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DRUG PRESCRIBING PATTERNS DURING ANTENATAL CARE IN A TERTIARY CARE RURAL TEACHING HOSPITAL: A CROSS-SECTIONAL STUDY

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ABSTRACT: Context: Drug treatment during pregnancy presents a special concern. All drugs should not be avoided. A better knowledge of parameters that determine teratogenicity may allow the physicians gain confidence. **Aims:** This study was conducted to understand the drug utilization practices during pregnancy in women from rural areas and poor socioeconomic background; classify them according to US-FDA category for determining the teratogenic potential; to provide feedback and recommendations to the health care providers. **Settings and Design:** This was a retrospective cross-sectional study carried out at rural tertiary hospital. **Methods and Material:** Case record forms of 300 patients admitted to the obstetrics ward from September to November 2009 were analyzed for demographic details, drug prescriptions and drug utilization patterns. The teratogenic potential of drugs was analyzed according to US-FDA risk categories for drugs and medication. Statistical analysis used: Statistical software SPSS was used for analysis. **Results:** Maximum prescriptions happened in the second trimester of pregnancy. Vitamins, mineral and nutritional supplements were prescribed in almost 100% cases. The patients receiving more than 3 drugs had co-morbidity. Though 100% cases had frequency of medications written, dose and duration was written in less than 50%. Fixed Dose Combination commonly prescribed was iron & folic acid supplement. Drugs from Category A-D were prescribed depending on the clinical condition of the patients. Antibacterials and antacids were the most commonly prescribed (25%) followed by antihistaminics (17%) and antiallergics (11%). **Conclusions:** Careful prescription behaviour to the pregnant women under antenatal care visiting a tertiary care rural hospital was noted.

INTRODUCTION: Drug treatment during pregnancy presents a special concern.

The major reasons being, physiologic adjustments in the mother and the threat of potential teratogenic effects of the drugs.[1] However, the recommendation to avoid all drugs during early pregnancy is unrealistic and may be dangerous. [2, 3] Prescribing drugs in pregnancy is an unusual risk-benefit situation. Rational drug prescribing practices, reducing medication errors, and improving patient safety are the important areas as

in addition to the mother, the health and life of her unborn child is also equally important.[4] It is felt that a better knowledge of the parameters that determine teratogenicity may allow the physicians to feel more confident in assessing the risks and benefits associated with drug prescribing in pregnancy.[5] Experts in different countries have set up risk classification systems based on data from human and animal studies to help physicians interpret the risk associated with drugs administered during pregnancy. The most well known classification was introduced by the US Food and Drug Administration (FDA) in 1979, using the letters A, B, C, D and X for five categories.[6]

US-FDA Risk categories for drugs and medications

Category A	Adequate clinical studies have shown no risk to fetus in any trimester
Category B	Animal studies have not shown adverse effect on the fetus and there are inadequate clinical studies
Category C	Animal studies have shown adverse effects, no adequate clinical studies. May be useful in pregnancy despite potential risks
Category D	There is evidence of risk to human fetus, but potential benefits may be acceptable despite potential risks (e.g. in a life-threatening situation).
Category X	Animal/human studies show foetal abnormalities. Risks involved clearly outweigh benefits. Contraindicated in women who are or may be pregnant

In common practice, drugs do get prescribed during pregnancy, more so if mother is suffering from has a medical condition but there can be situations when the prescribing physician may not be sure of the teratogenic potential of the medicine.

It is usually from the first trimester that a pregnant woman starts visiting the doctor and drug prescriptions can happen. In a country like ours, there can be a vast difference in the prescription patterns in cities and rural areas. e.g. doctors practising in tertiary care rural set up have to cater to hundreds of women visiting for antenatal check up, who could be semi-literate or illiterate and may not understand the significance of prescribed medications. Poverty, disparities in access to health-care, and not so developed drug distribution networks, may create additional issues for rural communities.[7] Since there exist numerous gaps in

knowledge about deleterious consequences for the fetus, prescription drug use by pregnant women should be viewed as a public health issue.[8] Drug utilization studies can help in minimizing the inherent risk of drug use in pregnancy, by establishing a profile of the safety and efficacy of drug consumption.[9] With this background, the following study was conducted to understand the patterns of drug utilization during pregnancy in women from rural areas and poor socioeconomic background.

Objectives
This study was conducted to understand the drug utilization practices (prescribing trends and pharmacological class wise drug consumption) in antenatal practice in the rural tertiary health care set up; to classify drugs prescribed during antenatal care according to the US-FDA category for determining the teratogenic potential; and to provide feedback and recommendations for the health care providers with this information

MATERIALS AND METHODS:
This was a retrospective cross-sectional study carried out at Acharya Vinoba Bhave Rural Hospital, Wardha, Maharashtra. Case record forms of 300 patients admitted to the obstetrics ward from September 2009 to November 2009 were analyzed. 100 patients each from the first, second and third trimester compromised this sample size of 300. The study was approved by the Ethics Committee of the hospital.

The data collected included the demographic details of the patients (age, address, occupation); socioeconomic status including the total monthly family income; and detailed medical history. We calculated monthly per capita income of the family for individual patient, socio-economic class of the patient using updated BG Prasad's classification for socioeconomic status linked with the All India Consumer Price Index[10] as shown in the following data.

Class	Monthly Per Capita Income	
	Original (1961)	As per February 2010 (₹)
I	100 and above	3147 and above
II	50 to 99	1558 to 3146
III	30 to 49	923 to 1557
IV	15 to 29	478 to 922
V	Less than 15	477 and below

The drugs prescriptions (number, frequency, dose, route, duration, whether generic or brand name) were analyzed. Further the drugs were classified according to the pharmacological class and their teratogenic potential according to USFDA risk categories for drugs and medication. [6] After completing the basic data collection, the medical records were analyzed for assessment of the drug utilization. Statistical analysis was done by using the statistical software SPSS.

The results are expressed as Mean $\pm$ SD. Data is presented descriptively.

RESULTS:

Total 300 case records of patients admitted to the obstetrics ward were analyzed. The average age of patients was 25.37 ± 5.75 years. **Table 1** shows the distribution of patients in different age groups. As is evident 281/300 (93.66%) patients were in the age group of 18 to 35 years.

TABLE 1: DEMOGRAPHIC CHARACTERISTICS

No	Age in Years	No. of patients	Percentage (%)
1	< 18	08	2.67
2	18-35	281	93.67
3	> 35	11	3.66

The socio-economic determinants of the study population are depicted in **Table 2**. Though the percentage of non-earning females is high (74%); many females quit their jobs as a result of pregnancy. Around 25% patients were working women. **Figure 1** shows the patient distribution as per the updated BG Prasad's classification for socioeconomic status. More than 60% patients had their monthly per capita income in the range of ₹478 to ₹1557.

TABLE 2: SOCIO-ECONOMIC DETERMINANTS OF THE STUDY POPULATION

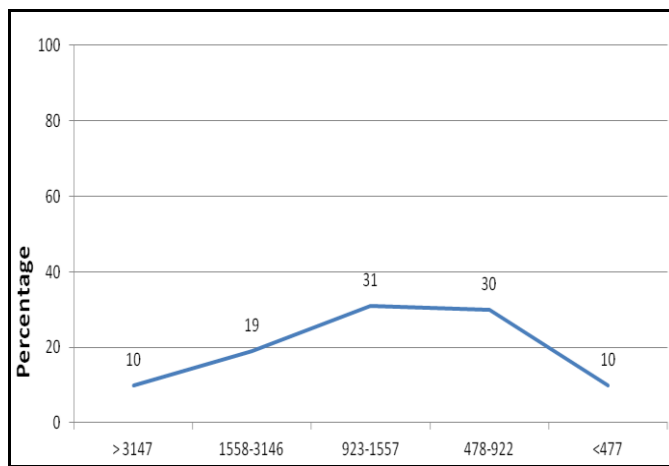| Occupation	No. on patients	Percentage (%)
Homemaker	222	74
Farmer	45	15
Service	18	6
Labourer	12	4
Student	03	1

FIGURE 1: SOCIO-ECONOMIC STATUS OF THE PATIENTS MONTHLY PER CAPITA INCOME IN RS.

The average number of drugs given to the patients is represented in **Table 3**.

TABLE 3: AVERAGE NUMBER OF DRUGS PRESCRIBED

Trimester (n=100 in each group)	Average number of drugs (Mean $\pm$ S.D.)
First	2.3 ± 1.6
Second	3.3 ± 1.1
Third	2.9 ± 1.8

It was seen that maximum drug prescriptions happened in the second trimester of pregnancy. Vitamins, mineral and nutritional supplements were prescribed in almost 100% cases. As these were antenatal cases they mandatorily received iron and folic acid, calcium supplement and protein supplement in the form of powder. The patients receiving more than 3 drugs were having co-morbid conditions. The analysis for completeness of prescriptions is shown in **Figure 2**.
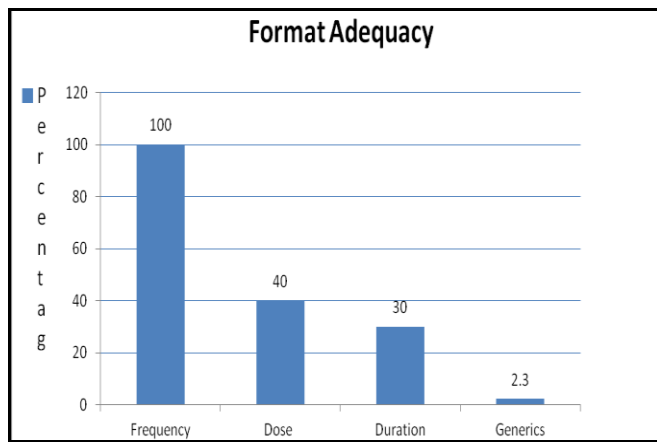

FIGURE 2: FORMAT ADEQUACY OF PRESCRIPTIONS

Though frequency of medications written was in 100% prescriptions, it was noted that the other details (dose as well as duration) was written in less than 50% of the prescriptions. Further it was noticed that generic drug prescribing was very low (2.3%) and constituted drugs like cabergoline, clomiphene citrate, tetanus toxoid and folic acid.

The most common Fixed Dose Combination prescribed was iron & folic acid supplement (**Table 4**). The essential combinations used were iron & folic acid and magnesium & aluminium hydroxides according to WHO and National list of Essential medicines.

TABLE 4: ANALYSIS OF FIXED DRUG COMBINATIONS PRESCRIBED

No.	Contents	Frequency	Essentiality
1	Iron + Folic acid	92	Essential
2	Doxyllamine + Pyridoxine	06	Non-essential
3	Magnesium hydroxide + Alluminium hydroxide	02	Essential
4	Serratio peptidase + Diclofenac	01	Non-essential
5	Pantoprazole + Domperidone	01	Non-essential
6	Folic acid + Vit C	01	Non-essential
7	Dicyclomine + Mephenamic acid	01	Non-essential

Table 5 lists all the drugs prescribed and their classification as per their ability to cause teratogenicity. It can be seen that varied drugs (Category A to D) were prescribed depending on the clinical condition of the patients and most of these were in the category B to C.

TABLE 5: DRUGS PRESCRIBED AS PER THE US-FDA RISK CATEGORY

Pharmacological Class	Drug category (US-FDA)
VITAMINS	
Vitamin C	A/C
Vitamin B complex	A/C
Folic Acid	A/C
ANTIBACTERIAL	
Ciprofloxacin	C
Amoxycillin	B
Ampicillin+cloxacillin	B
Metronidazole	B
Cephalosporins	B
Cotrimaxazole	B
Clindamycin	B
ANTACIDS	
Ranitidine	B
Pantaprazole	B
ANTIHISTAMINICS	
Cetrizine	B
Chlorpheneramine	B
ANALGESICS	
Paracetamol	B
Diclofenac	B/D
Ibuprofen	B/D
ANTIEMETICS	
Ondanseterone	B
Domperidone	C
Promethazine	C
Prochlorperazine	C
HORMONAL AGENTS	
HCG	D
Micronised Progesterone	D
Didrogesterone	D
CORTICOSTEROIDS	
Dexamethasone	C
Betamethasone	C
ANTICONVULSANTS	
Magnesium sulphate	B
Diazepam	D
ANTIASTHMATICS	B
(Nebulisation only) Terbutaline	
TOCOLYTICS	
Isoxuprine	C
ANTIHYPERTENSIVES	
α- methyl dopa	B
Nifedipine	C
Amlodipine	C
ANTICHOLINERGICS	
Scopolamine	C
ANTIDIABETICS	
Insulin	B
ANTIPLATELET	
Aspirin	C/D
DIURETICS	
Chlorthiazide	C/D
ANTHELMENTHICS	C
Mebendazole	
ANTIFUNGAL	
Fluconazole	C
THYROID	
Levothyroxine	A
Propylthiouracil	D

The percentage of drugs prescribed in patients demonstrating physiological changes in pregnancy according to pharmacological class is depicted in **Figure 3.** It was seen that antibacterials and antacids were the most commonly prescribed (25%) followed by antihistaminics (17%) and antiallergics (11%
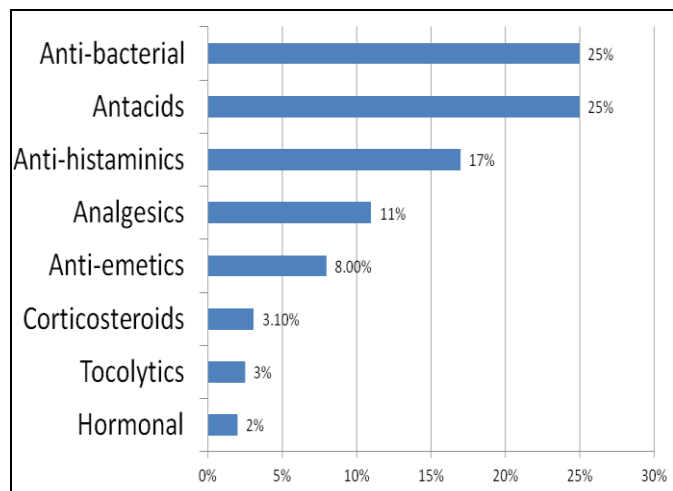
FIGURE 3: PERCENTAGE OF DRUGS PRESCRIBED IN PATIENTS DEMONSTRATING PHYSIOLOGICAL CHANGES IN PREGNANCY

The comparative analysis in the 3 trimesters **(Figure 4)** showed that for antibacterials, antacids, antihistaminics and analgesics. It was seen that maximum prescriptions happened in the 2nd trimester of pregnancy.
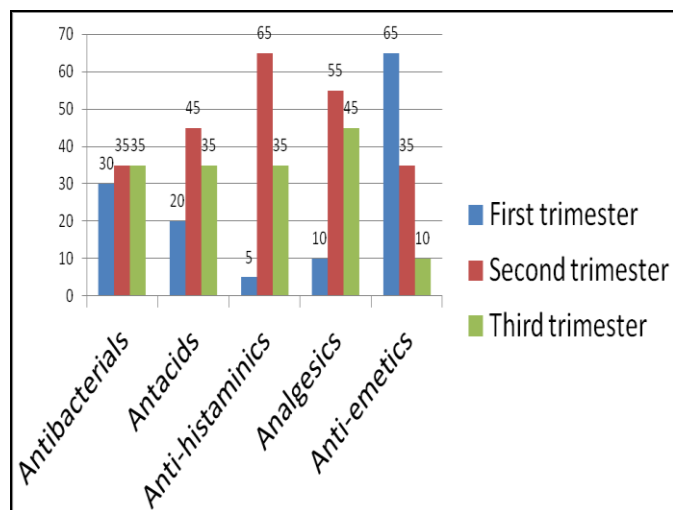

FIGURE 4: COMPARATIVE ANALYSIS OF PRESCRIPTIONS IN FIRST, SECOND AND THIRD TRIMESTER IN PATIENTS DEMONSTRATING PHYSIOLOGICAL CHANGES IN PREGNANCY

The percentage of drugs prescribed in patients with co-morbid conditions in pregnancy according to pharmacological class is illustrated in **Figure 5**. The overall drug prescription was negligible with antihypertensives prescribed in only 2% patients followed by anticholinergics in 1%. The rest of the drugs (antiasthmatics, antidiabetics, antiplatelets, etc) were prescribed in less than 1% of the patient population.
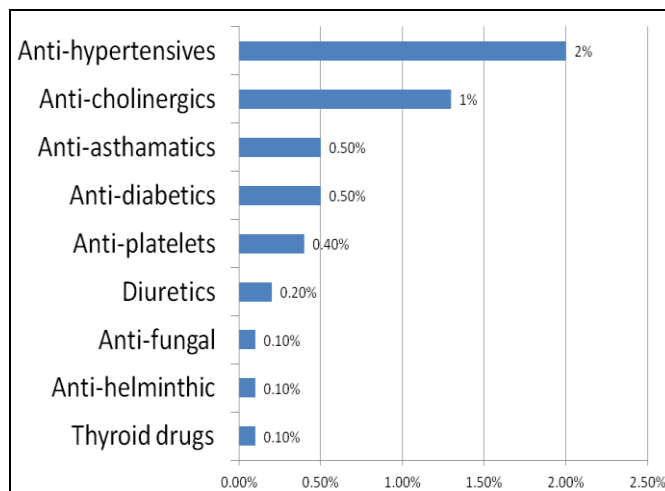

FIGURE 5: PERCENTAGE OF DRUGS PRESCRIBED IN PATIENTS WITH CO-MORBID CONDITIONS IN PREGNANCY

The comparative analysis in the 3 trimesters **(Figure 6)** showed that for hormonal agents, corticosteroids and tocolytics. Maximum prescriptions happened in the 2nd trimester of pregnancy, whereas diuretics were equally prescribed in 2nd and 3rd trimester of pregnancy
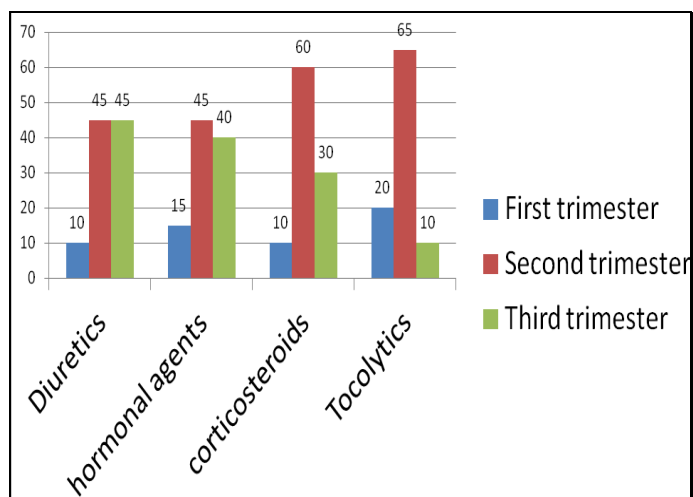

FIGURE 6: COMPARATIVE ANALYSIS OF PRESCRIPTIONS IN FIRST, SECOND AND THIRD TRIMESTER IN PATIENTS WITH CO-MORBID CONDITIONS IN PREGNANCY

DISCUSSION: Careful consideration of the benefit to the mother and risk to the fetus has to be given when drugs are prescribed during pregnancy.[11] The thalidomide tragedy in the 1960s and the teratogenicity with diethylstilboestrol in 1971 had raised concerns, which led US-FDA to establish strict regulations regarding the use of medications in pregnancy, requiring

demonstrations on safety and efficacy of drugs before they became commercially available. [11]

Pregnancy requires a special care. The present study helped us understand the drug utilization practices in antenatal practice in the rural tertiary health care set up. It made us aware of the attitudes and the factors influencing physician behavior which can be used for developing rational drug policies in rural areas. Supplementary drug treatment, that include iron, folic acid, calcium, vitamins and minerals, plays a pivotal role in the prevention of maternal and child mortality and morbidity.[11] In our study, majority of drugs used during pregnancy belonged to US-FDA category A, such as vitamins and mineral supplements. This was followed by category B drugs antibacterials, antacids, antihistaminics and analgesics (paracetamol). Category A drugs were used throughout the pregnancy, while Category B drugs were used more in the last two trimesters for pregnancy associated complications. Drugs from Category X were not prescribed in the samples analyzed.

These results varied when compared to other studies. A study done by Sharma R et al in North India reported that category-A drugs were commonly used followed by category-B and category-D[12]. In a study done by Andrade SE et al, it was seen that 5.8% of women were prescribed teratogenic drugs (US-FDA category D or X drugs)[13], whereas Tisonova J et al reported that drugs from Category C were prescribed the most in their practice.[14] Similarly, a study conducted in Pakistan regarding the drug-prescribing patterns during pregnancy documented that <1% of women were prescribed teratogenic drugs.[15]

In our study, iron plus folic-acid (fixed dose combinations) were the most commonly used drugs in pregnancy, with a frequency of 92 (**Table 4**). The trend noticed was similar to that reported from different parts of the world. In a prospective survey in Southwest Finland, iron and vitamin supplementation were the most frequently used drugs, followed by analgesics, tocolytic agents and drugs for chronic conditions and common pregnancy symptoms.[16] In another study from Australia, folate (70%), iron (38%) and

multivitamins (27%) were the most frequently consumed drugs by pregnant women.[17]

A large proportion of women surveyed had anemia in pregnancy. This was the main reason why iron and folic acid combination was prescribed to a majority of patients. Anemia was also a reason for admission in all the three trimesters. The poor socio-economic status may be responsible for the poor nutritional status of the pregnant females. This population may not have a proper meal and also find it difficult to purchase nutritional supplements. Efforts should be taken to improve the nutrition of women in child bearing age as a primordial prevention. Detection of anaemia at an early stage can avoid the risks associated with blood transfusion during pregnancy.

A noticeable fact was that maximum drug prescription (3.3 ± 1.1) happened in the second trimester of pregnancy. This was attributable to co-morbid conditions patients were suffering. On this basis we can say that drug prescription in our set up was rational. While the frequency of medications written was noticeable in 100% of patients, an area of concern was that other details like dose and duration of therapy was mentioned in <50% of patients. Considering the importance of documenting these facts as well as the lower literacy rates amongst the patients in our study, we feel, physicians should inculcate the habit of writing correct prescriptions.

A large percentage of patients visiting our hospital came from poor socio-economic background. Their purchasing power for branded drugs was limited. Hence, in practice, if generic drugs are prescribed, the cost of the treatment can be reduced.

Judicious use of drugs, adequate knowledge, positive approach and awareness towards rational drug use are mandatory prerequisites for good maternal and child health. Pharmacoepidemiological studies can help in minimizing the inherent risk of drug use in pregnancy, by establishing a profile of drug consumption, by evaluating the existing health services and by investigating the interventional measures.[8] But few such studies on drug audits during pregnancy have been conducted in India.

So, it becomes important to examine the pattern of drug utilization in pregnancy, to check as to up to what extent there may be a room for improvement in the light of current knowledge.[11] There is a need to educate and counsel women of child-bearing age regarding advantages and disadvantages of drug use during pregnancies.[17] Even the doctors need to be trained to give rational treatment to the pregnant women, by including community pharmacology studies in their academic curriculum

Our study had the following limitations. Since it was a cross sectional study, we were unable to determine the effects of drugs on pregnancy outcomes. Further we were unable to study the effect of factors like history of chronic diseases, bad obstetric history and parity on the pattern of the drug use. In India most pregnancies are unplanned and chances are, pregnant women may be taking drugs before they know are pregnant and also they may be having little knowledge on the drugs consumed[18]. Our study was done in rural tertiary care set up; however, conditions could be worse in the remote corners of India. Such studies in diverse environmental, social, educational and cultural conditions should be carried out periodically. These will aid in providing directions to rational drug usage in the community.

CONCLUSION: Our study revealed a careful prescribing behaviour by the physicians to the pregnant women under antenatal care visiting a tertiary care rural hospital. We can conclude that it is strongly recommended that the habit of prescription of drugs by generic names should be inculcated amongst the prescribers. Awareness of low cost prescribing practices should be initiated among prescribers because a large percentage of patients visiting this hospital are from poor socio-economic background. A further cost analysis study should be undertaken to determine if the cost per day is affordable to patients.

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