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Research Article

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Assessment of Drug prescription Pattern in pregnancy in A Tertiary Care Hospital: A Prospective Study

Hedieh Vafaeerokh [1*] and Mohammed Kazim Sheriff [2]

[1*] *Intern Department of Pharmacy Practice, Al-Ameen college of pharmacy, Bangalore, India.*

[2] *Faculty, Department of Pharmacy Practice, Al-Ameen College of Pharmacy, Bangalore, India.*

Abstract: Pregnancy is a special physiological condition and managing medical conditions during pregnancy is a challenge due to the teratogenic potential of many drugs. This cross-sectional prospective study was conducted for a period of 6 months to describe the prescription pattern and risk categorization of drugs among pregnant inpatients in a tertiary care hospital. Pregnant inpatients of OBG ward in any trimester who were prescribed with at least one drug were included. Demographic details and list of prescribed drugs were collected from medical records of patients. The drugs prescribed were grouped according to their pharmacological classes and US FDA pregnancy risk classification. Prescription pattern was assessed using WHO core prescribing indicators. A total of 951 drugs comprising 34 different drugs were prescribed for 420 pregnant women. The average number of drugs prescribed per encounter was 2.3 ± 0.9 (SD). Anti- anemic/vitamin and mineral supplements (288, 30.3%), followed by antibiotics (142, 14.93%) and antihypertensive drugs (127, 13.35%) were the most commonly prescribed classes of drugs. As per FDA Drug Risk Category, most of prescribed drugs belonged to category B (42.26%) and category A (32.9%) followed by category C (17%), category D (1.05%) and category X (0.84%). It was found that the overall prescription pattern of drugs among pregnant inpatients was safe and rational since the majority of prescribed drugs fell under category A and B pregnancy. Continuous drug utilization evaluation in this population and interaction of clinical pharmacist with healthcare team is crucial to have rational and safe prescription of drugs among hospitalized pregnant women.

Keywords: prescription pattern, pregnancy, drug, risk category, trimester, teratogen

***Corresponding Author**

Dr. Hedieh Vafaeerokh , Intern Department of Pharmacy Practice, Al-Ameen college of pharmacy, Bangalore, India.

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1. INTRODUCTION

Pregnancy is a special condition with physiological alteration in the body that affects pharmacokinetic parameters of administered drugs which can impose potential risks to the foetus due to teratogenicity of the drug itself and/or physiological adjustments of the body during pregnancy. Transferring of drugs through the placenta is one of the main factors that affects teratogenicity of a drug during pregnancy. Hence, well-judged prescription of drugs during pregnancy need to be considered.[1-3] Thalidomide incidence in 1960's and teratogenic effect of diethylstilbestrol in 1971 are two examples of historical tragedies that made FDA to establish safety and efficacy of drugs before they come to the market.[3] However, during drug development process, pregnant women are generally excluded in clinical trials and safety and efficacy information of drugs during pregnancy are collected from case reports, epidemiological studies, post marketing surveillance and animal reproductive toxicological studies.[4] Supplements like calcium, iron and vitamins are routinely prescribed during pregnancy to promote the health and nutritional status of the mother as well as fetus. Ideally use of drug should be avoided/ minimised during pregnancy.[5] But use of drugs during pregnancy is unavoidable in certain conditions including presence of pre-existing chronic morbidities like epilepsy, hypertension, diabetes, asthma, thyroid disorder, etc or in pregnancy related complications including hypertension or gestational diabetes as well as complications which are not directly related to pregnancy but have happened during pregnancy such as respiratory infections, gastrointestinal infection, urinary tract infection, etc.[3,6] In such conditions, risk/benefit assessment of selection of drugs in pregnancy is challenging for clinicians. Because maternal drugs can increase risk of abortion, premature labour, delayed labour, foetal abnormalities, birth defects, etc.[7] About 2-3% of all birth defects result from drugs that are taken during pregnancy.[3]Hence, continuous monitoring of drug utilization in pregnancy is necessary to promote rational use of drugs in this special population in order to ensure maternal and foetal safety and well-being. Drug utilization studies in pregnancy is of great concern. It can improve health outcomes and provide optimal care to pregnant women by critical evaluation of prescription patterns and comparing the observed pattern with available guidelines and recommendations, providing feedback and giving awareness to the healthcare team regarding the risks of potential harmful drugs during pregnancy.[8]There are limited drug utilization studies among pregnant women in South India. Hence this study aims to describe the prescription pattern and risk categorization of drugs in pregnant women who are admitted in a tertiary care hospital to know the extent of rational prescribing practice in this special population.

2. MATERIALS AND METHODS

This was a prospective, cross-sectional study conducted at the inpatient ward of Obstetrics and Gynecology (OBG) department of the hospital for a period of 6 months (from November 2018 to April 2019) after obtaining ethical clearance (with reference number of Al-Am/2018/159) from the Institutional Ethics Committee of the Hospital in Bangalore. The informed consent was obtained from all included study subjects. Pregnant women in any trimester who were admitted in OBG ward and were prescribed with at least one drug were included. Pregnant women who were not willing to participate in the study and those who were not prescribed with any drug were excluded. All data including demographic details of patients (age, gravidity and trimester of pregnancy), medical complaints, list of prescribed drugs including their generic or brand names, dose, frequency and their route of administrations were collected from medical records of pregnant women and were recorded in structured data collection form. The drugs prescribed were grouped according to their pharmacological classes and their safety for use in pregnancy was assessed according to US Food and Drug Administration (FDA) pregnancy risk classification groups of A, B, C, D, X. Description of each USFDA pregnancy risk category (initiated in 1979) is as following[9]:

(A) Adequate and well-controlled studies in pregnant women have not shown that the drug increases the risk of fetal abnormalities.

(B) Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

(C) Animal reproduction studies have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans and the benefits from the use of the drug in pregnant women may be acceptable, despite its potential risks.

(D) Based on human data, the drug can cause fetal harm when administered to pregnant women, but the potential benefits from the use of the drug may be acceptable, despite its potential risks.

(X) Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

The pregnant women were grouped into their respective trimesters and prevalence of drug use was analysed over the trimesters.

3. STATISTICAL ANALYSIS

Analysis was done using the Statistical Package for Social Science (SPSS) for Windows software (Version 22.0; SPSS Inc, Chicago). Descriptive statistics was used and results have been presented in terms of number, percentage and in terms of mean ± standard deviation (SD). The WHO core prescribing indicators including a) Average number of drugs prescribed per encounter (it was calculated by dividing the total number of drugs by the number of encounters), b) Percentage of drugs prescribed by generic name, c) Percentage of encounters prescribed with antibiotic, d) Percentage of encounters prescribed with injection, e) Percentage of drugs prescribed from essential drug list was used for drug utilization evaluation. FDA pregnancy safety categories of prescribed drugs were assessed using drug index online checker and available literatures.[10,11]

4. RESULTS

A total of 420 cases were included in the present study. The relevant characteristics of the enrolled study subjects are depicted in table No.1. Most pregnant women were in the reproductive age range of 21-24 years (175, 41.6%) and were of secundigravida (193, 45.9%). Around half enrolled

pregnant women (53.6%) were admitted during their third trimesters. Looking at reason for admission, the most common medical condition was anemia and vitamin deficiency (21.42%), followed by hypertension/pre-eclampsia (12.8%), urinary tract infection (9.5%), abdominal and body pain (8.5%), diabetes (8.5%), acidity (7.3%), hyperemesis (7.3%), asthma (5.9%), acute respiratory tract infection (5.2%) and hypothyroidism (3.5%).A total of 951 drugs comprising 34 different drugs were prescribed for 420 pregnant women in all trimesters. The frequency of prescription of classes of drugs and their trimester-wise distribution are shown in table No.2. Anti-anemic/vitamin and mineral supplements (288, 30.3%), followed by antibiotics (142, 14.93%), antihypertensive drugs (127, 13.35%), antacids (84, 8.85%) and anti-diabetic drugs (78, 8.2%) were the most commonly prescribed classes of drugs. The above-mentioned drugs accounted for around 75.63% of total prescribed drugs. The average number of drugs prescribed per encounter was 2.3 ± 0.9 (SD). Details of WHO core prescribing indicators evaluation is given in table No.3. Distribution of prescribed drugs according to US FDA pregnancy safety categories over different trimesters is shown in table No.4. Most of the prescribed drugs belonged to category B (440, 46.26%) and category A (312, 32.9%) while only 0.84% and 1.05% of prescribed drugs belonged to category X and D respectively. It was shown that category B was the most commonly prescribed category of drugs in all trimesters. Findings of the study showed that most frequently observed drugs of category B belonged to antibiotic class. Similarly, anti-anemic and multivitamins were the most frequently prescribed drugs in category A drugs. Of all 34 different prescribed drugs, antihypertensives and anti-asthmatics were most commonly observed classes of category C drugs. Frequency of various routes of administration of drugs over three trimesters are given in table No. 5. In general, most drugs were administered by oral route accounted for 87.38%. Comparison of routes of administration in different trimesters showed that oral route was the most common route of administration in all three trimesters. Inhalation route was the least given route of administration in first (0.71%) and second (0.59%) trimesters. Administration of drugs through the vaginal route was the least given route of administration in the third trimester (1.18%).

Table 1. Characteristics of study subjects

Characteristics	Frequency, n (%)
Age	
<=20	22 (5.3)
21-24	175 (41.6)
25-28	102 (24.3)
22-32	85 (20.3)
>=33	36 (8.5)
Gravida	
Primigravida	98 (23.4)
SecundiGravida	193 (45.9)
Multigravida	129 (30.7)
Trimester	
First	88 (20.9)
Second	107 (25.5)
Third	225 (53.6)

Table 2. Trimester-wise distribution of prescribed classes of drugs among pregnant inpatients

Name of Drugs	FDA Category	Frequency of prescription, n (%) trimesters			Total, n %)
		First	Second	Third	
Anti-Anemic/Vitamin and Mineral Supplements					
Ferrous Fumarate	A				
Iron/Folic Acid	A	90 (32.25)	110 (32.83)	88 (26.10)	288 (30.30)
Vitamin B Complex	A				
Multivitamin	A				
Calcium	C				
Antibiotic					
Cefixime	B				
Ceftriaxone	B				
Cefotaxime	B				
Amoxicillin+ Clavulanic Acid	B	45 (16.20)	56 (16.71)	41 (12.16)	142 (14.93)
Ampicillin	B				
Ciprofloxacin	C				
Metronidazole	B				
Azithromycin	B				
Anti-Fungal					
Clotrimazole	B	6 (2.15)	5 (1.49)	4 (1.18)	15 (1.57)
Analgesics					
Paracetamol	B	14 (5.01)	16 (4.70)	20 (5.93)	50 (5.25)
NSAID		8 (2.85)	12 (3.90)	9 (2.67)	29 (3.04)

Diclofenac	C/D				
Aspirin	D				
Anti-Hypertensive					
Methyldopa	B				
Nifedipine	C	28 (10.03)	45 (13.43)	54 (16.02)	127 (13.35)
Amlodipine	C				
Labetalol	C				
Antacid					
Esomeprazole	B				
Ranitidine	B	19 (6.81)	27 (8.05)	98 (11.27)	84 (8.85)
Cimetidine	B				
Anti-Diabetics					
Insulin	B	19 (6.81)	24 (7.20)	35 (10.38)	78 (8.20)
Metformin	C				
AntiEmetics					
Ondansetron	B				
Metoclopramide	B	31 (11.11)	15 (4.50)	8 (2.37)	54 (5.67)
Chlorpromazine	C				
Anti-Asthmatic					
Albuterol	C				
Budesonide	B(inhalation)	9 (3.22)	13 (3.80)	17 (5.04)	39 (4.10)
Beclometasone	C				
Thyroid Product					
Levothyroxine	A	10 (3.90)	12 (3.58)	15 (4.43)	37 (3.90)
Prostaglandin					
Misoprostol	X	-	-	8 (2.37)	8 (0.84)
Total		279(29.33)	335 (35.22)	337(35.43)	**951 (100)**

Table 3. WHO core prescribing indicators

Prescribing Indicator	Value Obtained	Reference Value
Average number of prescribed drugs per encounter	2.3 ± 0.9*	1.6-1.8
Percentage of drugs prescribed by generic name	92.8%	100%
Percentage of encounter with injection prescribed	9.9%	13.4-24%
Percentage of encounter with antibiotics prescribed	13.1%	20-26.8%
Percentage of drugs Prescribed from essential drug list	96.7%	100%

The value is mean ± SD.

Table 4. US FDA pregnancy categorization of prescribed drugs among pregnant inpatients

FDA category	1st trimester n (%)	2nd trimester n (%)	3rd trimester n (%)	Total
A	98 (35.12)	117 (34.92)	97(28.80)	312 (32.90)
B	125 (44.80)	146 (43.58)	169 (50.10)	440 (46.26)
C	48 (17.20)	60 (17.90)	54 (16.10)	162 (17.03)
C/D	5 (1.80)	8 (2.40)	6 (1.78)	19 (1.99)
D	3 (0.89)	4 (1.20)	3 (0.89)	10 (1.05)
X	-	-	8 (2.40)	8 (0.84)
Total	279 (100)	335 (100)	337 (100)	951 (100)

Table No.5: Route of administration of prescribed drugs among pregnant inpatients

Route of administration	1st trimester n (%)	2nd trimester n (%)	3rd trimester n (%)	Total n (%)
PO	279 (89.25)	290 (86.56)	291 (86.35)	830 (87.38)
IM	4 (1.43)	9 (2.70)	10 (2.96)	23 (2.41)
IV	18 (6.45)	29 (8.65)	25 (7.45)	72 (7.57)
Vaginal	6 (2.15)	5 (1.50)	4 (1.18)	15 (1.57)
Inhalation	2 (0.71)	2 (0.59)	7 (2.07)	11 (1.15)
Total	279 (100)	335 (100)	337 (100)	951 (100)

5. DISCUSSION

This study was conducted to provide an overview of prescription patterns of drugs prescribed for pregnant women admitted in OBG ward of a tertiary care hospital in Bangalore. As shown in table No.2, of a total of 951 prescribed drugs, anti- anemic/vitamin and mineral supplements, antibiotic and antihypertensive drugs were the most frequently prescribed classes of drugs. It was consistent with findings of other studies conducted in India and Swaziland that pregnancy supplements and antimicrobials were the major two prescribed classes of drugs.[12-14] In the current study, more than half (65.08%) of usage of pregnancy supplements and vitamins were observed in first and second trimesters. Iron, folic acid and vitamin B complex were the most frequently prescribed drugs of pregnancy supplement class. Consumption of folic acid and multivitamin supplements are essential during pregnancy as they can prevent or reduce the risk of most of the neural tube defects and other congenital abnormalities including urinary tract abnormalities (mostly obstructive defects) and cardiovascular malformations including ventricular septal defects.[15-17]Similarly, in the study of J. Z. Al-Hamimi et al, folic acid was the most prescribed drug in the first trimester.[18] Findings of the present study showed that ceftriaxone and metronidazole were commonly prescribed antibiotics that both fall under category B pregnancy which are relatively safe options for mother and baby. However, amoxicillin was the most commonly used antimicrobial (for treatment of respiratory tract infection) in another study conducted in Ahmedabad.[19] Clotrimazole was the only antifungal prescribed drug (1.57%) and it was given as a vaginal tablet for vaginal fungal infection. Paracetamol was the highly prescribed analgesic to manage abdominal and body pain. It was consistent with findings of Abubakar K et al.[20] Paracetamol is one of the widely used drugs during pregnancy. However, some animal studies have shown reduced production of testosterone and increased risk of cryptorchidism in male babies after prolonged use of analgesics including paracetamol during pregnancy.[21]Another study also showed reduced plasma testosterone and reduced seminal vesicle weight following 7 days of exposure to acetaminophen by using a xenograft model to expose human fetal testes to paracetamol dosage regimen.[22]Hence, while routine prescription of paracetamol being considered as a safe drug, second thought of its potential adverse effects should be brought into notice of clinicians. Awareness regarding its side effects should be given to pregnant women as well in order to encourage them to take paracetamol only if it is actually required. As it is widely available over the counter (OTC) drugs. Ondansetron and ranitidine were highly prescribed anti-emetic and antacid in the present study. Antiemetics were mostly prescribed in the first trimester (11.11%) to control hyperemesis gravidarum. Metoclopramide and ranitidine and promethazine were highly prescribed gastrointestinal drugs in other studies.[13,20] Though ondansetron belonged to category B pregnancy, but a recent case-control study showed 2-fold increased risk of cleft palate linked with ondansetron in the first trimester of pregnancy.[23] Moreover, FDA has issued a warning in September 2011 regarding possible serious QT prolongation and torsade de pointes in people administered with ondansetron.[24] Hence, it is recommended that ondansetron to be used with caution during pregnancy. Most antihypertensive drugs were prescribed during the third trimester (16.02%). The most prevalent prescribed antihypertensive agents were methyldopa and nifedipine. Likewise, methyldopa, labetalol, nifedipine, amlodipine and atenolol were drugs of choice for pre-eclampsia in the study of Kumarjit S et al.[14] Gestational diabetes was managed by prescribing insulin and metformin accounted for 8.2% of prescriptions. However, metformin prescription prevalence was higher than insulin. Albuterol was the most commonly prescribed anti-asthmatic drug that belonged to category C. Budesonide was prescribed in inhalation form that fell under B category. Metformin, levothyroxine, salbutamol and methyl dopa were continued during the hospitalization period for pregnant women who were having chronic disease before admission to hospital. Comparison of frequency of prescription of drugs in different trimesters showed similar prevalence of drug prescription over third (35.43%) and second trimester (35.22%). Whereas frequency of prescription of drugs were slightly lesser in the first trimester (29.33%). Lesser frequency of drug prescription in the first trimester was expected, as the first trimester is a critical stage of pregnancy in which major fetus organs are developing and exposure to drugs in this period should be minimized to avoid malformations and birth defects. With respect to the FDA pregnancy category of drugs prescribed during all trimesters, frequency of prescription of category A and B drugs was the highest in the first trimester (35.12%) and third trimester (50.1%) respectively. Whereas, results of study conducted in Puducherry showed that 3.6% of third trimester women were prescribed with category B drugs.[25] In the current study, category D drugs were prescribed in 1.05% of pregnant women whereas higher prevalence of prescription (9.3%) of category D drugs was reported in other study in Ethiopia.[26] Results of the current study showed that diclofenac belonged to category D and C in 1.78% and 4.2% of cases respectively. As per FDA guidelines use of diclofenac is not recommended during the last trimester of pregnancy (category D) and it can be used prior to 30 weeks of gestation when potential benefits justify the potential risks to the fetus (category C). In study of Gadisha DA, 3.27% of prescribed drugs belonged to category D including diclofenac, diazepam, ibuprofen, etc.[27] As per FDA pregnancy category, aspirin falls under category D if full dose is taken in the third trimester. However, in the current study, aspirin was prescribed in few cases with pre-eclampsia and/or history of miscarriage which is justifiable. Frequency of prescription of aspirin was relatively low due to its potential risk of maternal and fetal bleeding.[28] It was in line with findings of Amu AA et al.[13] In general, most prescribed drugs belonged to category A and B pregnancy which is appreciable and rational. As it could minimize the risks pertaining to maternal and fetal health. It was similar to findings of other two studies conducted in India.[14,29] Whereas in study of Farooq MO et al, most of prescribed drugs belonged to category C and D.[12] Misoprostol was the only prescribed drug of category X in the present study. It was prescribed only in 8 cases (2.37%) in the third trimester to induce labor which probably outweighed the risk. It was in consistent with findings of other studies carried out in Pakistan and US in which 0.8% and 1.1% of pregnant women were prescribed with teratogenic drugs respectively.[30,31] Whereas, higher prevalence (5.71%) of prescription of category X drugs during first trimester was reported in other study conducted in north India.[1] In other study conducted in Ethiopia, misoprostol (category X) was prescribed in first trimester to terminate pregnancy.[26] The average number of drugs prescribed per encounter was found to be 2.3 ± 0.9 (SD) which was slightly higher than the recommended range

of WHO. Our finding was similar to findings of other studies conducted in Nigeria and Oman.[18,32]Whereas, a study carried out in Saudi Arabia showed an average of 4.17 drugs per prescription.[33]As per WHO core prescribing indicator analysis, majority of drugs (92.8%) were prescribed by generic name which is appreciable and indicates the rational prescribing practice. Whereas Uchenna I. Eze et al found that most of drugs were prescribed by brand names in their setting.[32] In total, 9.9% and 13.1% of encounters were prescribed with injection dosage form and antibiotics respectively which are lesser than reference values recommended by WHO which is actually encouraging. High frequency of administration of drugs in injection dosage form may cause high plasma concentration of drugs leading to increased chance of drug toxicity.[34] Similar findings were reported by Gadisa DA et al.[27] In contrast to our findings, higher percentage of encounters prescribed with antibiotics and injections were reported in study of Abubakar K et al.[20] Findings of the present study also showed that the majority of drugs (96.7%) were prescribed from essential drug lists which suggests rational prescription of drugs from essential drug lists. It was higher than findings of Patel KP et al (80.79%).[19] Hence, it can be said that the overall prescription pattern of drugs in this study was found to be rational.

6. CONCLUSION

This study provided an overview of the current prescription pattern of drugs for hospitalized pregnant women in a tertiary care hospital of south India. Most drugs were prescribed from category A and B which reflects safe and rational practice of drugs in this setting. Prescription of high-risk drugs was low but not absent. Relatively low prevalence of prescription of high risks drugs showed that practice of medicines was compatible with FDA recommendations. However, interaction of clinical pharmacists with clinicians, continuous monitoring of drug utilization in this population and providing updated information of high-risk drugs to practitioners may further improve the safety of pregnant women and fetus.

7. ACKNOWLEDGEMENT

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8. AUTHORS CONTRIBUTION STATEMENT

Dr. Hedieh Vafaeerokh gathered and analysed the data with regard to this work and wrote the manuscript. Dr. Mohammed Kazim Sheriff conceptualized and supervised the study and contributed to the final manuscript.

9. CONFLICT OF INTEREST

Conflict of interest declared none.

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