evidence-based medicine in the decision-making process. Ultimately, an interdisciplinary collaboration among physicians, nurses, and pharmacists is paramount to achieving optimal therapeutic safety and efficacy.

4. Conclusion

This case report demonstrates that the management of Deep Vein Thrombosis (DVT) in the first trimester of pregnancy, particularly when complicated by multiple comorbidities such as hypertension and diabetes mellitus, requires a highly individualized and rigorous pharmacological approach. The clinical assessment revealed that while the majority of the 13 administered medications fell within the safer FDA Categories A and B, the judicious use of Category C agents—including heparin and insulin—was clinically justified to mitigate severe maternal risks. Although the Lexicomp™ analysis identified four moderate-to-minor drug interactions, predominantly affecting glycemic control, these were effectively managed through diligent monitoring and dose titration. Ultimately, this study underscores that while FDA categories provide a foundational safety framework, optimal obstetric outcomes depend on a meticulous risk-benefit analysis and robust interdisciplinary collaboration to ensure both therapeutic efficacy and fetal-maternal safety.

5. Acknowledgments

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6. Conflict of Interest

No conflict of interest is associated with this work.

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