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Assessing drug-associated adverse events of spontaneous abortion or fetal death: A disproportionality analysis based on FDA adverse event reporting system

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Abstract: **Background**: Spontaneous abortion and fetal death represent significant reproductive health challenges, affecting approximately 10-20% of recognized pregnancies. Certain medications are an acquired risk factor for spontaneous abortion or fetal death. **Objectives**: This pharmacovigilance investigation sought to systematically assess the disproportionality signal of medication-associated spontaneous abortion or fetal death by leveraging the most extensive publicly accessible database of adverse event reports. **Methods**: Reports from the FDA Adverse Event Reporting System (FAERS) were used to conduct disproportionality analysis, ranging from the first quarter of 2004 to the second quarter of 2025. Medications were categorized based on the Anatomical Therapeutic Chemical (ATC) classification system. **Results**: The analysis identified 43,199 reports of drug-related spontaneous abortion or fetal death, involving 1,001 different drugs. 119 drugs were identified as significantly associated with disproportionality by the disproportionality analysis. The largest therapeutic category was anti-infective for systemic use (J), comprising 41 drugs (34.5%). Following this were the genitourinary system and sex hormones (G), which had 22 drugs (18.5%), the nervous system (N) with 15 drugs (12.6%), the alimentary tract and metabolism (A) with 9 drugs (7.6%) and antineoplastic and immunomodulating agents (L) with 8 drugs (6.7%). **Conclusions**: A total of 119 medications were identified as potentially associated with spontaneous abortion or fetal death. This study emphasizes the elevated disproportionality signal associated with anti-infectives for systemic use, as well as the genitourinary system and sex hormones. Identification of specific medications linked to these adverse outcomes can guide targeted medication counseling for women planning pregnancy.

Keywords: Drug-related side effects and adverse reactions; Fetal death; FAERS; Pharmacovigilance; Spontaneous abortion

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INTRODUCTION

Spontaneous abortion, commonly referred to as miscarriage or fetal death, represents a significant reproductive health challenge, affecting approximately 10-20% of recognized pregnancies (Moradinazar *et al*., 2020; Nikitina *et al*., 2026). These events not only impose profound emotional distress on individuals and families (Ho *et al*., 2022) but also contribute to substantial economic burdens on healthcare systems due to the need for medical interventions and psychological support (Lin *et al*., 2022). Spontaneous abortion or fetal death primarily results from chromosomal abnormalities (Yang *et al*., 2020; Chen *et al*., 2025), maternal health conditions (Dan *et al*., 2021; Li *et al*., 2021), drug-induced factors (Abu-Tineh *et al*., 2023) and environmental factors (Lin *et al*., 2022; Zheng *et al*., 2025). Among these causes, drug-induced factors are of increasing concern because the use of medications for various indications during pregnancy is rising. However, extensive studies of drug-induced spontaneous abortion and fetal death are lacking. Identifying drugs that could lead to spontaneous abortion or fetal death is crucial for informed clinical medication decisions.

Existing research suggests that some categories of drugs, such as anti-inflammatory drugs (NSAIDs) (Ying *et al*., 2022), antibiotics (Muanda *et al*., 2017), certain antidepressants (Almeida *et al*., 2016) and antiepileptic medications (Zeytin Demiral *et al*., 2024) are associated with an elevated likelihood of spontaneous abortion or fetal death. According to a historical cohort study from Denmark, pregnant women who were prescribed antipsychotic drugs had a 34% higher likelihood of experiencing spontaneous abortion compared to those who did not use such medications (Sorensen *et al*., 2015). With the increased use and prolonged treatment durations of approved drugs, concerns about their potential to cause spontaneous abortion or fetal death have intensified. Accurately assessing drug-related risks for spontaneous abortion or fetal death is challenging due to frequently missing data on drug exposure during pregnancy. Numerous pharmacovigilance investigations have explored the association between specific pharmaceuticals and spontaneous abortion or fetal death. For example, the antiepileptic drug levetiracetam demonstrated significant

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disproportionality signals related to spontaneous abortion and stillbirth (Wang *et al*., 2024). Biologic agents like adalimumab, etanercept and ustekinumab are linked to a heightened risk of adverse pregnancy outcomes, including abortion (Liu *et al*., 2025). However, these studies did not cover most of the drugs involved in the analysis. Systematic investigations are required to assess the connection between drug exposure and negative outcomes in pregnancy, since drug therapy during pregnancy becomes more common. Conducting clinical trials to assess adverse effects caused by rarely used drugs is impractical (Zheng *et al*., 2025). Similarly, repeating similar studies for each drug is not feasible. Utilizing extensive real-world pharmacovigilance databases offers significant insights into the link between drug exposure and spontaneous abortion or fetal death.

Disproportionality analysis within spontaneous reporting systems is a well-established methodology in pharmacovigilance research. By contrasting the reporting rate of a particular adverse event for a target drug with the average frequency across all other drugs, this approach enables the rapid identification of potential associations between drugs and adverse events (Cai *et al*., 2025). This method serves as a reliable means for the early recognition of emerging safety signals (Michel *et al*., 2017). In this study, the FDA Adverse Event Reporting System (FAERS) was employed to thoroughly examine drugs associated with the reporting association of spontaneous abortion or fetal death and to evaluate whether their effects are independent. These insights are crucial for directing future research and creating effective interventions to reduce the risks of spontaneous abortion or fetal death associated with pharmacological treatments.

MATERIALS AND METHODS

Data source

Information from the FAERS database, covering the first quarter (Q1) of 2004 to the second quarter (Q2) of 2025, was collected, including demographics, drug details, reported adverse events, therapeutic indications, sources of the reports and patient outcomes. To ensure data integrity, duplicate reports were systematically eliminated in accordance with the FDA's recommended deduplication protocol (Kaz-Onyeakazi and Kim, 2025). This procedure involved selecting the record with the most recent FDA_DT (FDA receipt date) and the highest PRIMARYID (unique case identifier) when multiple entries shared an identical CASEID. As the FAERS database contains fully anonymized data, obtaining informed consent or securing approval from an institutional review board was not required for this analysis.

Spontaneous abortion or fetal death events and drug identification

This study standardized adverse event terminology using the Medical Dictionary for Regulatory Activities (MedDRA, https://www.meddra.org) (Zhang *et al*., 2024). In MedDRA, a Preferred Term (PT) represents a single medical concept—for example, spontaneous abortion, spontaneous abortion complete, spontaneous abortion complicated, spontaneous abortion incomplete, abortion threatened and fetal death. PTs are categorized under broader System Organ Classes (SOCs) (Tan *et al*., 2019), such as “Pregnancy, puerperium and perinatal conditions”. Each PT from the extracted reports underwent individual disproportionality analysis to detect positive signals. Subsequently, these positive signals were categorized by their corresponding SOCs to facilitate stratified analysis. This method enabled precise identification of signals associated with spontaneous abortion or fetal death at the detailed PT level prior to aggregation at the SOC level for comprehensive statistical analysis.

This study included drugs identified as 'primary suspect' (PS). The Anatomical Therapeutic Chemical (ATC) classification system (Parry et al., 2025) was used for drug categorization. Synonyms with the same active ingredient were manually consolidated to create the final list of drugs associated with spontaneous abortion or fetal death. To enhance identification accuracy, various forms of each drug's name and codes were gathered, encompassing drug codes, brand names, active pharmaceutical ingredients and generic names.

Disproportionality analysis

To investigate possible relationships between pharmaceuticals and spontaneous abortion or fetal death, disproportionality analysis was utilized. Drugs that were identified as the primary suspect (PS) in 10 or more reported cases of spontaneous abortion or fetal death were carefully selected as target drugs for further investigation. Representative drugs included levetiracetam, lamotrigine, isotretinoin, ulipristal, atazanavir, zidovudine and enoxaparin, among others. This specific frequency threshold was established to balance statistical significance and clinical relevance, effectively minimizing false positives that might arise from low-frequency events. Simultaneously, it prioritizes higher-frequency reports, thereby narrowing confidence intervals and allowing for a more accurate reflection of the underlying pharmacological mechanisms driving these outcomes (Tian *et al*., 2025). This study employed a range of metrics and computational methods, including the reporting odds ratio (ROR) (Trillenberg *et al.*, 2023), proportional reported ratio (PRR) (Khouri *et al*., 2021), Bayesian confidence propagation neural network (BCPNN) (Tada *et al*., 2020) and multi-item gamma Poisson shrinker (MGPS) (Heo and Jung, 2020). The combined application of these diverse algorithms was implemented to leverage their complementary strengths, thereby improving overall detection sensitivity and specificity in identifying potential safety signals.

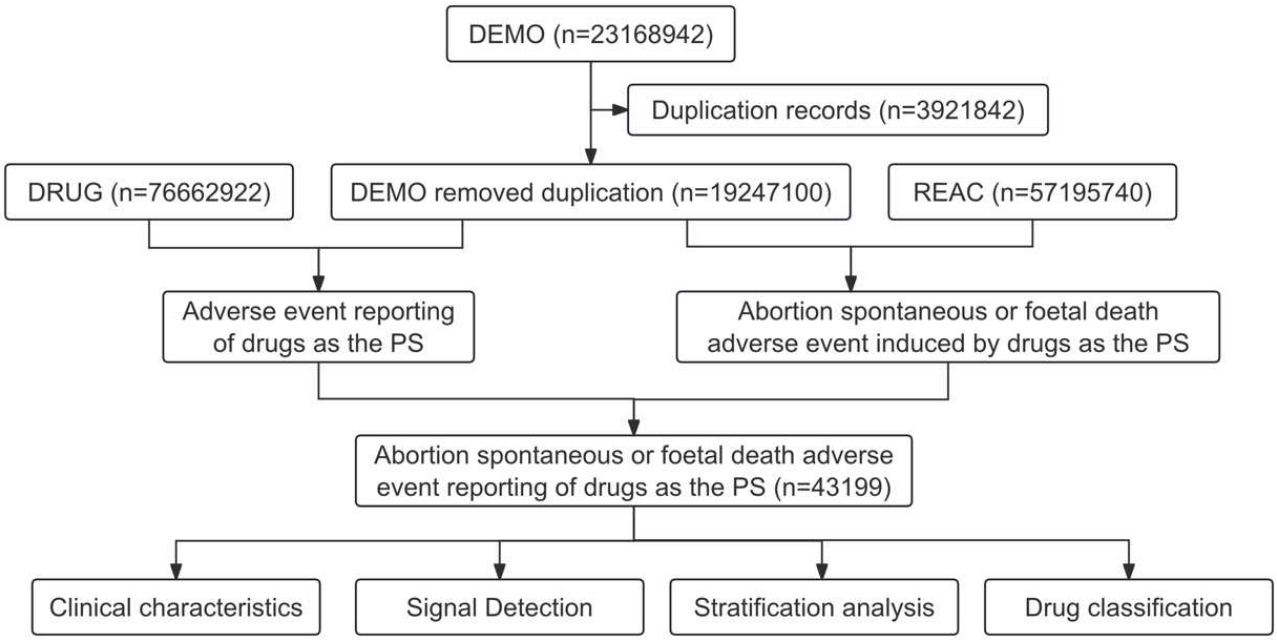

Fig. 1: Detailed technical roadmap of the study.
DEMO: refers to demographic and administrative data, while DRUG: pertains to drug information. REAC: denotes adverse events and PS: stands for the primary suspect.

Detailed descriptions of the specific calculation formulas and the criteria for establishing a positive signal are provided in Table S1. Only when the thresholds for all four algorithms were met simultaneously was a positive adverse event signal registered.

Statistical analysis

To delineate the clinical characteristics, such as patient demographics, countries of reporting, clinical outcomes and the occupations of reporters, descriptive statistical methods were employed. The expression of categorical variables was done through frequencies and percentages. In accordance with the READUS-PV guidelines for pharmacovigilance studies, this disproportionality analysis relies on individual case safety reports (Fusaroli *et al*., 2024). As this study involves multiple univariate analyses, the Bonferroni correction was applied to control the family-wise error rate. The adjusted significance threshold was calculated as α/n (0.05/392), resulting in a corrected p-value threshold of 0.000128. R software (version 4.3.2) was used for all analyses.

RESULTS

Clinical characteristics

The FAERS database included 19,247,100 AE reports from 2004 Q1 to 2025 Q2 after deduplication. A total of 43,199 reports of drug-related spontaneous abortion or fetal death were associated with 1,001 different medications (Fig. 1). Table 1 outlines the demographic characteristics related to drug-associated spontaneous abortion or fetal death. Most patients experiencing drug-related spontaneous abortion or fetal death were aged between 18 and 64 years (56.4%). Geographically, the largest percentage of reports, 34.85%, came from the United States, exceeding contributions from Canada (10.07%), the United Kingdom (8.05%), Germany (6.1%) and France (5.2%). In 40,834 reports, 94.53% specified the occupation of the reporters, with 13,310 (32.6%) being health professionals. “Other serious outcomes” were the most common reported at 86.3%, followed by “initial or prolonged hospitalization” (8.1%), “death” (2.6%) and “life-threatening outcomes” (1%). Fig. 2 depicts a marked upward trend in the annual case count from 2004 Q1 to 2025 Q2, peaking at 4,203 cases in 2019.

Disproportionality analysis

Disproportionality analysis was performed on 392 medications with a higher frequency of reported cases (>10 cases), identifying 119 medications that yielded positive safety signals (Table 2). According to the Anatomical Therapeutic Chemical (ATC) classification system, these 119 medications were sorted into 13 categories. The largest category was anti-infective for systemic use (J), comprising 41 drugs (34.5%). This was followed by genitourinary system and sex hormones (G) comprising 22 drugs or 18.5% of the total, nervous system (N) with 15 drugs (12.6%), alimentary tract and metabolism (A) with 9 drugs (7.6%) and antineoplastic and immunomodulating agents (L) with 8 drugs (6.7%).

Table 1: Demographic characteristics of the 43,199 reported cases of spontaneous abortion or fetal death.

Characteristics	Case reports	Percentage (%)
Gender		
Female	43199	100
Weight		
<50 kg	671	1.55
>100 kg	873	2.02
50~100 kg	8194	18.97
Unknown	33461	77.46
Age		
<18	420	0.97
18~64	24370	56.43
Unknown	18409	42.60
Reporter's occupation		
Health professional physician (MD)	13310	30.81
Non-healthcare professional consumer (CN)	12480	28.90
Other health professional (OT)	9684	22.42
Health professional (HP)	4160	9.63
Pharmacist (PH)	925	2.14
Lawyer (LW)	265	0.61
Registered Nurse (RN)	10	0.02
Unknown	2365	5.47
Outcome		
Hospitalization-initial or prolonged (HO)	3490	8.10
Death (DE)	1104	2.60
Life-threatening (LT)	411	1.00
Congenital Anomaly (CA)	371	0.90
Disability (DS)	118	0.30
Required intervention to prevent permanent impairment/damage (RI)	88	0.20
Other (OT)	37283	86.30
Unknown	334	0.80
Top 5 reported countries		
United States of America	15056	34.85
Canada	4349	10.07
United Kingdom	3476	8.05
Germany	2636	6.10
France	2232	5.20

The remaining categories consisted of blood and hematopoietic organs (B), dermatologicals (D), antiparasitic agents, insecticides and repellents (P), respiratory system (R), cardiovascular system (C), miscellaneous (V), hormonal preparations, excl. sex hormones and insulins (H) and the musculoskeletal system (M) (Fig. 3).

The 41 systemic anti-infectives were categorized into five ATC third-level subgroups: direct acting antivirals (J05A, 27 drugs, 65.9%), macrolides, lincosamides and streptogramins (J01F, 4 drugs, 9.8%), beta-lactam antibacterials, penicillins (J01C, 3 drugs, 7.3%), antimycotics for systemic use (J02A, 2 drugs, 4.9%) and tetracyclines (J01A, 2 drugs, 4.9%). Additionally, immunoglobulins (J06B), quinolone antibacterials (J01M) and other antibacterials (J01X) each comprised 1 drug, accounting for 2.4% each. The genitourinary system and sex hormones category, which includes 22 medications, can be categorized as follows: hormonal contraceptives for systemic use (G03A) account for 6 drugs (27.3%), gonadotropins and ovulation stimulants (G03G) comprise 5 drugs (22.7%), uterotonics (G02A) and progestogens (G03D) each contain 3 drugs (13.6%), other gynecological hormones (G02C) consist of 2 drugs (9.1%), while anti-infectives and antiseptics (G01A), intrauterine contraceptives (G02B) and other sex hormones and modulators (G03X) each represent 1 drug (4.5%). The 15 medications related to the nervous system can be categorized as follows: antiepileptics (non-barbiturates) (N03A) with 8 drugs (53.3%), antimigraine preparations (N02C) with 2 drugs (13.3%) and one drug each (6.7%) for antidepressants (N06A), anxiolytics (N05B), psychostimulants and agents used for attention deficit/hyperactivity disorder (ADHD) and nootropics (N06B), drugs used in addictive disorders (N07B) and antipsychotics (N05A).

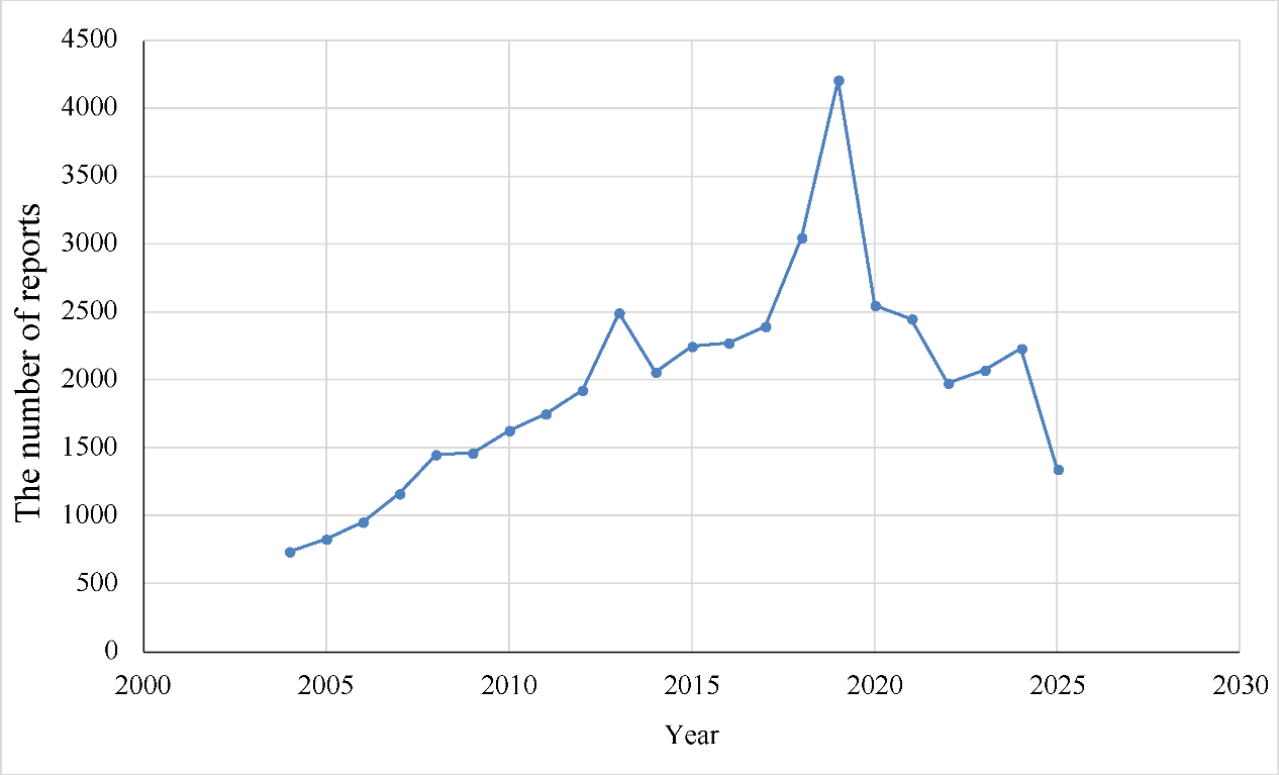

Fig. 2: Annual count of spontaneous abortion or fetal death reports in the FAERS database (2004 Q1 to 2025 Q2).

Supplemental Table S2 provides detailed classifications and summaries of medications linked to drug-associated spontaneous abortion or fetal death.

According to ROR values, ulipristal (IC 5.85, ROR 62.74), atazanavir (IC 5.36, ROR 43.59), nelfinavir (IC 5.23, ROR 39.53), lopinavir (IC 5.11, ROR 36.43) and zidovudine (IC 5.08, ROR 35.94) were the drugs with the highest ROR. All with $p < 0.001$.

DISCUSSION

Clinical implications

This research represents the most comprehensive and methodologically rigorous pharmacovigilance study to-date, employing the FAERS database to evaluate the potential reporting association of drug-induced spontaneous abortion or fetal death. It offers crucial real-world data to inform post-marketing updates and enhancements of drug package inserts. The analysis identified 119 medications that demonstrated a statistically significant association with a greater reporting of these negative pregnancy outcomes

Spontaneous abortion and fetal death are frequent and severe pregnancy complications, causing significant psychological and emotional burdens for pregnant women and their families. Spontaneous abortion or fetal death is commonly caused by infections, genetic factors, mental health issues and environmental toxins (Gong *et al*., 2022; Kaur *et al*., 2022; He *et al*., 2024; Gabrielli *et al*., 2025). Additionally, some medications administered while pregnant can significantly heighten the likelihood of spontaneous abortion and stillbirth (Wang *et al*., 2024). There are few large-scale clinical trials of drugs during pregnancy, so safety data for most drugs in this context have not been established. This study revealed 119 drugs significantly associated with these outcomes. These pharmaceuticals are classified into categories, including systemic anti-infectives, genitourinary agents and sex hormones, nervous system drugs, alimentary tract and metabolic regulators and antineoplastic and immunomodulating compounds.

Anti-infective drugs

The relationship between taking anti-infective medications while pregnant and the likelihood of spontaneous abortion or fetal death has been widely investigated. Studies suggest that the administration of antiretroviral drugs during pregnancy might increase the likelihood of adverse perinatal outcomes, including premature birth, low birth weight and small for gestational age infants (Tshivuila-Matala *et al*., 2020; Brooks *et al*., 2023; Hey *et al*., 2025). This result demonstrated that antiretroviral medications approved by the FDA for use during pregnancy, including dolutegravir (DTG), emtricitabine and tenofovir, could potentially increase the ROR of spontaneous abortion or fetal death.

Table 2: Signal values from four disproportionality analysis methods for drugs associated with spontaneous abortion or fetal death.

ATC _L1	Drug name	Case	ROR (95%Cl)	PRR (X2)	EBGM (EBGM05)	IC (IC025)	p-value
A	Vitamin B1	14	16.09 (9.48 - 27.34)	15.77 (193.83)	15.76 (9.28)	3.98 (2.24)	<0.001
A	Vitamin B6	30	15.81 (11.01 - 22.7)	15.49 (407.04)	15.48 (10.78)	3.95 (2.87)	<0.001
A	Vitamin B2	13	10.76 (6.23 - 18.62)	10.62 (113.43)	10.62 (6.14)	3.41 (1.88)	<0.001
A	Sapropterin	65	8.49 (6.65 - 10.84)	8.4 (423.76)	8.39 (6.57)	3.07 (2.56)	<0.001
A	Imiglucerase	72	7.54 (5.98 - 9.51)	7.47 (403.56)	7.46 (5.91)	2.9 (2.44)	<0.001
A	Vitamin E	13	6.88 (3.98 - 11.88)	6.82 (64.67)	6.82 (3.95)	2.77 (1.49)	<0.001
A	Sibutramine	31	6.41 (4.5 - 9.13)	6.36 (140.11)	6.36 (4.46)	2.67 (1.93)	<0.001
A	Velaglucerase alfa	35	6.37 (4.57 - 8.88)	6.32 (156.9)	6.32 (4.53)	2.66 (1.98)	<0.001
A	Ursodeoxycholic acid	23	5.77 (3.83 - 8.69)	5.73 (89.85)	5.73 (3.8)	2.52 (1.67)	<0.001
B	Enoxaparin	374	9.9 (8.94 - 10.97)	9.78 (2927.35)	9.71 (8.76)	3.28 (3.1)	<0.001
B	Tinzaparin	29	9.66 (6.7 - 13.94)	9.55 (222.09)	9.54 (6.61)	3.25 (2.36)	<0.001
B	Vitamin B9	41	4.92 (3.62 - 6.7)	4.9 (127.22)	4.89 (3.6)	2.29 (1.72)	<0.001
B	Dalteparin	28	4.47 (3.08 - 6.48)	4.45 (74.86)	4.44 (3.06)	2.15 (1.45)	<0.001
B	Acetylsalicylic acid	214	2.33 (2.04 - 2.67)	2.33 (161.35)	2.32 (2.03)	1.21 (1.01)	<0.001
C	Methyldopa	28	10.77 (7.42 - 15.65)	10.63 (244.45)	10.62 (7.31)	3.41 (2.46)	<0.001
C	Labetalol	17	5.05 (3.13 - 8.13)	5.02 (54.75)	5.02 (3.11)	2.33 (1.35)	<0.001
C	Nifedipine	53	3.89 (2.97 - 5.1)	3.88 (113.14)	3.87 (2.96)	1.95 (1.48)	<0.001
D	Finasteride	55	34.02 (25.95 - 44.58)	32.54 (1681.5)	32.5 (24.79)	5.02 (3.98)	<0.001
D	Tazarotene	16	11.69 (7.13 - 19.16)	11.52 (153.85)	11.52 (7.03)	3.53 (2.12)	<0.001
D	Isotretinoin	586	5.79 (5.33 - 6.28)	5.75 (2272.77)	5.69 (5.24)	2.51 (2.38)	<0.001
D	Ketoconazole	33	4.34 (3.08 - 6.12)	4.32 (84.39)	4.32 (3.07)	2.11 (1.48)	<0.001
G	Ulipristal	163	62.74 (53.45 - 73.64)	57.84 (9083.47)	57.63 (49.1)	5.85 (5.19)	<0.001
G	Clomifene	61	24.21 (18.75 - 31.24)	23.46 (1311.46)	23.43 (18.15)	4.55 (3.73)	<0.001
G	Progesterone	252	22.46 (19.8 - 25.46)	21.81 (4983.06)	21.7 (19.13)	4.44 (4.14)	<0.001
G	Follitropin	163	20.8 (17.8 - 24.32)	20.25 (2976.46)	20.18 (17.27)	4.34 (3.95)	<0.001
G	Chorionic gonadotrophin	74	14.44 (11.47 - 18.18)	14.18 (906.17)	14.16 (11.24)	3.82 (3.25)	<0.001
G	Human menopausal gonadotrophin	36	13.73 (9.87 - 19.09)	13.49 (416.65)	13.48 (9.69)	3.75 (2.85)	<0.001
G	Follitropin Beta	19	12.51 (7.95 - 19.69)	12.31 (197.68)	12.31 (7.82)	3.62 (2.32)	<0.001
G	Dinoprostone	29	12.24 (8.48 - 17.67)	12.06 (294.22)	12.05 (8.35)	3.59 (2.61)	<0.001
G	Dienogest	44	10.74 (7.97 - 14.46)	10.6 (382.56)	10.59 (7.86)	3.4 (2.69)	<0.001
G	Norgestrel	29	8.71 (6.04 - 12.56)	8.62 (195.44)	8.61 (5.97)	3.11 (2.25)	<0.001
G	Cabergoline	67	8.66 (6.81 - 11.03)	8.57 (448.25)	8.56 (6.73)	3.1 (2.59)	<0.001
G	Clotrimazole	19	5.57 (3.55 - 8.75)	5.53 (70.65)	5.53 (3.52)	2.47 (1.52)	<0.001
G	Methylergometrine	13	5.39 (3.12 - 9.3)	5.36 (46.14)	5.36 (3.1)	2.42 (1.26)	<0.001
G	Hydroxyprogesterone	210	5.37 (4.69 - 6.15)	5.34 (737.89)	5.32 (4.64)	2.41 (2.18)	<0.001
G	Etonogestrel	1258	4.09 (3.87 - 4.33)	4.08 (2840.65)	3.99 (3.77)	2 (1.91)	<0.001
G	Misoprostol	48	3.86 (2.9 - 5.12)	3.84 (100.86)	3.84 (2.89)	1.94 (1.45)	<0.001
G	Bromocriptine	18	3.83 (2.41 - 6.09)	3.82 (37.47)	3.82 (2.4)	1.93 (1.07)	<0.001
G	Desogestrel	29	3.59 (2.49 - 5.17)	3.57 (53.82)	3.57 (2.48)	1.84 (1.19)	<0.001
G	Intrauterine contraceptive device	1714	2.73 (2.6 - 2.87)	2.72 (1800.04)	2.66 (2.53)	1.41 (1.34)	<0.001
G	Norelgestromin	143	2.66 (2.26 - 3.14)	2.66 (147.41)	2.65 (2.25)	1.41 (1.15)	<0.001

Table. 2 is continue……..

ATC L1	Drug name	Case	ROR (95%Cl)	PRR (X2)	EBGM (EBGM05)	IC (IC025)	p-value
G	Levonorgestrel	1636	2.61 (2.48 - 2.74)	2.6 (1557.53)	2.54 (2.42)	1.35 (1.27)	<0.001
G	Medroxyprogesterone	217	2.35 (2.06 - 2.69)	2.35 (167.26)	2.34 (2.05)	1.23 (1.02)	<0.001
H	Ganirelix	21	5.76 (3.75 - 8.85)	5.72 (81.92)	5.72 (3.72)	2.52 (1.62)	<0.001
J	Atazanavir	214	43.59 (37.96 - 50.06)	41.19 (8362.33)	40.99 (35.7)	5.36 (4.91)	<0.001
J	Nelfinavir	49	39.53 (29.64 - 52.7)	37.54 (1743.06)	37.5 (28.12)	5.23 (4.02)	<0.001
J	Lopinavir	357	36.43 (32.75 - 40.54)	34.75 (11624.33)	34.48 (30.99)	5.11 (4.82)	<0.001
J	Zidovudine	493	35.94 (32.82 - 39.36)	34.31 (15785.47)	33.94 (30.99)	5.08 (4.86)	<0.001
J	Nevirapine	272	31.51 (27.9 - 35.59)	30.24 (7654.79)	30.06 (26.62)	4.91 (4.59)	<0.001
J	Saquinavir	11	27.61 (15.12 - 50.42)	26.63 (271.69)	26.63 (14.58)	4.73 (2.24)	<0.001
J	Dolutegravir	226	25.5 (22.32 - 29.13)	24.67 (5113.75)	24.55 (21.49)	4.62 (4.28)	<0.001
J	Lamivudine	787	23.94 (22.28 - 25.71)	23.22 (16456.45)	22.82 (21.24)	4.51 (4.37)	<0.001
J	Emtricitabine	1269	19.92 (18.82 - 21.08)	19.43 (21572.7)	18.9 (17.86)	4.24 (4.14)	<0.001
J	Darunavir	80	16.99 (13.61 - 21.21)	16.63 (1174.47)	16.6 (13.3)	4.05 (3.47)	<0.001
J	Efavirenz	342	16.7 (14.99 - 18.59)	16.34 (4895.54)	16.23 (14.57)	4.02 (3.8)	<0.001
J	Fosamprenavir	12	16.55 (9.34 - 29.33)	16.2 (171.35)	16.2 (9.14)	4.02 (2.09)	<0.001
J	Bictegravir	74	16.14 (12.82 - 20.33)	15.81 (1026.44)	15.79 (12.54)	3.98 (3.38)	<0.001
J	Didanosine	31	16.08 (11.26 - 22.96)	15.75 (428.6)	15.74 (11.03)	3.98 (2.91)	<0.001
J	Abacavir	201	16.04 (13.94 - 18.45)	15.72 (2761.06)	15.65 (13.6)	3.97 (3.66)	<0.001
J	Stavudine	45	15.89 (11.82 - 21.35)	15.57 (613.71)	15.55 (11.57)	3.96 (3.13)	<0.001
J	Tenofovir	1580	14.53 (13.81 - 15.28)	14.27 (18826.13)	13.8 (13.11)	3.79 (3.7)	<0.001
J	Telbivudine	14	14.34 (8.45 - 24.35)	14.09 (170.37)	14.08 (8.3)	3.82 (2.16)	<0.001
J	Raltegravir	91	13.88 (11.28 - 17.08)	13.64 (1064.96)	13.61 (11.06)	3.77 (3.28)	<0.001
J	Elvitegravir	66	13.55 (10.62 - 17.29)	13.32 (752.05)	13.3 (10.43)	3.73 (3.13)	<0.001
J	Cobicistat	75	12.32 (9.81 - 15.49)	12.14 (766.11)	12.12 (9.64)	3.6 (3.07)	<0.001
J	Rilpivirine	108	9.44 (7.81 - 11.42)	9.34 (803.01)	9.32 (7.7)	3.22 (2.83)	<0.001
J	Entecavir	37	8.65 (6.25 - 11.96)	8.56 (247.1)	8.55 (6.18)	3.1 (2.36)	<0.001
J	Fluconazole	196	8.51 (7.39 - 9.79)	8.42 (1277.45)	8.39 (7.28)	3.07 (2.81)	<0.001
J	Anti-D immunoglobulin	46	8.42 (6.3 - 11.27)	8.34 (297.17)	8.33 (6.23)	3.06 (2.43)	<0.001
J	Metronidazole	352	7.08 (6.37 - 7.86)	7.02 (1804.26)	6.97 (6.27)	2.8 (2.62)	<0.001
J	Clarithromycin	309	6.31 (5.64 - 7.06)	6.27 (1359.93)	6.23 (5.57)	2.64 (2.45)	<0.001
J	Adefovir	16	6.1 (3.73 - 9.98)	6.06 (67.62)	6.05 (3.7)	2.6 (1.52)	<0.001
J	Azithromycin	311	5.24 (4.68 - 5.86)	5.21 (1051.6)	5.18 (4.63)	2.37 (2.19)	<0.001
J	Ritonavir	762	4.93 (4.59 - 5.3)	4.91 (2332.16)	4.84 (4.5)	2.27 (2.16)	<0.001
J	Erythromycin	53	4.88 (3.73 - 6.4)	4.86 (162.36)	4.85 (3.7)	2.28 (1.78)	<0.001
J	Itraconazole	36	4.68 (3.37 - 6.5)	4.66 (103.48)	4.66 (3.35)	2.22 (1.61)	<0.001
J	Ampicillin	20	4.61 (2.97 - 7.16)	4.59 (56.25)	4.59 (2.96)	2.2 (1.34)	<0.001
J	Ciprofloxacin	501	3.49 (3.2 - 3.82)	3.48 (877.35)	3.45 (3.16)	1.79 (1.65)	<0.001
J	Minocycline	50	3.45 (2.61 - 4.55)	3.43 (86.31)	3.43 (2.6)	1.78 (1.31)	<0.001
J	Amoxicillin	344	3.42 (3.08 - 3.81)	3.41 (582.83)	3.39 (3.05)	1.76 (1.6)	<0.001
J	Cefalexin	41	3.39 (2.49 - 4.61)	3.38 (68.75)	3.38 (2.49)	1.76 (1.23)	<0.001
J	Clindamycin	128	3.29 (2.77 - 3.92)	3.28 (203.07)	3.28 (2.75)	1.71 (1.43)	<0.001
J	Oseltamivir	89	3.29 (2.67 - 4.05)	3.28 (140.94)	3.28 (2.66)	1.71 (1.37)	<0.001
J	Doxycycline	108	2.8 (2.32 - 3.39)	2.8 (124.64)	2.79 (2.31)	1.48 (1.18)	<0.001
J	Ribavirin	98	2.71 (2.22 - 3.31)	2.71 (105.31)	2.7 (2.22)	1.43 (1.12)	<0.001
L	Cetrorelix	10	10.97 (5.88 - 20.49)	10.82 (89.28)	10.82 (5.8)	3.44 (1.64)	<0.001
L	Peginterferon beta-1a	128	3.53 (2.97 - 4.21)	3.52 (230.79)	3.51 (2.95)	1.81 (1.53)	<0.001
L	Hydroxycarbamide	27	3.5 (2.4 - 5.1)	3.48 (47.87)	3.48 (2.39)	1.8 (1.13)	<0.001
L	Cladribine	50	2.84 (2.15 - 3.74)	2.83 (59.11)	2.83 (2.14)	1.5 (1.04)	<0.001
L	Natalizumab	1290	2.8 (2.64 - 2.95)	2.79 (1438.42)	2.74 (2.59)	1.45 (1.37)	<0.001
L	Certolizumab	668	2.46 (2.28 - 2.65)	2.45 (567.7)	2.43 (2.25)	1.28 (1.17)	<0.001
L	Mycophenolic acid	303	2.39 (2.14 - 2.68)	2.39 (243.1)	2.38 (2.12)	1.25 (1.08)	<0.001

Table. 2 is continue……..

ATC L1	Drug name	Case	ROR (95%Cl)	PRR (X2)	EBGM (EBGM05)	IC (IC025)	p-value
L	Tacrolimus	263	2.31 (2.04 - 2.6)	2.3 (192.94)	2.29 (2.03)	1.2 (1.01)	<0.001
M	Indometacin	17	3.25 (2.02 - 5.23)	3.24 (26.36)	3.24 (2.01)	1.7 (0.84)	<0.001
N	Levetiracetam	1923	18.43 (17.59 - 19.3)	18.01 (29597.43)	17.27 (16.49)	4.11 (4.03)	<0.001
N	Carbamazepine	457	6.58 (6 - 7.22)	6.53 (2122.66)	6.48 (5.9)	2.7 (2.54)	<0.001
N	Naratriptan	10	6.15 (3.3 - 11.46)	6.11 (42.77)	6.11 (3.28)	2.61 (1.19)	<0.001
N	Zonisamide	37	5.94 (4.3 - 8.21)	5.9 (150.71)	5.9 (4.27)	2.56 (1.91)	<0.001
N	Clobazam	45	5.3 (3.95 - 7.1)	5.26 (155.53)	5.26 (3.92)	2.4 (1.84)	<0.001
N	Modafinil	43	4.83 (3.58 - 6.53)	4.81 (129.79)	4.81 (3.56)	2.26 (1.71)	<0.001
N	Lacosamide	150	4.67 (3.97 - 5.48)	4.64 (427.77)	4.63 (3.94)	2.21 (1.94)	<0.001
N	Valproic Acid	403	4.63 (4.2 - 5.11)	4.61 (1130.99)	4.58 (4.15)	2.19 (2.04)	<0.001
N	Oxcarbazepine	118	4.35 (3.63 - 5.21)	4.33 (301.29)	4.32 (3.6)	2.11 (1.8)	<0.001
N	Buprenorphine	534	3.87 (3.55 - 4.22)	3.86 (1117.19)	3.82 (3.51)	1.93 (1.8)	<0.001
N	Fluvoxamine	15	3.76 (2.26 - 6.24)	3.74 (30.18)	3.74 (2.25)	1.9 (0.95)	<0.001
N	Lamotrigine	574	3.73 (3.43 - 4.05)	3.71 (1125.17)	3.68 (3.39)	1.88 (1.75)	<0.001
N	Topiramate	322	3.67 (3.28 - 4.09)	3.65 (616.7)	3.63 (3.26)	1.86 (1.69)	<0.001
N	Rizatriptan	20	3.34 (2.15 - 5.18)	3.33 (32.61)	3.33 (2.14)	1.73 (0.95)	<0.001
N	Aripiprazole	397	2.67 (2.42 - 2.95)	2.67 (409.87)	2.65 (2.4)	1.41 (1.25)	<0.001
P	Mebendazole	26	19 (12.87 - 28.05)	18.54 (431.77)	18.53 (12.55)	4.21 (2.93)	<0.001
P	Albendazole	29	12.52 (8.67 - 18.07)	12.32 (301.94)	12.32 (8.53)	3.62 (2.63)	<0.001
P	Proguanil	26	5.34 (3.63 - 7.85)	5.31 (90.93)	5.3 (3.61)	2.41 (1.64)	<0.001
P	Atovaquone	26	3.82 (2.59 - 5.61)	3.8 (53.7)	3.8 (2.58)	1.93 (1.23)	<0.001
R	Doxylamine	19	4.21 (2.68 - 6.61)	4.19 (46.24)	4.19 (2.67)	2.07 (1.21)	<0.001
R	Elexacaftor	94	4.07 (3.32 - 4.98)	4.05 (215.66)	4.04 (3.3)	2.02 (1.67)	<0.001
R	Tezacaftor	105	3.49 (2.88 - 4.22)	3.47 (184.83)	3.47 (2.86)	1.79 (1.48)	<0.001
R	Ivacaftor	115	2.46 (2.05 - 2.96)	2.46 (99.31)	2.45 (2.04)	1.3 (1.01)	<0.001
V	Iodine (131 I)	30	16.36 (11.39 - 23.49)	16.02 (422.69)	16.01 (11.15)	4 (2.91)	<0.001
V	Naloxone	292	6.09 (5.43 - 6.84)	6.05 (1225.19)	6.02 (5.36)	2.59 (2.4)	<0.001

Note: ATC refers to anatomical therapeutic chemical; L1 indicates level 1 or the first level; 95% CI denotes a 95% confidence interval; FAERS is the US FDA's Adverse Event Reporting System; X2 denotes chi-squared; PRR refers to the proportional reported ratio; ROR represents the reported odds ratio; IC denotes the information coefficient, while IC025 signifies the lower limit of the 95% confidence interval for the information coefficient; EBGM stands for empirical Bayesian geometric mean; EBGM05 represents the 95% confidence interval's lower boundary for EBGM. (A) digestive and metabolic systems; (B) hematopoietic system; (C) cardiovascular system; (D) dermatologicals; (G) genitourinary system and sex hormones; (J) systemic antiinfectives; (L) antineoplastic and immunomodulating agents; (M) musculoskeletal system; (N) nervous system; (V) miscellaneous.

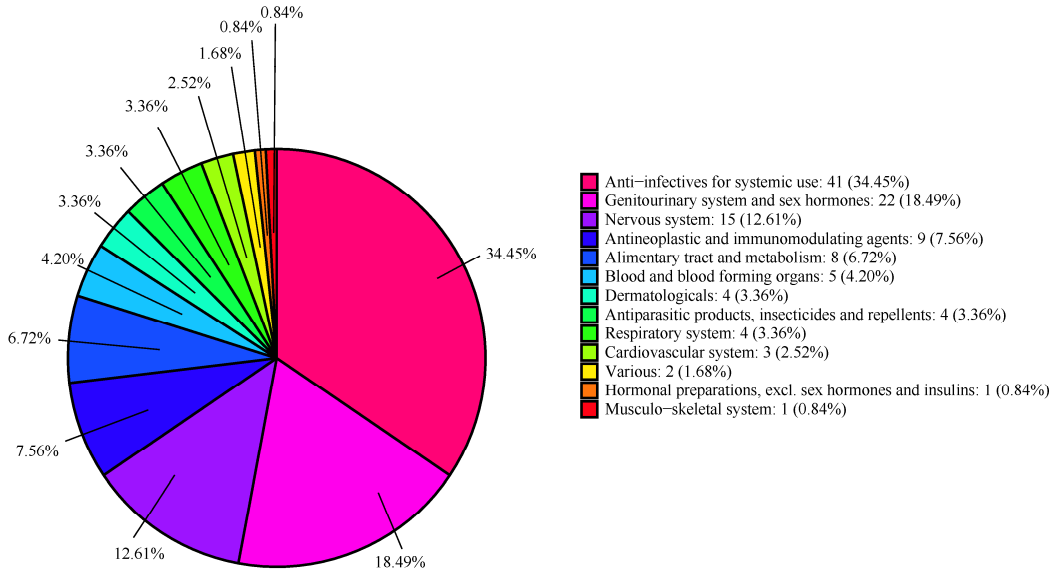

Fig. 3: Medications associated with spontaneous abortion or fetal death signals, categorized by the L1 of the ATC classification.

Nevertheless, the essential function of these antiretroviral agents in preventing mother-to-child HIV transmission is widely acknowledged (Lockman *et al*., 2021). A comprehensive systematic review revealed that macrolide antibiotics, notably azithromycin and clarithromycin, are correlated with a markedly elevated risk of spontaneous abortion (Omranipoor *et al*., 2020; Hegger *et al*., 2024). There is no evidence that amoxicillin use is associated with spontaneous abortion or stillbirth. However, some studies have suggested that amoxicillin may be linked to cleft lip and palate. Notably, the risk category for amoxicillin was changed from "compatible" to "risk in the first and third trimesters." This suggests that the use of amoxicillin during pregnancy is not absolutely safe (Leong *et al.*, 2019). Pregnant women exposed to metronidazole have a 70% higher risk of experiencing a spontaneous abortion (Nwosu and Bloom, 2021).

Genitourinary and hormonal drugs

Hormonal contraceptives for systemic use, along with gonadotropins and other ovulation stimulants, were the most frequently associated genitourinary and sex hormone drugs with spontaneous abortion or fetal death. Ulipristal is frequently utilized as an emergency contraceptive and for inhibiting uterine fibroid growth (Donnez *et al*., 2014; Glasier, *et al*., 2010). An observational study indicated no elevated risk of congenital anomalies, spontaneous abortion, or ectopic pregnancy after exposure to ulipristal during the implantation phase and early embryonic development (Wagner *et al*., 2020). Some studies indicated that levonorgestrel did not increase the risk of spontaneous abortion (Pohjoranta *et al*., 2024; Vanderhoff *et al*., 2024) but was associated with an increased risk of ectopic pregnancy (Kitani *et al*., 2019; Resta *et al*., 2021). Misoprostol and dinoprostone are abortifacients used in early pregnancy (Gornisiewicz *et al*., 2020; Pirrami and Reinert, 2025). Improper use of these drugs during pregnancy, including off-label use or incorrect timing, may elevate the likelihood of spontaneous abortion or fetal death. Progesterone is often used to prevent or treat spontaneous abortion (Van Leer, 2019). In this study, the reporting association between progesterone and spontaneous abortion or fetal death might be due to the underlying disease rather than the drug's toxicity.

Antineoplastic and immunomodulating drugs

Although exposure to natalizumab in individuals with multiple sclerosis (MS) is associated with a greater probability of spontaneous abortion, this risk does not exceed the baseline rate observed in the general population (Andersen *et al*., 2023). Pregnancies involving mycophenolic acid (MPA), 30–49.5% of cases result in miscarriage (Thai *et al*., 2020). While certain studies indicate that certolizumab pegol (CZP) use during pregnancy is relatively safe and does not elevate the risk of spontaneous abortion (Clowse *et al.*, 2015; Dai *et al*., 2022), a real-world pharmacovigilance study has suggested a potential link between CZP and spontaneous abortion (Liu *et al*., 2025). Further research is required to validate the safety of additional biologic agents in pregnant populations.

Nervous system drugs

A comprehensive review, which included data from 16,941,373 pregnancies, established a connection between taking antiepileptic drugs (AEDs) during gestation and an elevated likelihood of spontaneous abortion or fetal death (Berry-Noronha *et al*., 2025). According to an observational investigation, the incidence of spontaneous abortion showed a statistically significant increase when levetiracetam and lamotrigine were used in combination therapy (Tomson *et al*., 2015). Additionally, an Australian study found a dose-related increase in intrauterine death risk associated with carbamazepine exposure (Vajda *et al*., 2018). There is a lack of comprehensive evidence on the relationship between valproic acid exposure in pregnancy and spontaneous abortion, with existing studies providing inconsistent results (Trivedi *et al*., 2018).

Intrauterine device

The intrauterine device (IUD), a commonly used contraceptive method, is generally considered to be highly effective. Pregnancy can occur with an IUD, potentially impacting pregnancy outcomes negatively (Molino *et al*., 2025). Having an IUD is linked to a higher chance of pregnancy loss. A retrospective study showed a notable increase in spontaneous abortion rates among those who became pregnant while using a copper IUD. Research further indicates that removal of the IUD is linked to a decreased likelihood of spontaneous abortion, whereas retention of the device heightens the probability of pregnancy loss (Karakuş *et al*., 2023). Another study investigated the influence of copper IUDs on HLA-G and IGF-II levels during pregnancy, proposing that the IUD may interfere with embryonic development by altering chorionic IGF-II expression (Cao *et al*., 2022). This regulation could impair embryo development, raising the risk of spontaneous abortion.

Other drug categories

Medications that may elevate the risk of spontaneous abortion or fetal death encompass those used for dermatological conditions, blood and blood-forming organs, cardiovascular issues, antiparasitic treatments, insecticides and repellents and respiratory ailments. Isotretinoin is contraindicated during pregnancy because it can cause fetal defects (Havet *et al.*, 2025). However, induced and spontaneous abortions caused by isotretinoin misuse during pregnancy still occur (Yousif *et al*., 2022; Reinold *et al*., 2024). Research on the link between naloxone use and the reporting association of spontaneous abortion or fetal death is limited.

Limitations

This study acknowledges several inherent limitations. The FAERS database primarily contains reports submitted

voluntarily by healthcare professionals, consumers and other reporters, which can lead to recall bias and subjective interpretation. The quality and accuracy of these reports depend on the reporter's level of expertise. Secondly, there exists the possibility of under-reporting, over-reporting, or misreporting of adverse events (AEs), which can introduce significant reporting bias into the analysis. Furthermore, it is important to note that the United States is the predominant source of AE reports in the FAERS database, underscoring the critical need for extensive, long-term investigations that use regional data to validate the conclusions drawn from this study. Despite efforts to conduct a sensitivity analysis, unmeasured confounding factors may still have influenced the results, necessitating a cautious interpretation of the findings presented. Ultimately, due to its inherent nature as a passive surveillance system that is primarily focused on collecting adverse event case reports, the FAERS database is unable to definitively determine the incidence of spontaneous abortion or fetal death that may be caused by drugs. While the disproportionality analysis conducted in this study indicated an association, it did not confirm any causal relationships. Therefore, future research endeavors should incorporate experimental validation and place greater emphasis on longitudinal studies that meticulously track patient outcomes over time. By addressing these limitations, researchers can significantly strengthen the validity and reliability of the conclusions drawn from this study.

Future perspectives

Future studies should focus on prospective cohort validation, integration with clinical registries and mechanistic exploration to confirm the pharmacovigilance signals identified in this study.

CONCLUSION

This study identified 119 drugs with significant disproportionality signals associated with spontaneous abortion or fetal death. However, these findings should be interpreted as signal detection rather than evidence of causality. These results provide important real-world pharmacovigilance insights to support safer medication use in women of reproductive age. Further prospective and mechanistic studies are required to validate these associations.

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ChatGPT (version 5.0) was used to improve language.

Authors' contributions

H.L. and L.L: Wrote the manuscript, analyzed the data and created the graphs; W.L revised the manuscript; F.Z: Provided the research ideas and revised the manuscript. All authors contributed to the interpretation of the data, critically reviewed the manuscript, approved the final version and agreed to be accountable for all aspects of the work.

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Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval

This study utilized publicly available, de-identified data from FAERS. Therefore, institutional review board approval and informed consent were not required. This study was performed in adherence with the READUS-PV guidelines. See supplementary file for the READUS-PV checklist.

Conflict of interests

The authors declared no conflict of interest.

Supplementary data

https://www.pjps.pk/uploads/2026/06/SUP1780318678.pdf

REFERENCES

Abu-Tineh M, Ali EA, Alshurafa A, Nashwan AJ, Albsheer K, Ahmed A, Hailan Y, Rozi W, Aljaloudi E and Yassin MA (2023). The impact of tyrosine kinase inhibitors on fatherhood in patients with chronic myeloid leukemia: A mixed-method study. *Cureus J. Med Science*, **15**(1): e33407.

Almeida ND, Basso O, Abrahamowicz M, Gagnon R and Tamblyn R (2016). Risk of miscarriage in women receiving antidepressants in early pregnancy, correcting for induced abortions. *Epidemiology*, **27**(4): 538-546.

Andersen JB, Sellebjerg F and Magyari M (2023). Pregnancy outcomes after early fetal exposure to injectable first-line treatments, dimethyl fumarate, or natalizumab in Danish women with multiple sclerosis. *Eur. J. Neurol*., **30**(1): 162-171.

Berry-Noronha A, Manoleehakul P, Rottler A, McGuiness G, Chen Z, Kuhn R, Vajda FJ, Perucca E, Antonic-Baker A and Perucca P (2025). Risk of adverse pregnancy outcomes associated with antiseizure medications and their indications: A systematic review and meta-analysis. *Neurology*, **104**(3): e210233.

Brooks KM, Scarsi KK and Mirochnick M (2023). Antiretrovirals for human immunodeficiency virus treatment and prevention in pregnancy. *Obstet. Gyn. Clin. N. Am.*, **50**(1): 205-218.

Cai X, Chen G, Wang H, Wang L and Hu C (2025). Pharmacovigilance insights into drug-associated venous thromboembolism. *Int J Surg*, **111**(11): 7677-7685.

Cao L, Chen X and Huang L (2022). Effect of a copper intrauterine device on HLA-G and IGF-II levels during pregnancy. *Growth Horm IGF Res*, **62**: 101441.

Chen W, Zhang T, Chen C and Gao L (2025). A case of 8p12q11.21 chimeric duplication with normal pregnancy. *Clin Lab*, **71**(8): 10-7754.

Clowse MEB, Wolf DC, Forger F, Cush JJ, Golembesky A, Shaughnessy L, De Cuyper D and Mahadevan U (2015). Pregnancy outcomes in subjects exposed to certolizumab pegol. *J Rheumatol*, **42**(12): 2270-2278.

Dai F, Hu M, Zhang Y, Zhu R, Chen L, Li Z, Huang Y, Hu W and Cheng Y (2022). TNF-α/anti-TNF-α drugs and its effect on pregnancy outcomes. *Expert Rev. Mol. Med.*, **24**: e26.

Dan K, Lee JE, Han D, Kim SM, Hong S, Kim HJ and Park KH (2021). Proteomic identification of biomarkers in maternal plasma that predict the outcome of rescue cerclage for cervical insufficiency. *Plos One*, **16**(4): e0250031.

Donnez J, Vazquez F, Tomaszewski J, Nouri K, Bouchard P, Fauser BCJM, Barlow DH, Palacios S, Donnez O, Bestel E, Osterloh I, Loumaye E and PEARL IAPI (2014). Long-term treatment of uterine fibroids with ulipristal acetate ☆. *Fertil. Steril.*, **101**(6): 1565-1573.

Fusaroli M, Salvo F, Begaud B, AlShammari TM, Bate A, Battini V, Brueckner A, Candore G, Carnovale C, Crisafulli S, Cutroneo PM, Dolladille C, Drici M, Faillie J, Goldman A, Hauben M, Herdeiro MT, Mahaux O, Manlik K, Montastruc F, Noguchi Y, Norén GN, Noseda R, Onakpoya IJ, Pariente A, Poluzzi E, Salem M, Sartori D, Trinh NTH, Tuccori M, van Hunsel F, van Puijenbroek E, Raschi E and Khouri C (2024). The reporting of a disproportionality analysis for drug safety signal detection using individual case safety reports in pharmacovigilance (READUS-PV): Development and statement. *Drug Saf*, **47**(6): 575-584.

Gabrielli L, Pavoni M, Monari F, Baiesi Pillastrini F, Bonasoni MP, Locatelli C, Bisulli M, Vancini A, Cataneo I, Ortalli M, Piccirilli G, Cantiani A, Ambretti S, Facchinetti F and Lazzarotto T (2025). Infection-related stillbirths: A detailed examination of a nine-year multidisciplinary study. *Microorganisms*, **13**(1): 71.

Glasier AF, Cameron ST, Fine PM, Logan SJS, Casale W, Van Horn J, Sogor L, Blithe DL, Scherrer B, Mathe H, Jaspart A, Ulmann A and Gainer E (2010). Ulipristal acetate versus levonorgestrel for emergency contraception: A randomised non-inferiority trial and meta-analysis. *Lancet*, **375**(9714): 555-562.

Gong Y, Sun P, Fu X, Jiang L, Yang M, Zhang J, Li Q, Chai J, He Y, Shi C, Wu J, Li Z, Yu F, Ba Y and Zhou G (2022). The type of previous abortion modifies the association between air pollution and the risk of preterm birth. *Environ. Res.*, **212**(Pt A): 113166.

Gornisiewicz T, Kusmierska-Urban K, Huras H and Galas A (2020). Comparison of misoprostol versus dinoprostone for delivery induction among pregnant women without concomitant disease. *Ginekol Pol*, **91**(12): 726-732.

Havet A, Bouvard C, Moskal A, Chaneliere M, Massardier J, Lebrun-Vignes B, Jonville-Bera A, Payet C and Viprey M (2025). Compliance with the pregnancy prevention program among women initiating isotretinoin treatment between 2014 and 2021: A nationwide cohort study on the French Health Data System (SNDS). *J Eur Acad Dermatol Venereol*, **39**(4): 806-814.

He Y, Wang L, Tang R, Jin H, Liu B, Chen S, Mu H and Wang X (2024). Common mental disorders and risk of spontaneous abortion or recurrent spontaneous abortion: A two-sample Mendelian randomization study. *J. Affect. Disorders*, **354**: 258-266.

Hegger S, Levy A, Koren G, Lunenfeld E and Daniel S (2024). Exposure to macrolides during pregnancy and the risk for spontaneous abortions: A population-based retrospective cohort study. *J. Clin. Pharmacol.*, **64**(10): 1288-1294.

Heo S and Jung I (2020). Extended multi-item gamma Poisson shrinker methods based on the zero-inflated Poisson model for postmarket drug safety surveillance. *Stat. Med.*, **39**(30): 4636-4650.

Hey M, Thompson L, Portwood C, Sexton H, Kumarendran M, Brandon Z, Kirtley S and Hemelaar J (2025). Adverse perinatal outcomes associated with different classes of antiretroviral drugs in pregnant women with HIV. *AIDS*, **39**(2): 162-174.

Ho AL, Hernandez A, Robb JM, Zeszutek S, Luong S, Okada E and Kumar K (2022). Spontaneous miscarriage management experience: A systematic review. *Cureus J. Med Science*, **14**(4): e24269.

Karakuş SS, Karakuş R, Akalın EE and Akalın M (2023). Pregnancy outcomes with a copper 380 mm(2) intrauterine device in place: A retrospective cohort study in Turkey, 2011-2021. *Contraception*, **125**: 110090.

Kaur M, Sharma P, Kaur R and Khetarpal P (2022). Increased incidence of spontaneous abortions on exposure to cadmium and lead: A systematic review and meta-analysis. *Gynecol Endocrinol*, **38**(1): 16-21.

Kaz-Onyeakazi I and Kim H (2025). Revisiting disproportionality: Prescription-adjusted and TF-IDF-inspired metrics for post-market ADR detection. Amia ... Annual Symposium Proceedings. *Amia Symposium*, **2024**:585-594.

Khouri C, Revol B, Lepelley M, Mouffak A, Bernardeau C, Salvo F, Pariente A, Roustit M and Cracowski J (2021). A meta-epidemiological study found lack of transparency and poor reporting of disproportionality analyses for signal detection in pharmacovigilance databases. *J. Clin. Epidemiol.*, **139**: 191-198.

Kitani Y, Ishiguro T, Kobayashi A, Tamura R, Ueda H, Adachi S, Nishikawa N, Sekine M and Enomoto T (2019). Ectopic pregnancy following oral levonorgestrel emergency contraception use. *J Obstet Gynaecol Res*, **45**(2): 473-476.

Leong C, Chateau D, Dahl M, Falk J, Katz A, Bugden S

and Raymond C (2019). Prescription medication use during pregnancies that resulted in births and abortions (2001-2013): A retrospective population-based study in a Canadian population. *Plos One*, **14**(3): e0211319.

Li F, Niu A, Feng X, Yan Y and Chen Y (2021). The threshold effect of factors associated with spontaneous abortion in human-assisted reproductive technology. *Sci Rep-Uk*, **11**(1): 11368.

Lin S, Li J, Zhang Y, Song X, Chen G and Pei L (2022). Maternal passive smoking, vitamin D deficiency and risk of spontaneous abortion. *Nutrients*, **14**(18): 3674.

Lin S, Zhang Y, Jiang L, Li J, Chai J, Pei L and Shang X (2022). Interactive effects of maternal vitamin d status and socio-economic status on the risk of spontaneous abortion: Evidence from henan province, China. *Nutrients*, **14**(2): 291.

Liu M, Yin P, Fan R, Zhang G and Zhao K (2025). A real-world pharmacovigilance study of Certolizumab pegol based on FAERS database. *Sci Rep-Uk*, **15**(1): 28529.

Liu Q, Wang Y, Hu P and He P (2025). Abortion adverse events associated with adalimumab, etanercept, ustekinumab and dupilumab during pregnancy: A pharmacovigilance study based on FDA adverse event reporting system. *Drug Discov Ther*, **19**(3): 160-173.

Lockman S, Brummel SS, Ziemba L, Stranix-Chibanda L, McCarthy K, Coletti A, Jean-Philippe P, Johnston B, Krotje C, Fairlie L, Hoffman RM, Sax PE, Moyo S, Chakhtoura N, Stringer JS, Masheto G, Korutaro V, Cassim H, Mmbaga BT, Joao E, Hanley S, Purdue L, Holmes LB, Momper JD, Shapiro RL, Thoofer NK, Rooney JF, Frenkel LM, Amico KR, Chinula L, Currier J and IMPAACT VSTA (2021). Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate and efavirenz, emtricitabine and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): A multicentre, open-label, randomised, controlled, phase 3 trial. *Lancet*, **397**(10281): 1276-1292.

Michel C, Scosyrev E, Petrin M and Schmouder R (2017). Can disproportionality analysis of post-marketing case reports be used for comparison of drug safety profiles? *Clin. Drug Invest.*, **37**(5): 415-422.

Molino GOG, Santos ACFD, Dias MMF, Pereira AGA, Pimenta NDS and Silva PHCM (2025). Retained versus removed copper intrauterine device during pregnancy: An updated systematic review and meta-analysis. *Acta Obstet. Gyn. Scan*., **104**(5): 804-814.

Moradinazar M, Najafi F, Nazar ZM, Hamzeh B, Pasdar Y and Shakiba E (2020). Lifetime prevalence of abortion and risk factors in women: Evidence from a cohort study. *J. Pregnancy*, **2020**: 4871494.

Muanda FT, Sheehy O and Berard A (2017). Use of antibiotics during pregnancy and risk of spontaneous abortion. *CMAJ*, **189**(17): E625-E633.

Nikitina TV, Fonova EA and Lebedev IN (2026). Genomics of pregnancy loss. *J. Assist. Reprod. Gen.*, **43**(1): 3-18.

Nwosu OC and Bloom K (2021). The safety of metronidazole in pregnancy. *Health Care Women Int*, **42**(4-6): 726-738.

Omranipoor A, Kashanian M, Dehghani M, Sadeghi M and Baradaran HR (2020). Association of antibiotics therapy during pregnancy with spontaneous miscarriage: A systematic review and meta-analysis. *Arch. Gynecol. Obstet.*, **302**(1): 5-22.

Parry RE, Pera V, Verhamme KMC, de Wilde M, van Mulligen EM and Kors JA (2025). Aioli: Standardising drugs in the FDA adverse event reporting system (FAERS) to RxNorm and anatomical therapeutic chemical (ATC) codes. *Pharmacoepidem. Dr. S.*, **34**(9): e70216.

Pirrami RG and Reinert JP (2025). Efficacy and safety of mifepristone and misoprostol compared to misoprostol alone for the resolution of miscarriage and intrauterine fetal death: A systematic review and meta-analysis. *Ann Pharmacother*, **59**(7): 636-647.

Pohjoranta E, Suhonen S, Mentula M, Gissler M and Heikinheimo O (2024). Pregnancy outcomes following routine early provision of intrauterine device after first-trimester induced abortion-A secondary analysis of a randomized controlled trial with a 5-year follow up. *Acta Obstet. Gyn. Scan*., **103**(2): 342-350.

Portaccio E, Moiola L, Martinelli V, Annovazzi P, Ghezzi A, Zaffaroni M, Lanzillo R, Brescia Morra V, Rinaldi F, Gallo P, Tortorella C, Paolicelli D, Pozzilli C, De Giglio L, Cavalla P, Cocco E, Marrosu MG, Solaro C, Uccelli A, Laroni A, Pastò L, Giannini M, Trojano M, Comi G, Amato MP and MS SGOT (2018). Pregnancy decision-making in women with multiple sclerosis treated with natalizumab: II: Maternal risks. *Neurology*, **90**(10): e832-e839.

Reinold J, Kollhorst B, Wentzell N, Platzbecker K and Haug U (2024). Use of isotretinoin among girls and women of childbearing age and occurrence of isotretinoin-exposed pregnancies in Germany: A population-based study. *Plos Med.*, **21**(1): e1004339.

Resta C, Dooley WM, Malligiannis Ntalianis K, Burugapalli S and Hussain M (2021). Ectopic pregnancy in a levonogestrel-releasing intrauterine device user: A case report. *Cureus J. Med Science*, **13**(10): e18867.

Sørensen MJ, Kjaersgaard MIS, Pedersen HS, Vestergaard M, Christensen J, Olsen J, Parner E, Pedersen LH and Bech BH (2015). Risk of fetal death after treatment with antipsychotic medications during pregnancy. *Plos One*, **10**(7): e0132280.

Tada K, Maruo K, Isogawa N, Yamaguchi Y and Gosho M (2020). Borrowing external information to improve Bayesian confidence propagation neural network. *Eur. J. Clin. Pharmacol*., **76**(9): 1311-1319.

Tan X, Liu GF, Zeng D, Wang W, Diao G, Heyse JF and Ibrahim JG (2019). Controlling false discovery proportion in identification of drug-related adverse events from multiple system organ classes. *Stat. Med*.,

38(22): 4378-4389.

Thai TN, Sarayani A, Wang X, Albogami Y, Rasmussen SA and Winterstein AG (2020). Risk of pregnancy loss in patients exposed to mycophenolate compared to azathioprine: A retrospective cohort study. *Pharmacoepidem. Dr. S.*, **29**(6): 716-724.

Tian X, Luo D, Zeng W, Zhou X, Chen Y, Dai D, Fang C and Xiao J (2025). Disproportionality analysis of drug-induced erectile dysfunction using FAERS database. *Sci Rep-Uk*, **15**(1): 15760.

Tomson T, Battino D, Bonizzoni E, Craig JJ, Lindhout D, Perucca E, Sabers A, Thomas SV, Vajda F and EURAP SG (2015). Antiepileptic drugs and intrauterine death: A prospective observational study from EURAP. *Neurology*, **85**(7): 580-588.

Trillenberg P, Sprenger A and Machner B (2023). Sensitivity and specificity in signal detection with the reporting odds ratio and the information component. *Pharmacoepidem. Dr. S.*, **32**(8): 910-917.

Trivedi M, Jose M, Philip RM, Sarma PS and Thomas SV (2018). Spontaneous fetal loss in women with epilepsy: Prospective data from pregnancy registry in India. *Epilepsy Res.*, **146**: 50-53.

Tshivuila-Matala COO, Honeyman S, Nesbitt C, Kirtley S, Kennedy SH and Hemelaar J (2020). Adverse perinatal outcomes associated with antiretroviral therapy regimens: systematic review and network meta-analysis. *AIDS*, **34**(11): 1643-1656.

Vajda FJE, O'Brien TJ, Graham J, Hitchcock AA, Lander CM and Eadie MJ (2018). Anti-epileptic drug exposure and risk of foetal death in utero. *Acta Neurol. Scand.*, **137**(1): 20-23.

Van Leer P (2019). Preventing spontaneous abortion with progestin therapy. *Am. Fam. Physician*, **100**(1):

Vanderhoff A, Lanes A and Ginsburg E (2024). Impact of prior levonorgestrel intrauterine device use at the time of embryo transfer. *Reprod Fertil*, **5**(4): e240099.

Wagner JK, Dathe K, Schaefer C and Hoeltzenbein M (2020). Ulipristal acetate and pregnancy outcome-an observational study. *Hum Reprod*, **35**(4): 751-758.

Wang Q, Sun H, Huang J, Chen Y, Ni J, Tang Z and Liu J (2024). Investigation of spontaneous abortion and stillbirth adverse events in epilepsy patients treated with levetiracetam: A pharmacovigilance study. *Epilepsy Behav*, **160**: 110077.

Yang L, Tao T, Zhao X, Tao H, Su J, Shen Y, Tang Y, Qian F and Xiao J (2020). Association between fetal chromosomal abnormalities and the frequency of spontaneous abortions. *Exp Ther Med*, **19**(4): 2505-2510.

Ying X, Bao D, Jiang H and Shi Y (2022). Maternal non-steroidal anti-inflammatory drug exposure during pregnancy and risk of miscarriage: A systematic review and meta-analysis. *Eur. J. Clin. Pharmacol.*, **78**(2): 171-180.

Yousif J, Adlam T, Grant-Kels JM and Farshchian M (2022). The Supreme Court abortion ban impact on dermatology. *J. Am. Acad. Dermatol.*, **87**(5): 1225-1226.

Zeytin Demiral G, Betaş Akın S, Kayacık Günday Ö, Şahbaz FG and Turk Boru U (2024). Maternal and fetal outcomes of antiepileptic treatments during pregnancy: A retrospective study. *Epilepsy Behav*, **158**: 109937.

Zhang X, Feng Y, Li F, Ding J, Tahseen D, Hinojosa E, Chen Y and Tao C (2024). Evaluating MedDRA-to-ICD terminology mappings. *Bmc Med Inform Decis*, **23**(Suppl 4): 299.

Zheng J, Zhang Z, Ma L and Su L (2025). Real-world pharmacovigilance study on neonatal congenital anomalies associated with maternal drug exposure using the FDA adverse event reporting system. *Ther Adv Drug Saf*, **16**: 20420986251383765.

Zheng J, Zhang Z, Liang Y, Wu Q, Din C, Wang Y, Ma L and Su L (2025). Risk of congenital anomalies associated with psychotropic medications: A review of neonatal reports in the FDA adverse event reporting System (FAERS). *Arch Womens Ment Health*, **28**(4): 911-918.