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MEDICATION-RELATED IATROGENESIS AND ADVERSE DRUG EFFECTS IN PREGNANT WOMEN: RISKS, PATTERNS, AND CLINICAL IMPLICATIONS

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Abstract: Medication-related iatrogenesis is an increasingly recognized contributor to maternal morbidity and adverse pregnancy outcomes. Physiological changes during pregnancy alter pharmacokinetics and pharmacodynamics, increasing the risk of adverse drug reactions. This study aimed to evaluate the prevalence, types, and consequences of drug-related iatrogenic events in pregnant women, identify high-risk medications, and assess clinical outcomes. A retrospective review of 2018–2024 maternal hospital records was conducted, analyzing cases of maternal morbidity and mortality linked to drug therapy. Findings indicate that the most frequent adverse effects were hepatotoxicity, allergic reactions, hypotension, and preterm labor. High-risk medications included antibiotics, NSAIDs, antihypertensives, anticoagulants, and certain anti-epileptic drugs. Early recognition, careful prescription practices, and monitoring are essential to minimize harm. Multidisciplinary management and adherence to evidence-based guidelines significantly reduce maternal and fetal complications.

Keywords: Medication iatrogenesis, pregnancy, adverse drug reaction, maternal morbidity, high-risk drugs, pharmacovigilance

Introduction

Medication iatrogenesis refers to harm caused by drugs prescribed or administered in a medical setting. In pregnant women, physiological adaptations—including increased blood volume, altered renal clearance, and hepatic metabolism—can amplify the risk of adverse drug effects. According to the World Health Organization, indirect causes of maternal morbidity and mortality, including medication-related events, account for a significant proportion of maternal deaths globally.

Pregnant women are often prescribed medications for chronic conditions such as hypertension, diabetes, epilepsy, or infections, as well as for pregnancy-related complications. However, inappropriate dosing, drug interactions, or use of teratogenic agents can lead to serious complications, including organ injury, preterm labor, fetal malformations, and maternal death. Studies by Allanazarov Ismoiljon Musurmonqulovych and other researchers emphasize that medication-related iatrogenesis remains an underreported but critical contributor to maternal morbidity in tertiary care settings.

The aim of this study was to evaluate the patterns, prevalence, and outcomes of drug-related iatrogenic events in pregnant women and to identify high-risk medications. Specific objectives included identifying the most common adverse drug reactions, assessing the timing and severity of events, and recommending strategies for safer medication use during pregnancy.

Methods

This study was conducted as a retrospective observational and analytical study to investigate the prevalence, patterns, and outcomes of medication-related iatrogenesis in pregnant women. The research was carried out at a tertiary maternity hospital over a six-year period from 2018 to 2024. The study population included all pregnant women who experienced adverse drug reactions or complications directly related to prescribed or administered medications during antenatal care, labor, or postpartum hospitalization.[2]

Inclusion criteria consisted of cases where maternal morbidity or mortality was directly or indirectly associated with drug therapy, including both chronic medications and medications prescribed specifically for pregnancy-related complications. Exclusion criteria included maternal complications that were purely obstetric in origin (such as preeclampsia, spontaneous hemorrhage, or infection without medication exposure), or cases where the adverse drug reaction could not be reliably linked to the medication administered.

Data were collected from multiple sources to ensure comprehensive case identification. These included patient medical records, hospital pharmacy logs, medication administration charts, laboratory test results, imaging studies, and autopsy reports when available. Each case was carefully reviewed to confirm the presence of a drug-related adverse effect, determine the severity of the event, and assess maternal and fetal outcomes.

The adverse drug events were classified into multiple categories for analytical purposes: hepatotoxicity, nephrotoxicity, cardiovascular complications (hypotension, arrhythmia), hematologic disorders (thrombocytopenia, coagulopathy), allergic reactions (ranging from urticaria to anaphylaxis), preterm labor induction, and teratogenic effects. Medications were grouped by pharmacological class, including antibiotics, NSAIDs, antihypertensives, anticoagulants, anti-epileptics, sedatives/analgesics, and antiviral agents. For each drug, dosing, duration, and timing of administration relative to gestational age were recorded.

Several analytical components ("experiments") were incorporated to understand risk factors and outcomes. First, the severity of the adverse drug reaction was graded as mild, moderate, or severe, based on maternal clinical status, need for hospitalization, and impact on fetal outcomes. Second, trimester-specific risk assessment was performed to evaluate whether drug administration during the first, second, or third trimester correlated with higher rates of adverse outcomes. Third, a polypharmacy analysis was conducted to assess whether multiple simultaneous medications increased the risk of severe reactions. Fourth, the time between drug administration and onset of adverse effects was recorded to identify patterns of delayed versus immediate reactions.[13]

Variables analyzed included maternal age, parity, gestational age at the time of exposure, type and class of medication, severity of reaction, interventions required (drug discontinuation, supportive

therapy, hospitalization, or intensive care), and maternal and fetal outcomes. Statistical analysis included descriptive statistics (percentages, means, and ranges), cross-tabulation of drug classes versus complications, and correlation analysis to identify drugs or combinations most strongly associated with severe maternal or fetal outcomes.

Additionally, a problem-focused component was included. Preliminary review indicated that inappropriate dosing, delayed recognition of adverse effects, and failure to adjust therapy for pregnancy-specific pharmacokinetics were major contributors to severe maternal outcomes. To address these problems, the study analyzed modifiable factors, including prescription errors, lack of standardized monitoring protocols, and insufficient patient education regarding warning signs of adverse reactions. The goal was to generate evidence-based recommendations for safer medication practices during pregnancy, emphasizing early detection, prompt intervention, and multidisciplinary management.[15]

Results

During the six-year study period from 2018 to 2024, a total of 55 cases of medication-related iatrogenic events in pregnant women were identified. The mean maternal age was 29 years (range 18–42), and most cases (60%) occurred in multiparous women. Adverse drug reactions were observed across all trimesters, but the highest incidence occurred in the second and third trimesters, accounting for 65% of cases. This trend reflects both increased medication use for pregnancy-related complications and physiological changes that alter drug metabolism in later gestation.

Hepatotoxicity was the most frequently observed complication, affecting 15 patients (27%). Most of these cases were associated with antibiotics such as amoxicillin-clavulanate, erythromycin, and ciprofloxacin, as well as anti-epileptic drugs including valproate and phenytoin. Clinical manifestations included jaundice, elevated liver enzymes, abdominal pain, and in severe cases, acute liver failure requiring intensive care. Hypotension and other cardiovascular effects were noted in 12 cases (22%), primarily related to antihypertensives such as labetalol and methyldopa, and sedatives/analgesics such as midazolam and opioids. These events occasionally led to dizziness, syncope, or transient fetal distress, highlighting the need for careful hemodynamic monitoring during drug administration.

Allergic reactions occurred in 10 patients (18%), ranging from mild urticaria to severe anaphylaxis. The most common triggers were antibiotics and NSAIDs. Emergency interventions, including administration of epinephrine, corticosteroids, and antihistamines, were required in 5 cases, with no maternal deaths in this subgroup due to rapid management. Preterm labor induced or exacerbated by NSAIDs or inappropriate tocolytic therapy was recorded in 8 cases (15%), demonstrating the significant impact of certain medications on gestational timing and perinatal outcomes.

Nephrotoxicity was observed in 5 cases (9%), primarily related to aminoglycoside antibiotics and high-dose diuretics. Laboratory findings included elevated serum creatinine and urea, with some patients requiring temporary dialysis. Hematologic complications, including thrombocytopenia and coagulopathy, were reported in another 5 cases (9%), frequently associated with anticoagulants such as

heparin and warfarin. These cases were often complicated by postpartum hemorrhage, necessitating transfusions or surgical intervention.

Maternal mortality occurred in 5 cases (9%). These fatalities were associated with severe hepatotoxicity (3 cases), massive hemorrhage due to anticoagulant-induced coagulopathy (1 case), and combined nephrotoxicity with sepsis (1 case). Fetal outcomes were affected in 25% of cases, including preterm delivery (15%), low birth weight (6%), and congenital anomalies (4%), predominantly associated with anti-epileptic drugs and NSAIDs administered during early pregnancy.[9]

Analysis of risk factors revealed that polypharmacy, delayed recognition of adverse effects, and incorrect dosing were strongly correlated with severe outcomes. In contrast, early detection and prompt intervention, such as discontinuation of the offending drug and initiation of supportive therapy, resulted in favorable maternal and fetal outcomes in 85% of cases. Multidisciplinary involvement, including consultation with obstetricians, pharmacologists, and intensive care teams, was associated with significantly lower rates of morbidity and mortality.[6]

These results underscore that medication-related iatrogenesis in pregnancy is a multifactorial issue involving pharmacological, procedural, and monitoring components. The study highlights the importance of careful prescription practices, trimester-specific risk assessment, continuous maternal monitoring, and rapid response to adverse drug reactions to minimize maternal and fetal complications.

Analysis

A detailed examination of the 55 cases of medication-related iatrogenesis revealed that the severity and outcomes of adverse drug events were influenced by multiple factors. The most significant contributors included polypharmacy, incorrect dosing, delayed recognition of adverse effects, and failure to adjust therapy for physiological changes in pregnancy. Hepatotoxicity and hypotension emerged as the leading complications, particularly associated with antibiotics, anti-epileptics, and antihypertensives. Allergic reactions, preterm labor, nephrotoxicity, and hematologic disorders were also significant, with maternal mortality occurring primarily in severe hepatotoxic and coagulopathic cases.[10]

Trimester-specific analysis showed that exposure to high-risk medications during the first trimester was most closely associated with teratogenic effects, while late pregnancy exposure increased the likelihood of preterm labor, hypotension, and maternal organ dysfunction. Polypharmacy amplified risks across all trimesters, and inadequate monitoring often delayed the recognition of complications, contributing to maternal and fetal morbidity.[3]

Multidisciplinary management, including early involvement of obstetricians, pharmacologists, and intensive care teams, was associated with better outcomes. Prompt discontinuation of offending drugs, supportive therapy, and adherence to trimester-specific pharmacological guidelines were crucial in reducing complications. The analysis confirms that medication-related iatrogenesis is not only a pharmacological problem but also a systems-level issue, requiring improved protocols, staff training, and vigilant monitoring.[7]

Discussion

Medication-related iatrogenesis is a significant contributor to maternal morbidity and indirect maternal mortality. The study highlights that high-risk drugs, improper dosing, and delayed intervention are the primary drivers of adverse outcomes. Hepatotoxicity caused by antibiotics and anti-epileptics was the leading cause of severe maternal complications, sometimes resulting in mortality. Cardiovascular complications, particularly hypotension associated with antihypertensives and sedatives, contributed to both maternal and fetal distress.

The findings align with previous studies emphasizing that pregnancy-specific pharmacokinetics and physiological changes alter drug metabolism, heightening the risk of adverse reactions. Polypharmacy and lack of careful monitoring exacerbate this risk, especially in tertiary care settings where complex cases are more frequent. Early recognition and intervention were shown to significantly improve maternal and fetal outcomes, reinforcing the need for systematic pharmacovigilance and multidisciplinary care.

Allanazarov Ismoiljon Musurmonqulovych and colleagues have noted similar patterns in tertiary maternity hospitals, highlighting the importance of evidence-based prescribing, adherence to safety protocols, and active monitoring for adverse drug events. Preventive strategies should include standardized dosing charts, trimester-specific drug guidelines, patient education regarding warning signs, and rapid response protocols to manage complications efficiently.

The study also emphasizes the need for institutional interventions, such as enhanced pharmacy oversight, staff simulation training for recognizing and managing drug-related complications, and better documentation of maternal medication exposure. These strategies can help reduce both maternal morbidity and fetal complications such as preterm birth and congenital anomalies.

Limitations of the study include its retrospective design, reliance on medical record documentation, and a limited sample size. Despite these limitations, the findings provide critical insights into the patterns and risks of drug-related iatrogenesis in pregnancy and inform strategies for prevention and early intervention.

Conclusion

Medication-related iatrogenesis is a preventable but significant contributor to maternal morbidity and mortality. High-risk medications include antibiotics, NSAIDs, antihypertensives, anticoagulants, and anti-epileptics. Adverse outcomes range from hepatotoxicity, hypotension, and allergic reactions to preterm labor, fetal malformations, and maternal death.

Prevention requires a comprehensive approach: careful prescription practices, monitoring for early signs of adverse drug effects, and adherence to trimester-specific pharmacological guidelines. Multidisciplinary management involving obstetricians, pharmacologists, and intensive care teams significantly improves outcomes. Polypharmacy and delayed recognition of complications are major risk factors, and interventions such as patient education, protocol adherence, and rapid response systems are essential to reduce harm.

Overall, minimizing medication-related iatrogenesis in pregnant women requires a combination of individual vigilance, institutional protocols, and team-based clinical strategies to safeguard both maternal and fetal health.

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