

# Evaluation of Medicine Exposure During Pregnancy at a Tertiary Center of an Indian State

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## ABSTRACT

**Context:** Prescribing drugs in pregnancy is a challenging approach for doctors.

**Objective:** To evaluate drugs used in pregnancy.

**Method:** A prospective, cross-sectional, descriptive study was carried out by collecting and evaluating prescriptions on various parameters.

**Results:** More than 50% of antenatal care attendees belonged to the 18-24 age group, and 102 (41.46%) were primigravidae. The main presenting complaints were abdominal pain (25.16%), followed by nausea and vomiting (22.60%) and fever (11.14%); the maximum number of visits to hospital was seen in the first trimester (40.53%), followed by the third trimester (38.42%). It was observed that 25.78% of prescriptions did not contain any medicine. The average number of prescribed medicines was 2.32, with the lowest in the first trimester (1.77) and the highest in the second trimester (2.78). It was noticed that 74.11% and 71.26% of all prescribed medicines were from essential medicine list and generics, respectively. Of all prescribed drugs, 11.52% were antimicrobials, and 4.11% injectable dosage forms. Vitamins and minerals were the preferred prescribed medicines (34.82%), followed by antimicrobial agents (11.52%) and doxylamine plus pyridoxine (10.16%). Also, doctors who made the drug choice during antenatal visits were more confident in evidence-based safety as per New Pregnancy and Lactation Rule (PPLR); 45.37% of drugs were prescribed from category A, followed by 38.25% from category B and none from group X.

**Conclusion:** Doctors were concerned about prescribing safer drugs in pregnancy and were more confident in evidence-based medication.

**Keywords:** antenatal, pregnancy, prescription, medicine, generic.

## INTRODUCTION

Rational use of drugs has multi-dimensional aspects and is very important for the developing countries that lack a proper drug monitoring system, especially in pregnancy. Monitoring of drug

safety is crucial, given that pregnancy is associated with progressive and gradual anatomical and physiological changes, which are confined not only to the genital organs but also involve other systems of a woman's body. Physiological changes start after conception and affect almost every organ system (1). Drug exposure in pregnancy is

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an increasingly growing phenomenon due to an ascendant trend of chronic illnesses in mothers. In pregnancy, prescriber must take care of two lives, those of the mother and fetus, because placental barrier is incomplete, allowing lipid-soluble and lipid-insoluble drugs to cross it; also, drug transfer is more intense in the third trimester due to an increased maternal and placental blood flow, decreased thickness and increased surface area of the placenta (2). It is not possible to eliminate drug use during pregnancy because diseases must be treated in pregnancy too. An appropriate fetal growth and development is possible only if the mother is healthy. Prescribing the best possible medication to mothers poses challenges for doctors. Around 8% of pregnant women need permanent drug treatment due to pregnancy-induced complications and various chronic diseases (3). The prescriber must always focus on the safety profile of drugs to maximize the beneficial effect on both mother and fetus. A rational drug use during pregnancy promotes good maternal and fetal health. A study found that more than 90% of pregnant women take prescription or non-prescription (over-the-counter) drugs, or use social drugs such as tobacco or alcohol or illicit drugs at some time during pregnancy (4). A regular prescription audit and health education of mothers allows checking for drug misuse and retaining doctors from prescribing expensive drugs.

The aim of the present study was to explore the use of both prescription and non-prescription drugs during pregnancy, as an online search on PubMed, Science Direct, Google, and different specialized journals, conducted in Rajasthan, India, showed that there were very few studies published on this topic. The result of our study can help not only minimize the risk of irrational drug use in pregnancy by evaluating the drug profile, but also ensure a constructive feedback to all stakeholders. □

## MATERIAL AND METHOD

A prospective, cross-sectional, descriptive study was carried out by collecting and evaluating prescriptions from diagnosis of pregnancy to at term pregnancy (just before delivery) in a tertiary centre of Rajasthan, India. A prescription audit was done to find out if pregnant women took any prescribed or non-prescribed drugs.

## Sample size

Sample size was calculated by using single proportion formula, with a proportion of drug use during pregnancy of 90% (4), a margin of error of 5% and a confidence level of 99%. If 5% of women have a chance to become pregnant among 12 lakh female population of Jhalawar district, the population size would be 60 000. We also considered that 10% of subjects would drop out during follow up and added 5% more subjects to counter methodological contingency. The final estimated sample size was 274.

## Ethical permission

The study was conducted after obtaining permission from the institutional review board. Data was calculated regularly, as one of the authors – who was an active member of the prescription audit constituted by the Dean of Medical College to promote a rational drug use – requested from the competent authority permission to use data for research purposes. All data were kept confidential.

## Methodology

Pregnant women were coming for antenatal checkup at Jhalawar Medical College associated hospital and their prescriptions were included in the study. They were followed up during the nine months of pregnancy, Diagnosis of pregnancy was confirmed by clinical examination, history, pregnancy test or ultrasonography. History of drugs taken by pregnant women up to the due date of pregnancy and their prescriptions audit were performed and data were analyzed on per-forma given in Annexes 1 and II. For collection of data about drug intake by pregnant women, follow up was made at least once a month throughout the entire pregnancy either after each patient's visit at the obstetrics and gynecology department or during investigators' home visits or telephone contact with their subjects. Thus, detailed data were collected and evaluated in order to: (a) study the pattern of drug prescribing by obstetricians or clinicians – the average number of medicines *per* prescription were calculated by dividing the total number of drugs by the number of prescriptions; percentage prescriptions for generics, antimicrobial agents and products from the essential medicine list were

studied; (b) assess the rational use of prescribed drugs based on “WHO guideline for good prescribing: a practical manual” and Rajasthan state standard treatment guidelines (RSSTGs); (c) see whether any teratogenic drugs were prescribed, using US Food and Drug Administration classification of medicines associated with fetal risk based on information provided in the physician’s drug handbook and New Pregnancy and Lactation Labeling Rule (PLLR); (d) see whether there was an intake of unprescribed drugs – a brief history was taken to look for self-medication, over the counter drugs, homeopathic products, herbal drugs and tobacco use during pregnancy.

**Inclusion and exclusion criteria**

All subjects who agreed to participate in the study, came to our hospital for antenatal care visit at the beginning of the first trimester of preg-

nancy and adhered to follow up to at term (just before delivery) were included in our research. Women suffering from chronic diseases (e.g., diabetes, hypertension) before getting pregnant, those who either did not participate in the study for the whole period or faced problems during follow up such as miscarriage or abortion were excluded from the study.

**Data collection and statistical analysis**

Data were registered in the case record form and analyzed using statistical package for social sciences (SPSS 16.0) and Microsoft excel. Descriptive statistics was used according to study objective. □

**RESULTS**

A total of 274 patients have been initially included in the study, but only 246 remained

Demographic profile (parameter)	Total number of pregnant women (N%)
Age (years)	
18 to 24	124 (50.40)
25-31	88 (35.77)
32-38	27 ((10.98)
39-45	7 (2.85)
>45	Nil
<b>Education status</b>	
Primary (V <sup>th</sup> class)	82(33.33)
Secondary (VI -X class)	61(24.80)
Senior secondary (XI -XII)	64(26.02)
Graduate	18 (7.32)
Post graduate	4 (1.6)
Illiterate	17 (6.9)
<b>Monthly family income (Rupees)</b>	
< 12000	76 (30.89)
12001 -25000	93 (37.80)
> 25000	77 (31.30)
<b>Gravida</b>	
Primigravidae	102 (41.46)
Secudigravidae	98 (39.84)
Multigravidae	46 (18.70)

**TABLE 1.** Demographic profile of antenatal care attendees

Reason for visit to the hospital	First trimester	Second trimester	Third trimester	Total no. (%)
Nausea and vomiting	198	4	1	203 (22.60)
Pain in abdomen	64	74	88	226 (25.16)
Fever	18	44	38	100 (11.13)
Burning micturation	8	24	38	70 (7.79)
Sore throat	8	24	30	62 (6.90)
Edema	0	6	33	39 (4.34)
Diarrhoea	4	16	17	37 (4.12)
Weakness	24	3	7	34 (3.79)
Itching	0	4	18	22 (2.45)
Bleeding	8	9	5	22 (2.45)
Blood pressure	0	0	12	12 (1.33)
Insomnia	0	4	7	11 (1.22)
Headache	3	5	2	10 (1.11)
Toothache	2	3	5	10 (1.11)
Pain in ear	2	5	2	9 (1.00)
Seizure	1	1	1	3 (.33)
Others	10	7	11	28 (3.11)
	350	233	315	898

TABLE 2. Reason for visiting antinatal care (ANC)

after follow up. Our research considered drug prescription and brief history of 246 patients. To eliminate bias, clinicians were kept unaware about the study.

Eight hundred ninety-eight prescriptions for 246 pregnant women were audited during their complete period of pregnancy in the entire study. Out of the 898 prescriptions, only 667 contained drugs, and these were considered for analysis in our study. It was observed that the total number of drugs indicated by the 667 prescriptions was 1 545.

Table 1 shows the demographic profile of antenatal care attendees. Of all subjects, 50.40% were aged 18-24, 102 (41.46%) were primigravida, 98 (39.84%) secundigravida and 46 (18.70%) multigravida. Also, 33.33% of subjects had primary education and 37.80% had a family income ranging from 12001 to 25001 Indian rupees.

Table 2 shows the pregnant women’s reasons for visiting OPD. Abdominal pain was the most frequently encountered presenting complain

(25.16%), followed by nausea and vomiting (22.60%), and fever (11.14%), whereas seizure was observed in only one attendee. The major complaint was nausea and vomiting in the first trimester, and abdominal pain in both the second and third trimesters.

Table 3 shows the prescribing pattern of medicines to pregnant women during their visit to hospital. The maximum number of visits was seen in the first trimester (40.53%), as subjects were selected in their first trimester of pregnancy and followed up to the third trimester (38.42%). Also, 25.78% of prescriptions did not contain any medicine. The average number of prescribed medicines was 2.32, with the fewest drugs being prescribed in the first trimester (1.77) and most of them in the second trimester (2.78). It was noticed that 74.11% and 71.26% of all medicines were chosen from the essential medicine list and generics, respectively. Antimicrobials accounted for 11.52% of all prescribed drugs, and injectable dosage forms for 4.11%.

TABLE 3. Prescribing pattern and frequency of visits to hospital

Prescribing pattern for pregnant women during visits to hospital	First trimester	Second trimester	Third trimester	Total
No. of visits to hospital	364 (40.53%)	189 (21.04%)	345 (38.42%)	898
No. of drug prescriptions	264 (39.58%)	73 (10.94%)	340 (50.97%)	667
Average number of medicines per visit	1.77 (645)	2.78 (527)	1.98 (373)	2.32 (1545)
Percentage of prescribed medicines from essential medicine list	78.45 (506)	80.45 (424)	57.64 (215)	74.11 (1145)
Percentage of prescribed medicines by generic name	62.48 (403)	79.32 (418)	75.06 (280)	71.26 (1101)
Percentage of prescribed antimicrobials	5.81 (36)	11.76 (62)	21.45 (80)	11.52 (178)
Percentage of prescribed injectable medicines	20 (3.10)	1.89 (8)	11.80 (44)	72 (4.66)

Table 4 shows different drugs or drug groups prescribed during pregnancy. Vitamins and mineral were the preferred prescribed medicines (34.82%), followed by antimicrobials (11.52%) and doxylamine plus pyridoxine (10.16%). Paracetamol was preferred among analgesics and antipyretics, while sodium valproate and insulin were prescribed to a single patient.

Table 5 shows the various categories of drugs which were included based on US Food and Drug Administration (FDA) before 2014 and New Pregnancy Lactation Rule, and a separate group “N”, in which calamine lotion ORS and urine agents were kept. It was found that 45.37% of all drugs were prescribed from A category, followed by B category (38.25%), while no drug was prescribed from X group,

Table 6 shows which drugs and remedies were taken by women during antenatal period without any prescription from their doctors. There was no history of alcohol tobacco or other illicit drug consumption.

**Rationality of drug used in pregnancy**

It was observed that the majority of prescriptions had followed standard treatment guidelines and almost all pregnancies were unplanned, except three postgraduate and five undergraduate women. □

**DISCUSSION**

Our study differs from other previously published studies that collected all prescriptions either prospectively or retrospectively, because we have enrolled subjects immediately after diagnosing pregnancy at baseline and full follow up was done just before delivery.

The mean maternal age was 26.79 years in our study, 25.16 year in a Nigerian report (5) and 25 years in a Nepal one (6). A study from Ethiopia (7) observed that 54.5% of subjects were aged 18 to 24, as compared to 50.4% in our study, and 41.46% of subjects were primigravidae as compared to 35.5% in studies of Nigeria (5) and India (8), and less than 44% in a study of Kerala (a Southern state of India) (9).

The presenting complains, partially similar to those reported in the Nepal study (6), included gastrointestinal problems (nausea and vomiting, dyspepsia) and vaginal spotting/bleeding, which was comparable to our study (59.09% cases of nausea and vomiting, abdominal pain and fever). The maximum number of pregnant women’s hospital visits were in the last trimester, according to a Sokoto study (41.9%) (10) and other studies, while our subjects made more visits in the first trimester (40.53%), when they were enrolled, and less visits in subsequent trimesters

TABLE 4. Drug prescribed during pregnancy

Drug or group of prescribed drugs	First trimester	Second trimester	Third trimester	Total number of prescribed drugs	Percentage of drugs in different groups
Vitamins, minerals (other than Iron)	246	246	46	538	34.82
Antimicrobials	36	62	80	178	11.52
Doxylamine + pyridoxine	145	12	0	157	10.16
Paracetamol	38	39	38	115	7.44
Drug for cough	43	20	12	75	4.85
Antihistaminics	20	16	19	55	3.56
Urine alkalinising agents	4	6	38	48	3.11
Drug for peptic acid disorder	24	15	8	47	3.04
NSAIDs	10	24	11	45	2.91
Anthelmintic	18	20	0	38	2.46
Oral rehydration powder	4	16	17	37	2.39
Uterine relaxants	0	0	36	36	2.33
Antiemetics	14	8	8	30	1.94
Antispasmodics	6	8	12	26	1.68
Antimalarial drugs	8	12	3	23	1.49
Progesterone	9	10	6	25	1.62
Calamine lotion	0	0	18	18	1.17
Laxative	12	4	1	17	1.10
Labetalol	0	0	10	10	0.65
Antifungals	6	4	0	10	0.65
Hypnotics and sedatives	0	3	4	7	0.45
Thyroxin	2	2	2	6	0.39
Methyldopa	0	0	2	2	0.13
Insulin	0	0	1	1	0.06
Valproate	0	0	1	1	0.06
	645	527	373	1545	100

(38.42% in the third trimester), as follow up was done during the entire pregnancy.

The average number of drugs *per* prescription was 2.32, which is slightly above (1.6 to 1.8) the

WHO standard (11). We had excluded prescriptions that did not recommend drugs in order to calculate the average number of drugs *per* prescription. In our study, the number of prescribed

**TABLE 5.** Pregnancy categories as per Food Drug Administration (FDA), non-FDA and PPLR

Pregnancy categories prior to new pregnancy and lactation rule (PPLR) (between 1979 and 2014)			PPLR in December 2014 effective in June 30, 2015
No risk to the fetus	A	544 (45.37)	Drug approved before June 30, 2001 would not be treated as pregnancy category or readily available to provider. They include both older medications and over the counter medicines
Animal reproduction studies showing adverse effect but not in pregnancy	B	591 (38.25)	
No animal reproduction studies and no well controlled studies in humans	C	117 (7.57)	
Positive evidence of fetal risk	D	33 (2.14)	
Positive evidence of fetal risk	X	0	
Not classified under FDA category (ORS, calamine lotion and urinary alkalisers)	N	103 (6.67)	

**TABLE 6.** Unprescribed drugs and remedies taken by pregnant women

Unprescribed and alternative medicine	Drug/remedy used during pregnancy
Over the counter drug	12
Homeopathic drug	36
Ayurvedic drug	9
Home remedy (certain problems)	45
Total	102

drugs was less than that reported by other studies such as Eze Ul *et al.* (5), Das *et al.* (6), and Krause *et al.* (12). There were 0 to 4 drugs per prescription, which was far better than the study of Eze Ul *et al.* (up to 10 drugs per prescription) (5). Polypharmacy not only increases the cost of prescriptions, but also decreases patient compliance. It also augments the chances of adverse events and drug-drug interactions. Most of the medicines were prescribed from generics (71.26%) and essentials medicine list (74.11%), maybe due to government guidelines to prescribe drugs by their generic name and from essential list of medicines. The government has established free drug distribution centres and jan aushdhi pharmacy shops to ensure availability of generic drugs. Problems related to availability of generic medicines, given the high demand at the level of drug distribution centres, forced doctors to prescribe drugs by their brand name. More than

70% of generic and essential medicine prescriptions show a clear trend towards rational prescription. There were only few prescriptions of injectable forms (4.66%), which was below the WHO reference value of 13.4 to 24.1; this is very encouraging, although we had not counted tetanus toxoid immunization, which were mandatory during antenatal visits. Antimicrobial agents accounted for 11.52% of all prescribed drugs, which was lower than WHO guideline and less than reported by the study conducted in Kerala (13).

The FDA classification of teratogenic drugs using a five-letter system according to fetal risk was valid till implementation of the Pregnancy and Lactation Labelling Rule (PLLR). In the present study, 701 (45.37%) of all prescribed medicines were in category A, 38.25% in category B, 117 (7.57%) in category C, 33 (2.4%) in category D, and 6.67% pertained to none of

the established categories, whereas another study, conducted by Uchenna I. Eze *et al.*, had shown that 48.1% of all prescribed drugs were in category A, 25.7% in category B, 17.2% in category C, and 5.0% in category D (5). The pattern of prescribing was similar to that of the present study, with a variation in percentage, but differed sharply from that of an Ethiopian study, in which 84.88% of drugs were prescribed from category A and 8.75% from category B. The maximum drugs were from category A, which included the safest products. In all three studies mentioned above there were no drugs prescribed from category X, which contains the most harmful medicines. This is explained by the fact that doctors were taking precautions regarding well established harmful drugs. The reason for prescribing drugs from B, C and D categories can be understood by the statement of Sandra Kwede, Deputy Director of the Office of New Drugs in the FDA Centre for Drug Evaluation and Research: "Prescribing decision during pregnancy and lactation are individualized and involve complex maternal, foetal, and infant risk-benefit considerations. The latter category system was overly simplistic and was misinterpreted as a grading system, which gave an oversimplified view of the product risk." (14).

We observed that only valproate, progesterone and alprazolam or diazepam were prescribed from D category. Valproate was used to control seizures in one pregnant woman, as no other drugs were helpful at that time. Progesterone and its analogue had also favourable foetal outcome in patients with vaginal bleeding, abdominal pain and risk of abortion (15, 16).

Albandazole was included in category C, but WHO suggested that using single-dose albendazole (400 mg) or mebendazole (500 mg) was recommended as a public health intervention for pregnant women after the first trimester, with several other drug being also prescribed from categories B and C for patients' benefit. Numerous medicines that belong to categories B and C are used safely and effectively in pregnancy, with minimal risk to the foetus and mother, which is also reflected by our findings.

The new rule has also several potential limitations. Older medications and over-the-counter products approved prior to June 30, 2001 will have neither a pregnancy category nor a narrative summary readily available to providers. The

requirement of close collaboration between FDA and manufacturers to ensure timely updates may also be problematic (18). It was observed that doctors who selected drugs during antenatal visits were more confident in evidence-based safety of chosen medicines as *per* PPLR. No drugs were prescribed from category X. The majority of pregnancies were unplanned.

We have also seen that only 12 subjects took over the counter drugs, while most of pregnant women were trying home remedies for certain condition such as sore throat, loose motion, dyspepsia, etc. No illicit or illegal drugs were used by our subjects, while the literature reported that 3.6 and 8.8% of pregnant women were taking illicit substances and 19.6% were consuming alcohol (20). Thus, our findings show an encouraging situation, most probable due to family and cultural values of our country.

### Study limitations

Our study was based only on information from prescriptions and brief interviews of patients. The older classification of FDA has been also used. □

### CONCLUSION

The present study reflected that drugs were prescribed in all three trimesters, with the maximum number of medicines being recommended in the first trimester. Average number of drugs *per* prescription were as *per* WHO limit. Gastrointestinal discomfort and fever were important presenting complaints. Doctors took care to prescribe safer drugs and the choice of medicines during antenatal visits showed they were more confident in evidence-based medication as *per* PPLR. Drugs in categories C and D have been also prescribed in certain diseases, where benefits could outweigh risks. There were no prescriptions of drugs from category X. The majority of pregnancies were unplanned. Education and counselling of women of childbearing age regarding planned pregnancy and drug intake would be beneficial. □

*Conflicts of interest and financial support: The present research was conducted while the author was working as associate professor at Jhalawar Medical College, Jhalawar, Rajasthan.*

**ANNEX 1. Case record form**  
**Analysis of drug use during pregnancy at a tertiary center of Rajasthan**

**Consent form**

The investigator has explained the purpose of the study. I have no objection regarding copies or photographs of the prescription and taking history on mentioned performa.

Patient signature

**Information collected by investigator through taking patient history and analysis of prescription**

Name ..... Age..... Gravida ..... Income per capita .....

Level of education..... Occupation .....

Reason for visit:

Time of the first antenatal visit ..... Duration of the present pregnancy .....

Total number of antenatal visits ..... Hb..... %

Treatment of any chronic condition.....

Non prescribing drugs

(a) Self-medication ..... (b) Over the counter drugs ..... (c) Herbal medicines.....

(b) Any other things not related to treatment (eg, tobacco, Bidi, etc)

Immunization with TT .....

Drugs use in pregnancy dangerous in (trimester) 1<sup>st</sup> ..... 2<sup>nd</sup> ..... 3<sup>rd</sup> ...

Drug use in pregnancy dangerous to mother ..... Fetus ..... Both.....

Planned or unplanned pregnancy .....

Type of contraceptive use.....

**ANNEX 2. Prescribing indicator form**

Location .....

Investigator .....

S. No.	Date	Age (years)	Drugs from EDL	Generic	Antimicrobial agent 0/1	Injection 0/1	Total drugs	Diagnosis/ presenting complain
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								

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