BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Drug exposure characteristics and related pregnancy outcomes in pregnant women: an observational cohort study

Ping Zhang[1]

Jing Xu[1]

Guorong Han[1]

Author details can be found at the end of this article

Correspondence to: Guorong Han (njyy033@njucm.edu.cn)

Abstract

Aims/Background The relationship between drug exposure and pregnancy outcomes is still unclear. The study was designed to characterise the overall condition of drug exposure during pregnancy and uncover related pregnancy outcomes.

Methods Pregnant women were enrolled in the study from 1 October 2019 to 31 April 2022, at a tertiary hospital in Jiangsu Province, China. Basic maternal information and data regarding drug exposure during different pregnancy trimesters were gathered using the 'Eugenic Baby' platform. Based on drug use data and the pregnancy and lactation labelling rule, pregnant women were divided into three groups to explore the relationship between drug exposure and pregnancy outcomes.

Results Analysis revealed that fetal protection drugs were used in 43.99% of early pregnancy cases. Pregnant women utilised more unrecommended drugs (according to the pregnancy and lactation labelling rule) in the first trimester than in the following trimesters. Regarding pregnancy outcomes, 56 of the 837 live infants had a malformation, and congenital heart disease was the main type. Gestational age, mode of delivery, birth weight, height, and head circumference were significantly different ($p < 0.05$) among the three groups. According to multivariate logistic regression analysis, preterm birth (odds ratio=3.226, 95% confidence intervals: 1.447–7.194, p=0.004) and low birth weight (odds ratio=4.270, 95% confidence intervals: 1.299–14.034, p=0.017) predicted increased risk of maternal drug exposure after adjusting for covariates.

Conclusion Drug exposure of various types is common during pregnancy. Compared to the second and third trimester, unrecommended drugs are used more frequently in the first trimester. Drug exposure is associated with adverse pregnancy outcomes and these associations need to be further confirmed. It is vital to fully consider treatment benefits and potential risks before medication initiation during pregnancy.

Key words: Birth defect; Drug exposure; Infants; Pregnancy

Submitted: 27 March 2024; Revised: 28 April 2024; Accepted: 10 May 2024

Introduction

Due to the country's massive population base, the number of women of childbearing age in China greatly outnumbers that of other countries. According to figures released by the National Bureau of Statistics, China had a total of 10.62 million births in 2021 (The National Bureau of Statistics, 2021). Meanwhile, data from the Ministry of Health showed that the birth defect rate was 5.6% in China each year (Gazette of the National Health Commission of the People's Republic of China, 2018). Birth defects are the main cause of miscarriage, stillbirth, and postnatal disability, which not only affect fetal and neonatal survival and quality of life, but also cause a significant socio-economic burden. Therefore, neonatal birth defects have received increased attention.

Birth defects have a complicated aetiology that involves a combination of genetic and environmental factors. Known teratogenic drugs include valproic acid, fluoxetine, β-blockers, etc. (Harris et al, 2017; Lee et al, 2021), as drugs are one of the high-risk factors. According to the analysis of recent surveys on drug usage, about 91.1%–97.1% of pregnant women have taken drugs due to physiological changes, pregnancy complications, and the risk of new diseases (Haas et al, 2018; Bérard et al, 2019; de Waard et al, 2019). However, the

How to cite this article: Zhang P, Xu J, Han G. Drug exposure characteristics and related pregnancy outcomes in pregnant women: an observational cohort study. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0124

risks of some drugs adopted by pregnant women are unknown. Firstly, studies reveal that many pregnant women may take drugs without realising they are pregnant, potentially exposing the foetus to drugs during critical developmental stages. Secondly, despite animal studies are conducted before the launch of new drugs, experimental false-positive or false-negative results do exist. For example, hydrocortisone may cause cleft lip and palate in mice but not in clinical trials (Erickson et al, 2005). In mice, thalidomide is weakly teratogenic, while it is significantly teratogenic in primates, including humans (Kim and Scialli, 2011). Moreover, pregnant women are frequently excluded from drug clinical trials due to scientific and ethical concerns. It is unclear whether drugs with pregnancy toxicity indicated by preclinical animal research or with unknown toxicity will affect fetal birth outcomes. As drug usage becomes more common, physicians and pharmacists confront a challenge: an increasing number of patients are inquiring about the safety of drug usage during pregnancy. On this basis, we aimed to investigate current drug exposure in pregnant women and to explore the relationship between maternal drug exposure during pregnancy and pregnancy outcomes, to establish an evidence-based foundation for clinical drug usage.

Methods

Participants

Pregnant women were enrolled in the study from 1 October 2019 to 31 April 2022, at a tertiary hospital in Jiangsu Province, China. The inclusion criteria were pregnant women at < 14 gestational weeks who voluntarily participated in the survey. Pregnant women with mental illness or physical disability were excluded due to poor compliance and difficulty with completing the questionnaire. The study enlisted the participation of 1019 pregnant women; among them, there were 8 spontaneous/induced abortions, 2 stillbirths, 1 intrauterine death, and 11 induced labours, and 176 did not have delivery information at the time. Thus, 821 pregnant women and 837 infants (including 16 pairs of twins) were included to examine the relationship between maternal drug exposure and pregnancy outcomes. The study was approved by the Ethics Committee of the West China Second University Hospital (K2019022) on 06 June 2019. All participants provided informed consent.

Questionnaire

Using a structured electronic questionnaire based on the ‘Eugenics Baby’ platform designed by China's National Birth Defects Monitoring Centre, we gathered basic demographic data and information regarding personal habits, diseases, drug exposure, and pregnancy outcomes. Women enrolled needed to complete the questionnaire under the guidance of the investigator at enrolment, at 24–28 gestational weeks, before delivery, and 42 days after delivery. To avoid memory bias, we gathered data on drug exposure in accordance with physician or pharmacist prescription or recall. The questionnaire was divided into four parts: basic information, pre-pregnancy habits, disease information, and drug exposure during pregnancy and pregnancy outcomes.

Research design

Based on the results of the questionnaire and according to the pregnancy and lactation labelling rule (PLLR), and after excluding the use of traditional Chinese medicine (TCM) and Chinese patent medicine (CPM), the enrolled women were divided into three groups: women in Group A did not use drugs during pregnancy, women in Group B used drugs currently considered safe by PLLR during pregnancy, and women in Group C used drugs with potential benefits and risks during pregnancy. Overall drug exposure and its relationship with pregnancy outcomes were analysed. The flowchart of the observational cohort study is shown in Figure 1.

Statistical analyses

The ‘Eugenics Baby’ system data were exported and statistically evaluated using SPSS 26.0 (IBM, Chicago, IL, USA) software. The prevalence of drug exposure at various gestational periods was described using descriptive statistics. Categorical variables were

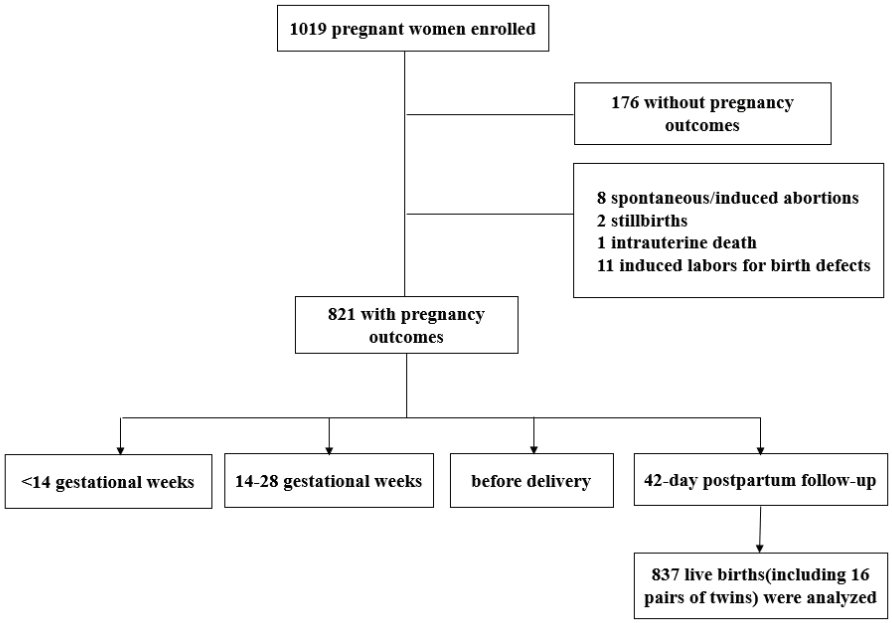

Figure 1. Study process and follow-up timing.

presented as counts with proportions, while continuous variables were presented as the mean ± standard deviation for normally distributed variables or the median and interquartile ranges for variables not normally distributed. Differences among groups were assessed using Pearson's chi-squared test or Student's *t*-test. The association between drug exposure and adverse pregnancy outcome was evaluated using univariable and multivariable logistic regression analyses, with adjustment for potential confounders. Adjusted odds ratios (AOR) and 95% confidence intervals (95% CI) were presented. The p values < 0.05 were considered statistically significant.

Results

Baseline characteristics on the participants

The data of 821 pregnant women were statistically analysed. The mean age was 30.27 ± 4.09 years, and the mean pre-pregnancy body mass index (BMI) was 22.03 ± 3.74 kg/m^2. Table 1 shows basic demographic and pregnancy-related information. 59.93% (n=492) of women had a history of multiple pregnancies, with one case reporting 10 pregnancies. 44.21% (n=363) of women had an adverse pregnancy history, mainly involving induced/drug abortions (30.93%), stillbirths (9.13%), and spontaneous abortions (8.89%). From 6 months before pregnancy to the first trimester (FT), 33.98% of spouses smoked and 23.14% of spouses drank, indicating that the spouses had a generally unhealthy lifestyle.

Comparisons of drug exposure at various stages of pregnancy

821 pregnant women with complete birth outcome information were analysed regarding drug exposure throughout pregnancy, with a cumulative total of 2092 drug usages during pregnancy and a per capita drug exposure of 2.5. Figure 2 indicates that 81.61% (n=670) of pregnant women were exposed to at least one drug, and 8 pregnant women were exposed to up to more than 5 categories of drugs, with reproductive assistance being the most common reason for drug usage.

Compared with the FT, the drug exposure rate in the second trimester (ST) and the third trimester (TT) showed an increasing trend, with 44.58% (n=366), 51.40% (n=422), and 60.90% (n=500), respectively. For the types of drugs, western medicine was the most common, with 81.13% (n=533), 74.84% (n=476), and 72.47% (n=579) in FT, ST, and TT, respectively. Figure 3 depicts the type of drug exposure at different pregnancy trimesters. The reasons for their usage were also investigated (Figure 4). As 7.92% (n=65) of women

Table 1. Basic information about women and the distribution of pregnancy risk

	Characteristic	Number	Percent (%)
Pre-pregnancy BMI (kg/m^2)	< 18.5	84	10.23
	18.5–23.9	576	70.16
	24–28	115	14.01
	> 28	46	5.60
Age (years)	< 20	3	0.37
	20–34	696	84.77
	≥ 35	122	14.86
Gravidity	1	329	40.07
	> 1	492	59.93
Level of education	Primary school and below	12	1.46
	Middle or high school	251	30.57
	College	224	27.28
	Bachelor degree	275	33.50
	Master or above	59	7.19
Mode of conception	Spontaneous conception	757	92.20
	Assisted conception	64	7.80
Adverse pregnancy history	Yes	363	44.21
	No	458	55.79
Unintended pregnancy	Yes	361	43.97
	No	460	56.03
Folic acid	Yes	786	95.74
	No	35	4.26
Smoking	No	801	97.56
	Smoking pre-pregnancy	12	1.46
	Smoking from pre-pregnancy to FT	8	0.97
Drinking	No	799	97.32
	Drinking pre-pregnancy	17	2.07
	Drinking from pre-pregnancy to FT	5	0.61
Smoking (husband)	No	509	62.00
	Smoking pre-pregnancy	33	4.02
	Smoking from pre-pregnancy to FT	279	33.98
Drinking (husband)	No	578	70.40
	Drinking pre-pregnancy	53	6.46
	Drinking from pre-pregnancy to FT	190	23.14

Pre-pregnancy: Half a year before pregnancy. Folic acid: Taking folic acid 3 months before pregnancy or in early pregnancy. Abbreviations: BMI, body mass index. FT, the first trimester.

conceived through assisted reproduction in the total population, 20.85% (n=137) of drugs were for assisted reproduction, and 43.99% (n=289) were for fetal protection in FT, indicating that this group had a high risk of miscarriage. Drug categories are shown in Table 2. According to the Anatomical Therapeutic Chemical (ATC) classification system that was developed by The WHO Collaborating Centre for Drug Statistics Methodology (CCDSM), genitourinary system drugs and sex hormones, systemic anti-infective drugs, and other types such as liver-protective drugs were the most common in the FT (43.99%, 19.03%, and 19.33%), while systemic anti-infective drugs, haematological drugs, and other types of drugs were the most common in the ST (41.51%, 26.42%, 19.18%) and TT (41.43%, 37.67%, 9.26%). After excluding TCM and CPM, the usage rate of drugs with unknown risk levels and need consideration of potential benefit and risk (25.74%, 21.34%, and 12.52% for the FT, ST and TT, respectively), indicated that there was still unknown drug safety for

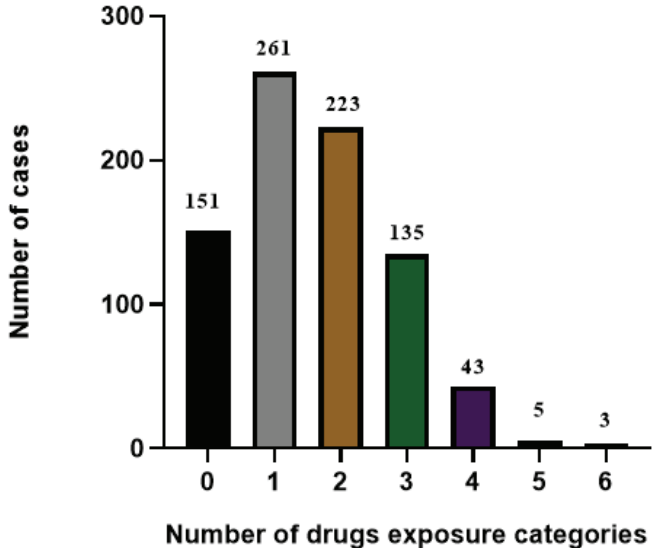

Figure 2. Distribution of drug exposure among pregnant women.

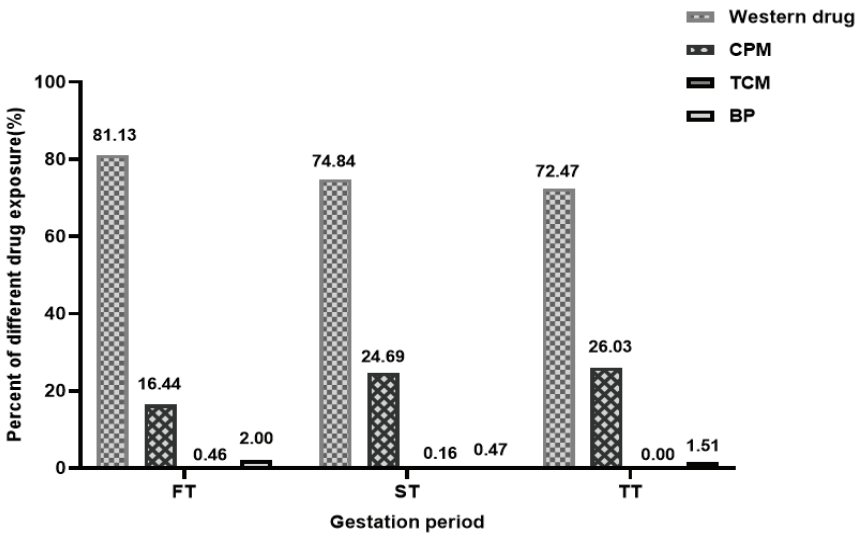

Figure 3. Distribution of drug types in various stages of pregnancy. Abbreviations: FT, the first trimester. ST, the second trimester. TT, the third trimester. CPM, Chinese patent medicine. TCM, traditional Chinese medicine. BP, biological products. Diet pills are not shown due to few data.

pregnant women. In the FT, drugs with unknown risk levels (8.98% vs. 2.52% vs. 2.13%, respectively) and unrecommended drug (5.63% vs. 0.00% vs. 0.13%, respectively) usages were significantly higher in comparison to that in ST and TT, indicating potential risk for fetal growth and development and adverse pregnancy outcomes. The most common drugs during pregnancy were prednisone acetate, efavirenz, methimazole, heparin, aspirin, and

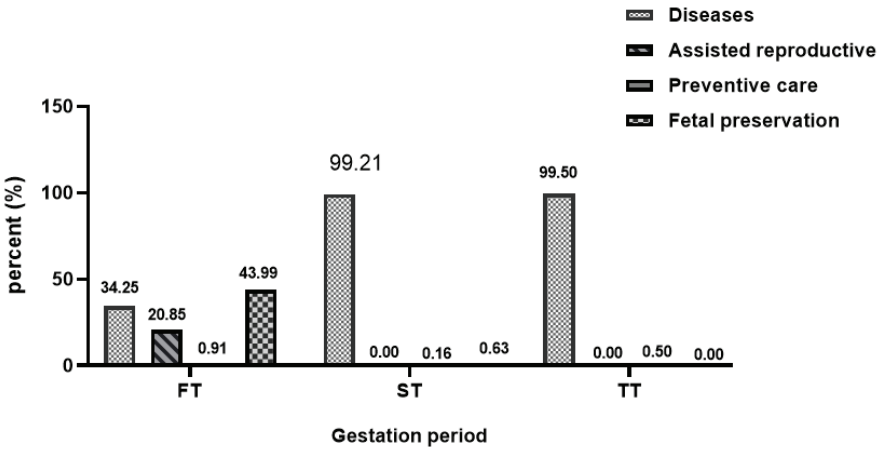

Figure 4. Distribution of drug usage reasons in various stages of pregnancy. Abbreviations: FT, the first trimester. ST, the second trimester. TT, the third trimester.

Table 2. Distribution of drug categories at different gestational weeks

Drug categories	FT	Percent (%)	ST	Percent (%)	TT	Percent (%)
Alimentary tract and Metabolism	15	2.28	19	2.99	34	4.26
Blood and blood forming organs	30	4.57	168	26.42	301	37.67
Cardiovascular system	17	2.59	5	0.79	7	0.88
Dermatologicals	–	–	7	1.10	9	1.13
Genito urinary system and sex hormones	289	43.99	4	0.63	4	0.50
Systemic hormonal preparations, excel sex hormones and insulins	36	5.48	42	6.60	34	4.26
Anti-infectives for systemic use	125	19.03	264	41.51	331	41.43
Anti-neoplastic and immunomodulating agents	5	0.76	–	–	–	–
Musculo-skeletal system	6	0.91	3	0.47	1	0.13
Nervous system	6	0.91	1	0.16	1	0.13
Anti-parasitic products, insecticides and repellents	1	0.15	–	–	–	–
Respiratory system	1	0.15	–	–	–	–
Sensory organs	–	–	1	0.16	–	–
Various	127	19.33	122	19.18	74	9.26

Abbreviations: FT, the first trimester. ST, the second trimester. TT, the third trimester.

hydroxychloroquine sulphate. The most common fetal preservation drugs were progesterone and dydrogesterone, but the use of these drugs requires consideration of potential benefit and risk, especially oestradiol and chorionic gonadotropin.

Pregnancy outcomes

This study included complete information from 821 pregnant women and 837 live births (16 pairs of twins) during follow-up. The live birth rate was 97.44% and causes of embryo/foetus death included 1 spontaneous abortion (0.12%), 7 induced abortions for personal reasons (0.81%), 1 induced abortion for intrauterine death (0.12%), 2 deliveries of a stillborn baby (0.23%), and 11 induced labours for birth defects (1.28%). The rate of caesarean delivery was 52.69% (n=441). In addition, 5.02% (n=42) babies were delivered with a low birth weight (< 2500 g), 5.73% (n=48) babies had macrosomia (> 4000 g), and 8.60% (n=72) babies were premature (< 37 weeks). When the pregnancy outcomes of mothers in Groups A, B, and C were compared, we discovered significant disparities in gestational age, mode of delivery, birth weight, height, and head circumference among the three groups (Table 3). Further multivariate analyses revealed an association between drug exposure and premature delivery (OR, 3.226; 95%CI, 1.447 to 7.194), low birth weight (OR, 4.270; 95%CI, 1.299 to 14.034), and caesarean delivery (OR, 0.727; 95%CI, 0.528 to 0.999) after controlling for potential confounding factors (Table 4). There were 56 birth defects among all live infants (Table 5), with a birth defect rate of 6.69%. Among the 56 malformations (32 boys, 24 girls), 17 mothers reported no drug exposure during their pregnancy. For infants with malformations whose mothers reported drug exposure (n=39), a total of 110 drugs

Table 3. Pregnancy outcomes for live infants

Characteristic	Total	Group A (n=217)	Group B (n=545)	Group C (n=75)	F or $\chi 2$	*p* value
Gender (n, %)						
Male	425 (50.78)	108 (49.77)	278 (51.01)	39 (52.00)	0.145	1.407
Female	412 (49.22)	109 (50.23)	267 (48.99)	36 (48.00)		
Gestational age (n, %)						
< 37 weeks	72 (8.60)	7 (3.23)	41 (7.52)	24 (32.00)	61.009	< 0.001
≥ 37 weeks	765 (91.40)	210 (96.77)	504 (92.48)	51 (68.00)		
Mode of delivery (n, %)						
Spontaneous delivery	396 (47.31)	118 (54.38)	255 (46.79)	23 (30.67)	12.742	0.001
Caesarean delivery	441 (52.69)	99 (45.62)	290 (53.21)	52 (69.33)		
Birth weight (n, %)						
< 2500 g	42 (5.02)	3 (1.38)	26 (4.77)	13 (17.33)	24.114	< 0.001
2500–3999 g	747 (89.25)	200 (92.17)	490 (89.91)	57 (76.00)		
≥ 4000 g	48 (5.73)	14 (6.45)	29 (5.32)	5 (6.67)		
Birth height (cm), range	49.82 ± 1.55	50.02 ± 0.70	49.90 ± 0.94	48.61 ± 4.17	16.609	< 0.001
Head circumference (cm), range	34.09 ± 1.73	34.34 ± 1.19	34.09 ± 1.77	33.32 ± 2.42	16.935	< 0.001
Apgar score 1 min, range	9.87 ± 0.63	9.88 ± 0.67	9.89 ± 0.54	9.72 ± 0.97	5.716	0.057
Apgar score 5 min, range	9.97 ± 0.27	9.96 ± 0.23	9.98 ± 0.20	9.91 ± 0.60	2.916	0.233
Birth defects (n, %)						
Yes	56 (6.69)	17 (7.83)	33 (6.06)	6 (8.00)	1.013	0.628
No	781 (93.31)	200 (92.17)	512 (93.94)	69 (92.00)		

The p value represents the comparison among the three groups.

were administered, consisting of anti-infectives drugs, hepatoprotective drugs, CPM, sex hormone drugs, and haematological drugs.

For neonatal height, head circumference, Apgar score 1 min and Apgar score 5 min, analysis of covariance showed no significant difference.

Discussion

Drugs can serve as teratogens during critical periods of embryonic development, causing birth abnormalities (Buhimschi and Weiner, 2009). When drugs are consumed before conception, developmental abnormalities can also be observed (Neri et al, 2015). It is estimated that prescription drug consumption could reach 80% in Italy (Fortinguerra et al, 2021) and 93% in France (Araujo et al, 2021). In addition, the pharmacokinetics of drugs in pregnant women change (Xia et al, 2016) due to physiological changes during pregnancy, such as changes in enzyme activity, cardiac output, tissue blood flow, renal function, body fluid, and fetoplacental function. This could result in fetal exposure to drugs by raising the levels of active medicines or metabolites in the blood. As a result, pregnant women must be guided to make informed decisions about therapeutic medicine during pregnancy.

The results of the present study indicated that sex hormones drugs, such as progesterone, dydrogesterone, and levothyroxine, were the commonly utilised drugs in the FT for fetal preservation and impaired thyroid function. Threatened abortion is a prevalent issue that

Table 4. Logistic regression analysis of drug exposure and adverse pregnancy outcomes in pregnant women

	Univariate regression analysis			Multivariate regression analysis		
	OR	**95%CI**	***p***	**OR**	**95%CI**	***p***
Premature delivery	3.514	1.586–7.786	0.002	3.226	1.447–7.194	0.004
Caesarean delivery	0.682	0.500–0.930	0.016	0.727	0.528–0.999	0.050
Low birth weight	4.788	1.464–15.657	0.010	4.270	1.299–14.034	0.017
Macrosomia	0.841	0.442–1.600	0.598		—	
Birth defects	1.266	0.701–2.289	0.434		—	

Premature delivery: adjusted for mode of conception. Caesarean delivery: adjusted for age, mode of conception low birth weight: adjusted for BMI, mode of conception. 95%CI, 95% confidence intervals; OR, odds ratio.

Table 5. Malformations encountered in our cohort and prevalence rates

Birth defects	Number	Percent (%)
Congenital heart defect	43	5.14
Asymmetric crying syndrome	3	0.36
Cleft palate	1	0.12
Craniocerebral dysplasia	1	0.12
Malformation of the external ear and atresia of the external auditory canal	3	0.36
Hypospadias	1	0.12
Polydactyly	1	0.12
Congenital adrenal hyperplasia	1	0.12
Syndactyly	1	0.12
Webbed penis	1	0.12

affects 25% of clinical pregnancies (Xu et al, 2017). The current consensus recommends that patients with threatened abortion use progesterone to reduce the rate of miscarriage. Progesterone is the safest exogenous progesterone supplement. The safety of dydrogesterone in offspring has attracted much attention because of its different pharmacodynamics and pharmacological mechanisms. In a study of 8,508 foetuses exposed to dydrogesterone in FT, an increased incidence of fetal anomalies including hypospadias, cardiovascular malformations, spina bifida, and hydrocephalus was discovered. However, there is not enough evidence to prove the teratogenic effect of dydrogesterone, and the conclusion remains to be further verified (Koren et al, 2020). According to a recent meta-analysis, progesterone supplements do not appear to be effective for threatened abortion (Yan et al, 2021). There is still a need for further verification in terms of the safety and efficacy of progesterone in pregnancy.

The prevalence of maternal morbidity (at least one physical morbidity) during pregnancy was 93.95%, which was similar to the prevalence in other studies (McCauley et al, 2022). Given the focus of our hospital, infectious disease accounted for the major part, (mainly hepatitis B, syphilis, hepatitis C). Tenofovir disoproxil fumarate (TDF), telbivudine (Ltd), tenofovir alafenamide (TAF), lamivudine (LAM), and other nucleotide analogues were used in our study population (37.44%). Ltd and TDF are safe, whereas the safety of LAM, TAF, and entecavir still needs to be further verified. According to the Antiretroviral Pregnancy Registry, the rate of birth defects among women undergoing antiretroviral therapy for HIV and/or HBV infection is similar to that of the general population (2.70% vs. 2.72%). Tenofovir disoproxil fumarate is currently recommended as a first-line antiviral drug for pregnant women. However, it raises the risk of osteoporosis and worsens kidney function in patients. It is not advocated for pregnant women with osteoporosis, or with high-risk factors for kidney damage. Entecavir should be avoided because of the potential for teratogenicity and should be replaced with TDF in women planning to become pregnant or who are already pregnant (Kumar et al, 2022). The newly marketed TAF has been recommended for the treatment of chronic hepatitis B in many regions of the world because it is safer for the kidneys and bones than TDF. Regarding maternal and infant safety, multiple studies have shown that TAF is safe in terms of adverse reactions, infant development, and deformity (Ding et al, 2020; Zeng et al, 2021).

In this study, CPM was also one of the most commonly utilised drug categories during pregnancy, with usage frequency up to 26.03% across the entire pregnancy. There are 16 various kinds of CPM drugs, including anaemia supplements, adjuvant liver disease drugs, fetal preservation drugs, etc. However, the medication guidelines for pregnant women in the CPM instructions are not perfect, and the ambiguity of their safety information still causes problems in guiding the usage of CPM during pregnancy. As a result, clinicians should strictly adhere to the relevant provisions in the drug instructions and syndrome differentiation when guiding the usage of CPM in pregnant women.

Anaemia is a common complication in pregnant women and the main causes include the deficiency of iron, cobalamin, and folic acid. It not only affects women's health, but is also associated with adverse pregnancy outcomes such as premature delivery, low birth weight, and nervous system dysplasia (Bicakci, 2015; Geng et al, 2015). As shown in a survey, the prevalence of gestational anaemia in China ranged from 40% to 10% between 2000 and 2019, with a downward trend over time (Liu et al, 2021). According to this study, approximately 34.10% of pregnant mothers were anaemic, with 20.02% using the CPM and 17.27% using western medicine to treat anaemia. In this study, 95.74% of pregnant women took folic acid, with 303 taking pure folic acid, 461 taking compound folic acid, and 22 taking the two folic acids. However, only 30.09% (n=247) of pregnant women took folic acid before pregnancy. The explanation for this could be that unintended pregnancies are common in the cohort. Unfortunately, information on maternal cobalamin intake and average haemoglobin levels throughout pregnancy was unavailable from the database.

During the study period, 837 infants were registered, with 56 birth defects diagnosed, resulting in a prevalence of 670 per 10,000. Congenital heart disease (CHD) was the most common birth defect, with a rate of 5.14%. It included atrial septal defect (55.36%), patent foramen ovale (17.85%), patent ductus arteriosus (12.50%), and so on. There were no infants that died from CHD. One possible reason is that our institution strictly implemented the

neonatal CHD screening programme. In 2020, the screening rate for neonatal CHD was 96.77%, with a positive rate of 4.17%. The actual cause of CHD, however, is unknown. The use of certain cold medicines, antibiotics, salicylates, antifungals, and other drugs in the FT, and viral infections in pregnant women, such as hepatitis B virus, coxsackievirus-b, human cytomegalovirus, and rubella virus, have been linked to an increased risk of CHD in newborns (Wang et al, 2022). This could account for our research population's high rate of CHD. However, more research is needed to confirm the findings.

Conclusion

In this study, we described the characteristics of drug exposure during pregnancy and analysed related pregnancy outcomes. We found a correlation between drug exposure during pregnancy and preterm labour and caesarean delivery, low birth weight, and fetal malformations. These results demonstrate that epidemiological studies of drug exposure during pregnancy are important for the promotion of the rational use of drugs, and such studies could also serve as a reference for drug usage safety during pregnancy. The study revealed a link between drug exposure during pregnancy and adverse pregnancy outcomes, providing evidence-based support for the impact of drug use during pregnancy.

Key points

- The study described the characteristics of drug exposure during pregnancy and analyzed related pregnancy outcomes.
- The study revealed a link between drug exposure during pregnancy and adverse pregnancy outcomes.
- The study provided evidence-based pharmacy support for drug use during pregnancy.

Author details

[1]Department of Obstetrics and Gynecology, The Second Hospital of Nanjing, Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China

Availability of data and materials

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

Author contributions

GRH designed the investigation and provided support. PZ wrote the manuscript. All authors contributed to important editorial changes in the manuscript. PZ and JX collected the data and performed the data analysis. All authors reviewed and approved the final version of the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the West China Second University Hospital (K2019022) on 06 June 2019. The project is sponsored by the West China Second University Hospital. Informed consent was obtained from all individual participants included in the study.

Acknowledgement

Not applicable.

Funding

The funding source for the research was the Chinese National Research Grant of the 13th Five-Year Plan for the Key Projects in Infectious Diseases (Grant No. 2017ZX10201201-002–001).

Conflict of interest

The authors declared that they have no competing interests.

References

Araujo M, Hurault-Delarue C, Sommet A et al. Drug prescriptions in French pregnant women between 2015 and 2016: A study in the EGB database. Therapie. 2021;76(3):239–247. https://doi.org/10.1016/j.therap.2020.07.002

Bérard A, Abbas-Chorfa F, Kassai B et al. The French pregnancy cohort: medication use during pregnancy in the French population. PLoS One. 2019;14(7):e0219095. https://doi.org/10.1371/journal.pone.0219095

Bicakci Z. Growth retardation, general hypotonia, and loss of acquired neuromotor skills in the infants of mothers with cobalamin deficiency and the possible role of succinyl-CoA and glycine in the pathogenesis. Medicine. 2015;94(9):e584. https://doi.org/10.1097/MD.0000000000000584

Buhimschi CS, Weiner CP. Medications in pregnancy and lactation: part 1. Teratology. Obstet Gynecol. 2009;113(1):166–188. https://doi.org/10.1097/AOG.0b013e31818d6788

de Waard M, Blomjous BS, Hol MLF et al. Medication use during pregnancy and lactation in a dutch population. J Hum Lact. 2019;35(1):154–164. https://doi.org/10.1177/0890334418775630

Ding Y, Cao L, Zhu L et al. Efficacy and safety of tenofovir alafenamide fumarate for preventing mother-to-child transmission of hepatitis B virus: a national cohort study. Aliment Pharmacol Ther. 2020;52(8):1377–1386. https://doi.org/10.1111/apt.16043

Erickson RP, Karolyi IJ, Diehl SR. Correlation of susceptibility to 6-aminonicotinamide and hydrocortisone-induced cleft palate. Life Sci. 2005;76(18):2071–2078. https://doi.org/10.1016/j.lfs.2004.08.036

Fortinguerra F, Belleudi V, Poggi FR et al. Medication prescriptions before, during and after pregnancy in Italy: a population-based study. Ann Ist Super Sanita. 2021;57(3):249–258. https://doi.org/10.4415/ANN_21_03_09

Gazette of the National Health Commission of the People's Republic of China. Circular of Issuing the National Comprehensive Prevention and Treatment Program for Birth Defects. 2018. http://www.nhc.gov.cn/fys/s3589/201812/9644ce7d265342779099d54b6962a4e0.shtml (Accessed 01 September 2018)

Geng F, Mai X, Zhan J et al. Impact of fetal-neonatal iron deficiency on recognition memory at 2 months of age. J Pediatr. 2015;167(6):1226–1232. https://doi.org/10.1016/j.jpeds.2015.08.035

Haas DM, Marsh DJ, Dang DT et al Prescription and other medication use in pregnancy. Obstet Gynecol. 2018;131(5):789–798. https://doi.org/10.1097/AOG.0000000000002579

Harris BS, Bishop KC, Kemeny HR et al. Risk factors for birth defects. Obstet Gynecol Surv. 2017;72(2):123–135. https://doi.org/10.1097/OGX.0000000000000405

Kim JH, Scialli AR. Thalidomide: the tragedy of birth defects and the effective treatment of disease. Toxicol Sci. 2011;122(1):1–6. https://doi.org/10.1093/toxsci/kfr088

Koren G, Gilboa D, Katz R. RETRACTED ARTICLE: fetal safety of dydrogesterone exposure in the first trimester of pregnancy. Clin Drug Invest. 2020;40(7):679. https://doi.org/10.1007/s40261-019-00862-w

Kumar M, Abbas Z, Azami M et al. Asian Pacific association for the study of liver (APASL) guidelines: hepatitis B virus in pregnancy. Hepatol Int. 2022;16(2):211–253. https://doi.org/10.1007/s12072-021-10285-5

Lee KS, Choi YJ, Cho J et al. Environmental and genetic risk factors of congenital anomalies: an umbrella review of systematic reviews and meta-analyses. J Korean Med Sci. 2021;36(28):e183. https://doi.org/10.3346/jkms.2021.36.e183

Liu XX, Yi YJ, Feng YK, Wang F. Analysis on the prevalence of anemia among Chinese pregnant women. Chin J Reprod Health. 2021;32(03):210–215. https://doi.org/10.3969/j.issn.1671-878X.2021.03.003

McCauley M, White S, Bar-Zeev S et al. Physical morbidity and psychological and social comorbidities at five stages during pregnancy and after childbirth: a multicountry cross-sectional survey. BMJ Open. 2022;12(4):e050287. https://doi.org/10.1136/bmjopen-2021-050287

Neri M, Bello S, Turillazzi E, Riezzo I. Drugs of abuse in pregnancy, poor neonatal development, and future neurodegeneration. Is oxidative stress the culprit? CPD. 2015;21(11):1358–1368. https://doi.org/10.2174/1381612821666150105124510

The National Bureau of Statistics. China Statistical Yearbook2021. China Statistics Press: Beijing. 2021.

Wang T, Li Q, Chen L et al. Maternal viral infection in early pregnancy and risk of congenital heart disease in offspring: a prospective cohort study in central China. Clin Epidemiol. 2022;14:71–82. https://doi.org/10.2147/CLEP.S338870

Xia Y, Stadler D, Lucifora J et al. Interferon-γ and tumor necrosis factor-α produced by T cells reduce the HBV persistence form, cccDNA, without cytolysis. Gastroenterology. 2016;150(1):194–205. https://doi.org/10.1053/j.gastro.2015.09.026

Xu Q, Chen J, Wei Z et al. Sex hormone metabolism and threatened abortion. Med Sci Monit. 2017;23:5041–5048. https://doi.org/10.12659/MSM.904500

Yan Y, Chen Z, Yang Y et al. Efficacy of progesterone on threatened miscarriage: an updated meta-analysis of randomized trials. Arch Gynecol Obstet. 2021;303(1):27–36. https://doi.org/10.1007/s00404-020-05808-8

Zeng QL, Yu ZJ, Ji F et al. Tenofovir alafenamide to prevent perinatal hepatitis B transmission: a multicenter, prospective, observational study. Clin Infect Dis. 2021;73(9):e3324–e3332. https://doi.org/10.1093/cid/ciaa1939