

**PATTERN OF DRUG PRESCRIBING DURING PREGNANCY IN NEPALESE WOMEN**

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**\*Corresponding author e-mail:** priyastha82@gmail.com, bhandarishiva11@gmail.com**ABSTRACT**

Objective of this study is to assess the utilization pattern and the teratogenesis risk of the drugs prescribed among pregnant women in Nepal. The drugs that were prescribed during pregnancy were assessed retrospectively in 94 Nepalese pregnant women who attended the prenatal clinic of the two Hospitals in Nepal. From Patient medical record, FDA drug category of prescribed drugs was identified. Maximum number of pregnant women was from age grouping 15 to 25 (72%). According to FDA drug category, our finding reveals that two drugs prescribed of FDA category X were oxytocin and dydrogesterone. A majority of drugs prescribed were from category B (42%). A majority of drugs were given as an oral dosage form i.e. Tablet form (56%) and in severe cases injection was preferred i.e. 24%. Anthelmintic was prescribed to all pregnant women during their second trimester. The most commonly prescribed drugs were nutritional supplements like Iron, Folate, Calcium, Vitamins followed by Tetanus Toxoid.

**Key words:** prescribing pattern, pregnancy, drug use, Nepalese women**INTRODUCTION**

The presence of antigen (hCG) in the urine or serum with antibody either polyclonal or monoclonal available commercially by 8-11 days after conception ensures pregnancy. Pregnancy is a time of profound physiological changes in a woman's body. These unique changes challenge clinicians managing disease states during pregnancy in the selection of medications best suited to treat their patients. <sup>[1]</sup> Altered physiology during pregnancy demands special care in the use of drugs. <sup>[2]</sup> Immense precautions need to be taken for the use of drugs during pregnancy as in addition to health of the mother and health of the fetus too may be affected. <sup>[3]</sup> No doubt drug treatment may be beneficial to the mother in some circumstances but the same agents may be hazardous to the unborn. Selection of drugs best suited to be administered to a pregnant woman is a challenging task to the doctors in view of the unique physiological changes. <sup>[4]</sup> Though teratogenic

risk is a biggest risk in the use of many drugs, it is unrealistic to recommend, not using any drugs at all during pregnancy. This decision may even prove dangerous for the health of the mother. <sup>[5]</sup> Risk benefits situation need to be carefully analyzed by the physicians in managing medical conditions in a pregnant women. <sup>[6]</sup> Despite the absence of adequate studies on the safety and effectiveness of prescription drugs for pregnant women, evidence available shows that physicians prescribe, and pregnant women take a surprisingly large number of drugs. <sup>[7]</sup>

**Pregnancy duration:** The Pregnancy is measured in trimesters from the first day of your last menstrual period, totaling 40 weeks. Each pregnancy stage, also known as a trimester, holds unique and different growth, developments, emotions and feelings

1. First trimester
2. Second trimester
3. Third trimester

The first trimester consists of the first 1-12 weeks of pregnancy. Morning sickness is inconsistently present in about 50% cases, more often in the first pregnancy than in the subsequent one. It usually appears soon following the missed period and rarely lasts beyond the first trimester. Its intensity varies from nausea on rising from the bed to loss of appetite or even vomiting. But it usually does not affect health status of the mother... Breast discomfort in the form of feeling of fullness and 'pricking sensation' is evident as early as 6-8<sup>th</sup> week specially primigravidae. Fatigue is also a frequent symptom which may occur early in pregnancy. This is a time when baby does the most of its developing, and is also the time where fetus stands the biggest chance of developing any complications. Second trimester consists of 13-28 weeks. Feeling of life or active fetal movement is felt by the women about 18<sup>th</sup> week. Progressive enlargement of the lower abdomen is seen by the growing uterus. Breasts are more enlarged with prominent veins under the skin. Third trimester or the last trimester consists of 29-40<sup>th</sup> weeks after the 2<sup>nd</sup> trimester. Enlargement of the abdomen is clearly visualized. Fetal movement is felt more intensively [8].

**FDA categories for drug use in Pregnancy:** In 1979, the Food and Drug Administration developed a system determining the teratogenic risk of drugs by considering the quality of data from animal and human studies. It provides therapeutic guidance for the clinician. Category A is considered the safest category but some drugs from categories B, C and D are also used during pregnancy. Category X is the only rating that denotes a drug is absolutely contraindicated for use during pregnancy. Some of the drugs have been proved to be harmful to the fetus and so their use during pregnancy is contraindicated. [9]

## METHODOLOGY

This retrospective study was carried among pregnant women in two Hospitals Koshi Zonal Hospital (Morang district) and Dhulikhel Hospital (Kavre District). Different Stages of pregnant women including First trimester, Second trimester and last i.e. Third trimester were interviewed individually. Each woman was interviewed only once, regarding drugs used in their present pregnancy since conception to study drug utilization practices during pregnancy, in women attending the ante-natal clinics. A set of in-depth format was developed for investigation of drug prescribing pattern during pregnancy in these two hospitals, for both quantitative and qualitative data and information. The

questionnaire is both open- and close-ended. The study is based on six months from Sep 2012 to Feb 2013 of wide study of drug utilization pattern. The data entry was started immediately after the completion of data collection. The collected data was checked, verified and then entered into the data sheet. Data was analyzed manually. The test statistics used to analyze the data will be descriptive statistics.

## RESULT AND DISCUSSION

The study was carried out among different age group of woman and the maximum age group was 15-25 (i.e. 72%) and others were 26-35 (i.e. 26%) and 35 above (i.e. 2%) as shown in figure 1. The maximum numbers of pregnant women were in third trimester i.e. 52 % and others were in first and second trimester i.e. 5 % and 43% respectively as shown in Table 2 and Figure 2. Among the 50 drugs prescribed during ANC, most of them (56%) were prescribed in tablet form. The rest were injection (24%), capsule (8%), syrup (8%) and cream (4%) as shown in table 3 and figure 3. Different drug category assigned by FDA which has been used during pregnancy is shown in table 1.

- The frequently prescribed drugs was from FDA category B (42%) and rest were C (30%), A (14%), D (4%), X (4%) and not categorized (4%) shown in table 4 and figure 4. But the FDA category varies according to the dose use and in which trimester the drug is being used.

Around 61% women were hospitalized during their pregnancy and rest 39% were not hospitalized during their pregnancy stage out of 94 pregnant women.

### Reasons for hospitalization are:

1. Hyperemesis Gravidarum
2. Pre-eclampsia
3. High fever, severe cough and cold
4. Vaginal bleeding
5. Urinary tract infection
6. Back ache, abnormal position of fetus and abdomen pain
7. Severe nausea and vomiting
8. Sweating and drowsiness
9. Vaginal discharge

### List of medical test administered during pregnancy

1. Urine test  
Color, reaction, albumin, sugar, acetone
2. Blood test

White blood test, platelets, hemoglobin, Blood group, Rh, H.I.V. Antibody I & II, Hbs Ag, V.D.R.L.

3. Microscopic examination  
R.B.C, Casts, epithelial test
4. Stool test
5. Ultrasonography i.e. video-X ray.
6. Blood pressure
7. Glucose level.
8. CTG ( Cardiotocography)

#### **Drugs prescribed for pregnant women during their ANC follow: (Table: 5)**

#### **Category D and category X drugs prescribed and their indication: (Table: 6)**

The most frequently prescribed drugs in each trimester were: antibiotics, anti emetics, vitamins, proton pump inhibitors /histamine H2 blockers during 1st trimester; antibiotics, cotrimoxazole, iron folate (Fe Fol), antacids and anti emetics during 2nd trimester; antibiotics, iron folate, antacids and anti D during 3rd trimester.

#### **DISCUSSION**

The information was collected from the pregnant women who have visited or admitted to the two hospitals. 94 women were interviewed. The study was carried out to describe the pattern of drug prescribing by the physicians during pregnancy in Nepal. But the prescribing pattern may vary according to geographical change and change in season. Because women from different geographical reason has different physical state and also change in season affects lot in prescribing pattern of drug by the physicians to the pregnant women. Pregnant women may easily get affected from various diseases during winter and rainy season and need more drug but it may not be same in the summer season. And also, rational drug use in pregnancy requires the balancing of benefits and potential risks associated with the use of the drug. The results of the present study show that maximum number of pregnant women was from age group 15 to 25 i.e. 72% .The maximum number of drugs was given as an oral dosage form (tablet) i.e. 56% and in severe cases injection was given. From this study it is also found that the physician prescribed the safe drug FDA category B in highest number i.e.42 % and rest were category C, A, D and X . Among the total drugs prescribed during ANC, 2% were category D, namely Povidone–Iodine and Phenobarbital, 2% were category X namely

dydrogesterone and oxytocin, 2% were not categorized (Table 3.6 and 3.7). From this we come to know that the drug used in maximum were safe drugs i.e. category B. FDA categorized this drug after animal reproduction studies which has failed to demonstrate a risk to the fetus but there are no adequate and well-controlled studies in pregnant women. Category A drugs prescribed in this study were only 7 out of 50 drug prescribed. Majority of the pregnant women were admitted for the hyper emesis gravid arum (HG) and Urinary tract infection in which they took different parenteral drugs such as anti emetics, anti pain, IV fluids, antibiotics and others per drug encounter and other reasons were pre-eclampsia, vaginal discharge, high fever, abdomen pain etc., Globally pregnant women and young children are at high risk of anemia with iron deficiency contributing to 50% of this. WHO has estimated that prevalence of anemia during pregnancy in developed countries is 14% and developing countries 51 percent. [10] More than half of pregnant women in developing countries suffer from iron deficiency anemia. As Nepal is one of the developing countries, result of our study implies that hospitals in Nepal supply iron supplement from the 1<sup>st</sup> trimester to prevent prevalence of anemia during pregnancy. And it is mandatory to consider iron supplement during pregnancy so as to minimize the risks associated with anemia. And also some pregnant women who were admitted to OBS ward give birth without taking any medication.

#### **CONCLUSION**

The study was carried out to describe the pattern of drug prescribing by the physicians during pregnancy in Nepal. But the prescribing pattern may vary according to geographical change and change in season. Because women from different geographical reason has different physical state and also change in season affects lot in prescribing pattern of drug by the physicians to the pregnant women. Pregnant women may easily get affected from various diseases during winter and rainy season and need more drug but it may not be same in the summer season. And also, rational drug use in pregnancy requires the balancing of benefits and potential risks associated with the use of the drug. Prescription to pregnant women should be easy known by the pharmacist either by direct communication with the health care provider working in GYN/OBS ward and OPD.

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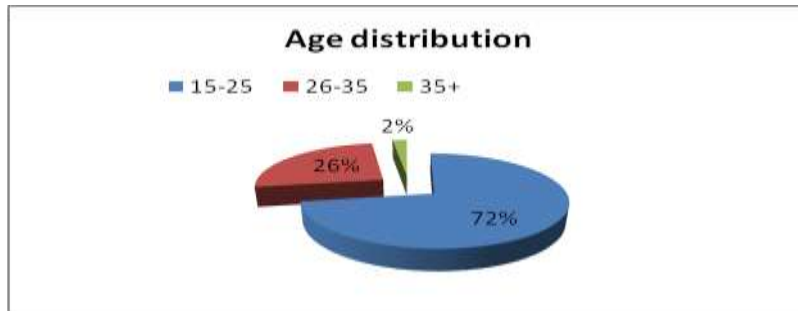


Figure: 1 Age distribution of pregnant women

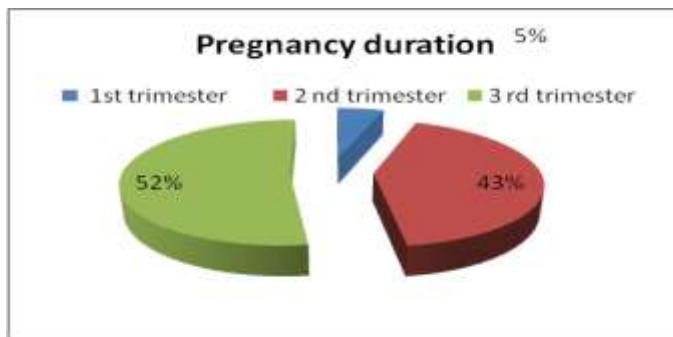


Figure: 2 Duration of pregnancy

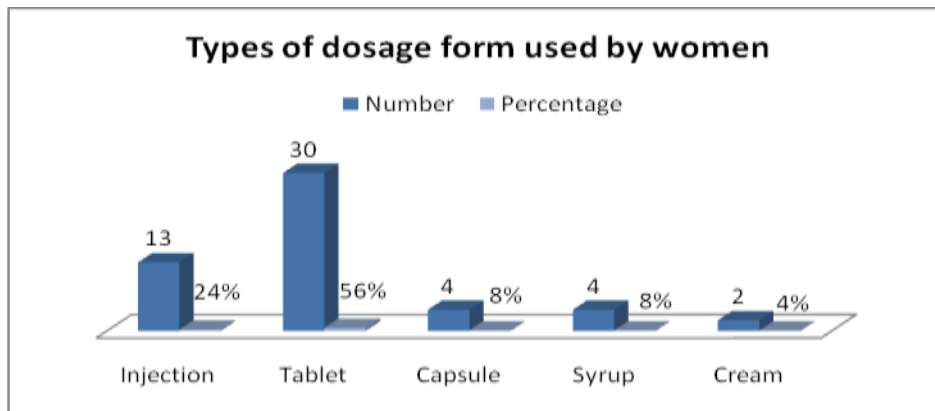


Figure: 3 Dosage Form of drugs prescribed to pregnant women

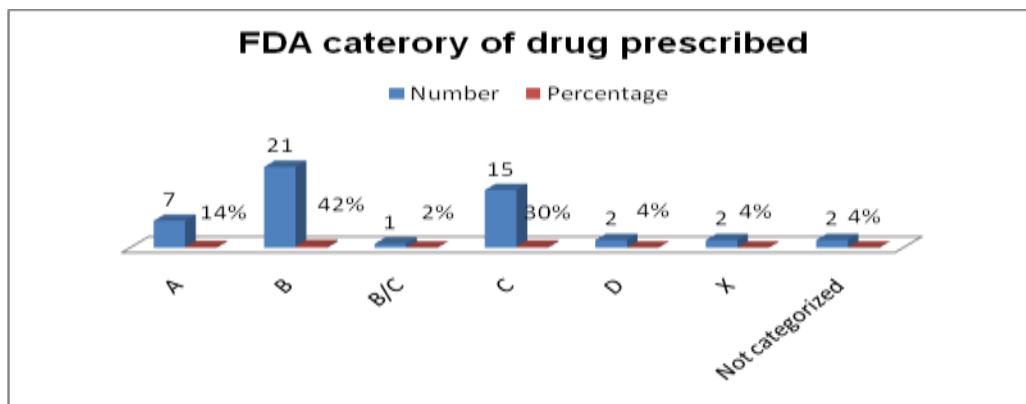


Figure: 4 Different FDA categorized drugs used by pregnant women

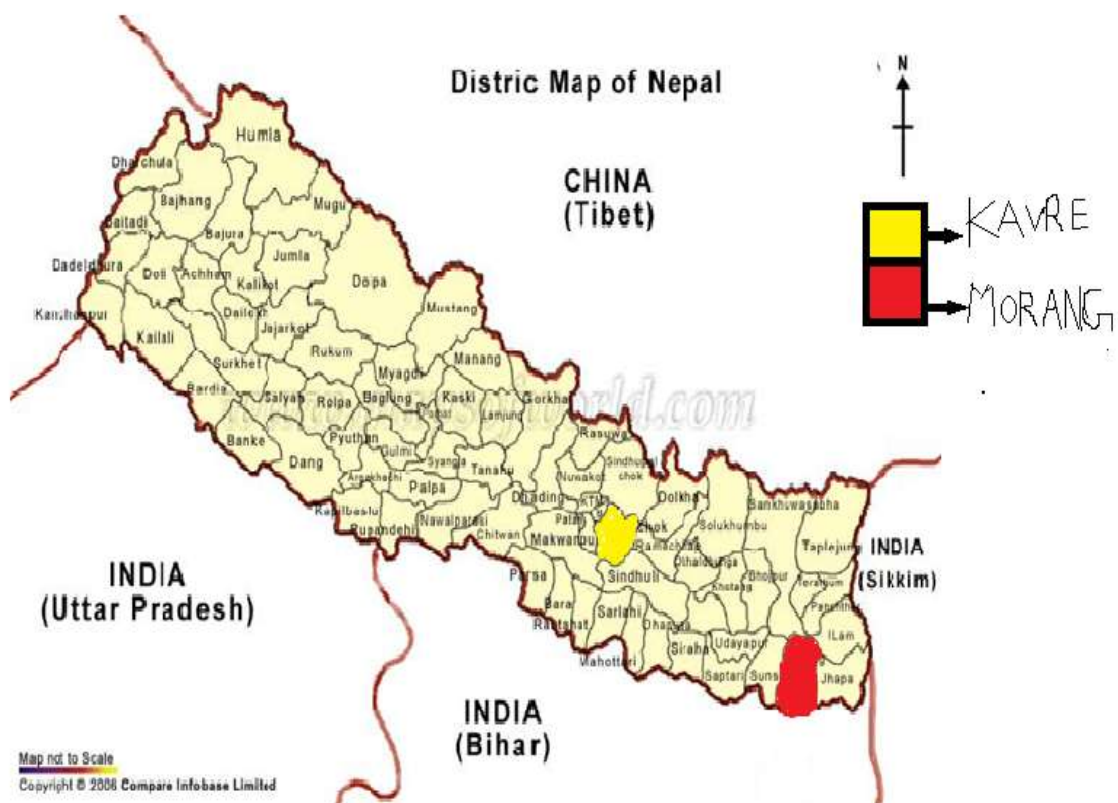


Figure: 5 Showing Kavre and Morang district (study area) of Nepal.

Table: 1 FDA categories for drug use in pregnancy

Category	Description
A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities
B	Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well controlled studies in pregnant women. Or Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus
C	Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women. Or No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women.
D	Studies, adequate well-controlled or observational, in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
X	Studies, adequate well-controlled or observational, in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.

Table 2: Pregnancy duration

Pregnancy duration	Number	Percentage
1st trimester	5	5%
2 nd trimester	40	43%
3 rd trimester	49	52%

**Table 3: Dosage form of drugs prescribed to pregnant women**

Dosage form	Number	Percentage
Injection	13	24%
Tablet	30	56%
Capsule	4	8%
Syrup	4	8%
Cream	2	4%

**Table 4 Table showing different drug category assigned by FDA which have been used during pregnancy**

FDA category	Number	Percentage
A	7	14%
B	21	42%
B/C	1	2%
C	15	30%
D	2	4%
X	2	4%
Not categorized	2	4%

**Table: 5 Drugs prescribed for pregnant women during their ANC follow up**

FDA category	Generic name	Trade name	Dosage form	Use
B	Ranitidine	Aciloc	Tablet	Gastritis
B	Ampicillin		Tablet	Antibiotic
C	Hyoscine Butylbromide 10mg	Busecopan	Tablet	Abdomen ache
B/C	Iron	Afee	capsule	Iron
B	Amoxicillin		capsule	Antibiotic, Urinary tract infection, Throat/Posterior pharyngeal wall congested
B	Albendazole		Tablet	Roundworm. Anthelmintic
C	Fexofenadine hydrochloride	Allegra-180	Tablet	Allergy
D	Povidone-Iodine	Betadine Gargle	Liquid	Tosilitis, Throat/Posterior pharyngeal wall congested, Oral germicide for fast and soothing relief of sore throat and mouth sores.
C	Clotrimazole Mucoadhesive	Vaginal Candid V6	Tablet	Vaginal candidiasis, antifungal
B	Cefixim		Tablet, Injection	Antibiotic
B	Cefadroxil	Odoxi 500mg	Tablet, IV	Antibiotic
B	Clotrimazole		Cream	Antifungal
C	Decadron	Dexona 0.5 mg	Tablet	Hormone system disorders, allergies and arthritis
A	Calcium with vitamin D <sub>3</sub>	Decal	Tablet	Used as calcium with vitamin D3
B	Drotaverine	Drotin DS-80	Tablet	Abdomen ache. Antispasmodic
A	Dextrose	Dextrose	IV	To maintain body fluid
A	Folic acid	Foliden	Tablet	Folic acid, fetus development
Not categorized	Iron/vitamin C/vitaminB12/Folic Acid	Ferric Plus	Tablet, capsule	To prevent anemia
X	Dydrogesteron	Gestofit 200mg	Tablet	To treat hormone deficiency during pregnancy and to treat secondary amenorrhea, manage luteal phase deficiency, prevent endometrialhyperplasia, amelioratemdysfunctional uterine bleeding, and treat endometriosis.
B	Ondansetron	Grandem	Tablet	Treat nausea and vomiting
A	vitamins	G vital	Syrup	Dietary supplement
C	Gentamycin		Injection	Antibiotic, bactericidal
C		Hydralazine	Tablet	To treat high blood pressure, preeclampsia
B	Hydroxy Progesteron	Injection	Injection	Reducing the risk of delivering a baby too early (preterm birth)

C	Isoxsuprine Hcl	Isox 10mg	Tablet	To prevent premature labor.
B		Ibuprofen	Tablet	Pain killer, abdomen ache
C	Saline	Normal saline	Saline	Electrolyte balance
A	Vitamin B-complex with	Nebula	Syrup	Vitamins
B	Pyrantel Pamoate	Nemocid 250 mg	Tablet	Treat parasitic infections and worm infections
A	Magnesium sulphate		Intravenous	Used to delay preterm labor, hypomagnesemic , seizures, Prevention or control of seizures in eclampsia
C	Calcium	Ossad 500mg	Tablet	Fetus bone development
X	Oxytocin		Intravenous	Increase uterus contraction
B	Ondansetron	Ondem 4 mg	Tablet	Treat nausea and vomiting
B	Metoclopramide	PerinoRM <sup>R</sup>	Tablet	Antiemetic
B	Acetaminophen	Paracetamol	Tablet, IV	Antipyretic, pain reliever
C	Promethazine	Phenergen 25 mg	Tablet	Abdomen ache
A	Multi-Vitamins+Minerals	Polybion	syrup	Nutrition
D	Phenobarbital	Phenobarbitone	Tablet	Helps reduce seizure frequency and severity and in a lot of cases stops seizures altogether.
B	Ritodrine HCl	Ritodrine	IV	Delay uterus contraction, to stop premature labor
B	Rabeprazole sodium IP	RAB-20	Tablet	Gastritis
C	Sodium Chloride IP	Rhine	Normal saline	Maintains electrolyte balance
C	Chlorpheniramine-	Suprin	Tablet	Cough, cold, fever
B	Tranexamic Acid Tablet	Transtat	Tablet 500mg	Stop PV bleeding
C	Benzydamine hydrochloride	Tantrum gargle	Liquid	Mouthwash, antibacterial
B	Cefotaxime	Taxim	Injection	Antibiotic
C	Chlorpheniramine Maleate	TusQD	syrup	Used to treat dry cough
B	Ceftriaxone	Taxone-P	Tablet	Antibiotic
C	Tetanus Toxoid	Tetanus vaccine	Injection	To prevent tetanus of mother as well as her baby.
Not categorized	Folic Acid, Iron (III) Hydroxide Polymaltose	Tisfer	Capsule	Nutrition, dietary supplements
B	Helminthic	Warmin	Tablet	Anthelmintic

\*B/C safety differs according to the trimester they are given.

**Table: 6 List of Category D and Category X drugs prescribed and their indication**

Drug	FDA category	Adverse effect	Indication
Povidone -Iodine	D	Irritation of the lining of the mouth and throat	Tosilitis, Throat/Posterior pharyngeal wall congested
Phenobarbital	D	Mother-Dizziness, drowsiness,excitation, headache, tiredness, loss of appetite, nausea, vomiting Fetus- Addiction or withdrawal symptoms in a newborn	Helps reduce seizure frequency and severity and in a lot of cases stops seizures altogether
Fexofenadine hydrochloride	C	Headache, drowsiness, dizziness and nausea.	Allergy
Chlorpheniramine-Acetaminophen/Paracetamol-Phenylehrine	C	nausea, drowsiness, dry mouth, rashes	Cough, cold, fever
Hyoscine Butylbromide	C	Dryness of the mouth, Rash, itching, increases heart rate, Producing less sweat than normal	Abdomen ache
Clotrimazole vaginal Mucoadhesive	C	Vaginal irritation, burning/stinging, and itching	Vaginal candidiasis, antifungal
Decandron	C	Difficulty sleeping, increased appetite ,feeling of a whirling motion ,increased sweating, mood changes, indigestion ,nervousness, appetite loss, tarry or black stools, convulsions, dizziness	Hormone system disorders, allergies and arthritis

Gentamycin	C	Nausea, vomiting, stomach upset, or loss of appetite, Pain/irritation/redness	Antibiotic, bactericidal
Hydralazine	C	Headache, pounding/fast heartbeat, loss of appetite, nausea, vomiting, diarrhea, or dizziness	To treat high blood pressure, preeclampsia
Isoxsuprine Hydrochloride	C	Dizziness, low blood pressure, palpitations, fast heart rate, lung swelling, nausea, vomiting and abdominal distress Rash and allergic reactions	To prevent premature labor.
Sodium chloride	C	Febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation and hypervolemia	Maintains electrolyte balance
Calcium	C	Constipation and upset stomach may occur	Fetus bone development
Promethazine	C	Drowsiness, Sedation, somnolence, blurred vision, dizziness; confusion, disorientation ,	Abdomen ache
Benzylamine hydrochloride	C	Burning, stinging or numbness in the mouth or throat. Throat irritation, cough, dry mouth with thirst, and headache	Mouthwash, Antibacterial
Chlorpheniramine Maleate	C	<i>Seizures, in a newborn baby if used in the final of 3 months of pregnancy</i>	Used to treat dry cough
Tetanus Toxoid	C	Mild fever, joint pain, muscle aches, nausea, tiredness, or pain/itching/swelling/redness at the injection site may occur	To prevent tetanus of mother as well as her baby.
Oxytocin	X	Allergic reaction, difficulty urinating, confusion, loss of appetite, nausea or vomiting.	Increase uterus contraction
Dydrogesterone	X	Dizziness, nausea, headache, fatigue, emotional lability, irritability; abdominal pain, musculoskeletal pain. Fetus- may cause fetal death	To treat hormone deficiency during pregnancy

**Table: 7 Drug lists of different types used by pregnant women with their common and serious side effects if taken more**

Drugs	Adverse effect
1. Amoxicillin	Confusion, convulsions, diarrhea, dizziness, insomnia, nausea, rash, vomiting.
2. Albendazole	Stomach pain, nausea, vomiting, headache, dizziness or temporary hair loss
3. Ampicillin	Irritation of the mouth or throat, diarrhea, nausea, vomiting, stomach pain/cramps or vaginal irritation or discharge
4. Acetaminophen	Skin rashes or hives, weakness, tiredness, sores
5. Benzylamine hydrochloride	Drowsiness, dryness of the mouth with thirst, headache , local burning or stinging sensation, local numbness
6. Clotrimazole Vaginal Mucoadhesive	Vaginal irritation, burning/stinging, and itching
7. Cefixim	Diarrhea, loose or frequent stools, abdominal pain, nausea, stomach upset and flatulence, vaginal inflammation/fungal infection and skin disorders.
8. Cefadriol	Allergic reactions including rashes, itching (pruritus), hives (urticaria), serum sickness-like reactions with rashes, fever and diarrhoea
9. Clotrimazole cream	Mild burning or irritation (immediately on use) , rash, itchiness
10. Chlorpheniramine-Acetaminophen/Paracetamol-Phenylephrine	Nausea, drowsiness, dry mouth.
11. Cefotaxime	Skin rash, bruising, severe tingling, numbness, pain, muscle weakness



12.	Chlorpheniramine Maleate	Drowsiness, dizziness, headache, constipation, stomach upset, blurred vision, decreased coordination, or dry mouth/nose/throat
13.	Ceftriaxone	Dizziness, headache, mild diarrhea
14.	Decadron	Headache, dizziness, weakness, confusion, insomnia, anxiety.
15.	Drotaverine	Headache, dizziness, nausea, constipation, hypertension.
16.	Gentamycin	Allergic reactions, such as rash, convulsion. Inflammation of the lining of any part of the mouth, such as cheeks, gums, tongue, throat and lips
17.	Fexofenadine hydrochloride	Headache, drowsiness, dizziness and nausea.
18.	Hydroxy Progesteron	Blood clots, allergic reactions, fluid retention, hypertension, migraine, depression, and jaundice.
19.	Hyoscine Butylbromide	Dryness of the mouth, Rash, itching, increases heart rate, Producing less sweat than normal.
20.	Isoxsuprine Hcl	Severe allergic reactions (rash, hives, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips, or tongue), chest pain, fast or irregular heartbeat, severe or persistent dizziness.
21.	Magnesium sulphate IV	Flushing, sweating, muscle weakness, dizziness, drowsiness, muscle weakness, slowed/shallow breathing or other breathing trouble.
22.	Metoclopramide	Restlessness, drowsiness, dizziness, fatigue, constipation and focal dystonia.
23.	Oxytocin	Nausea, vomiting, cramping, stomach pain, irregular heart beat of mother, headache, rash.
24.	Ondansetron	Headache, lightheadedness, dizziness, drowsiness, tiredness, or constipation, rash, itches.
25.	Promethazine	Drowsiness, dizziness, constipation, blurred vision, or dry mouth.
26.	Phenobarbital	Dizziness, drowsiness, excitation, headache, tiredness, loss of appetite, nausea, or vomiting.
27.	Rabeprazole sodium IP	Headache, diarrhoea, nausea, abdominal pain, rhinitis, vomiting, constipation, cough.
28.	Povidone-Iodine	Local irritation and skin sensitivity, Increased sodium in the blood (hypernatraemia), Increased acid levels in the blood (metabolic acidosis).
29.	Ritodrine HCl	Increase in heart rate, rise in systolic pressure, decrease in diastolic pressure, chest pain and arrhythmia.
30.	Tranexamic Acid Tablet	Back pain, headache, joint pain, muscle pain, spasms, or cramps, nasal or sinus congestion, stomach pain, tiredness.

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