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Research Article

DRUG UTILIZATION ASSESSMENT IN PREGNANCY WOMEN: A CROSS SECTIONAL STUDY

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ABSTRACT

Background: It is difficult to prescribe the right medication to pregnant women, because of so many complications and conditions. Women are prescribed with drugs according to food and drug administration (FDA) pregnancy drug list. They categorized drugs as A, B, C, D and X. some drugs are not categorized by FDA, they come under N (Not classified) category. Method: A cross-sectional observational study was conducted in Department of Gynecology. Information from subjects was collected in a designed proforma based on study criteria. Results: In this study there are total 247 members who visited antenatal hospital, more number of cases ware collected in the age group of 23-27 with the percentage of 44.53%. Complications were observed in the age group of 23-27 with the percentage of 36.28%. Pain was most commonly observed condition (37.24%). In our study c category drugs were most commonly prescribed class of drugs with the percentage of 39.84% among X drugs Human chorionic gonadotropin (HCG) was given in highest percentage of 0.63%. Conclusion: All the visited pregnant women were prescribed with at least one medication. A large number of complications and conditions during pregnancy were observed. However (0.21% of total drugs) X category drugs were also found to be prescribed.

Keywords: Pregnancy, FDA Drug Category, Complications, Drug Utilization

INTRODUCTION

Prenatal or antenatal is the developmental process which starts with embryo-genesis which is the fertilization stage and continues with foetus development. Prenatal development is divided or measured in trimesters. They are: first trimester, second trimester, third trimester. The first trimester is the first development stage where the rudiments of all the major organ systems appear. The first trimester lasts from the first day of last period and until the last day of week 12. The second trimester is the second developmental stage where almost all the organ systems are completely developed. The second trimester lasts from 14th week to the end of 28th week. By the end the foetus appears with complete human features. Third trimester lasts from 29th week to the end of 40th week. In the early stages of third trimester most of the organ systems are fully functional.[1]The child bearing age of women is from 15 to 44 years. Periconception care is very much needed to avoid exposure to harmful substances that cause teratogenic effects.[2] Thus, it is very important that the prescriber should be well aware of all the drug induced teratogenic effects before prescribing the medicines.[3] The pregnant women are excluded from the clinical trial studies due to ethical reasons.[4] That is why, for the safe prescribing of drugs in pregnancy USA-Food and Drug Administration has classified drugs into different categories .They are A, B, C, D and X drugs.[5]Therapeutic approach in pregnant women is not safe and effects drugs risk benefit ratio. The variables that affect the drugs risk benefit ratio are -Foetal age, Dose of drug, Duration of exposure, Drug distribution, Drug metabolism, Drug excretion. Therefore, the prescription should not only based on the category of drug but also on the right drug, right dose, right route of administration, right frequency The most commonly occurred complications in prenatal women are: Anaemia, Urinary Tract Infection (UTI), Thyroid dysfunction, Hypertension, Diabetes, Eclampsia, Loss of pregnancy, Other conditions like Gastroesophageal reflux disease (GERD), constipation, diarrhoea, nausea, vomiting, itching, p.v discharge and bleeding, headache, fever, pains.[6,7] Anemia occur due to transfer of iron and folic acid to the fetus. There in two types of anemia in prenatal period . Pathological anemia includes deficiency and haemorrhagic anemia. Physiological anemia of pregnancy is caused when an disproportionate increase in RBC volume, plasma volume and hemoglobin mass occurs Hemo-dilution occurs when plasma volume increases more than Red Blood Cells (RBC) mass which leads to physiological anemia in pregnancy. Urinary tract infection is a very common complication during pregnancy. It is due to growth of microorganisms in urinary tract. Examples of gram negative organisms are E.coli, klebsiella, proteus and gram positive organisms are streptococcus, staphylococcus, enterococcus species. Prevalence of asymptomatic UTI during pregnancy in India accounts for 6.2% and symptomatic UTI accounts for 1-18%.[10] Eclampsia is generalized tonic-clonic convulsion that occur during pregnancy. The incidence of eclampsia in UK is 4.9 per 10,000 and in USA 4.3 per 10,000. It is higher in India and is 220 per 10,000.[11] Thyroid hormones are important for fetal growth and development. Their requirement increases during pregnancy.[12] Gestational Hypertension is 6-8% of women are affected with gestational hypertension. Hypertension in pregnancy is of 3types. They are **Chronic hypertension** occurs before 20 weeks of pregnancy or 12 weeks beyond postpartum. **Gestational hypertension is** increased blood pressure during pregnancy. Half percentage of women acquiring gestational hypertension is between 24 to 35 weeks of gestation. **Pre-eclampsia** is associated with hypertension and protinuria occurs after 20th week of prenatal period.[13] Miscarriage is the loss of pregnancy that occur before 20 weeks of gestation. Risk of loss of pregnancy includes: increased age, history of loss of pregnancy or infertility. 15% of total pregnancy women experiences spontaneous pregnancy loss.[14, 15, 16] Gestational diabetes mellitus is the occurrence of diabetes during pregnancy. The women who are at high risk of

acquiring gestational diabetes mellitus are: Age greater than 25years, Overweight, Past history of gestational diabetes mellitus, Large baby (macrosomia)[17,18.]

The main aim of the study to assess medication utilization among pregnant women visiting antenatal hospital. The primary objective of the study is to assess the drug utilization pattern in antenatal women and the secondary objectives are to assess various categories of drugs according to their trimesters, to assess X category drugs in the prescriptions, to assess percentage distribution of conditions in pregnant women, to assess complications in pregnant women according to their age group.

MATERIALS AND METHODS

A hospital based cross sectional observational study was conducted in gynecology department. This study was conducted for a period of six months (August 2017– January 2018). We collected 247 prescriptions in these six months study, after obtaining the consent from patient. The study inclusion criteria include pregnant women at any gestational age, women visiting outpatient department, pregnant women acquiring any complication during gestational period and the exclusion criteria include women who are not willing to participate in the study.This cross-sectional observational study was carried out after obtaining the permission of institutional ethical committee on 19th august 2017, Creative Educational Society's College of Pharmacy, Kurnool, A.P, India. The pregnant women visiting out patient department were included in the study. A specially designed proforma was used for collecting data which includes patient demographics, birth history, history of consanguinity, complications, lab investigations and past and present medications prescribed for each patient. The data was obtained by direct patient interview and from patient case profiles. Total 247 cases were collected from gynaecology wards, according to study criteria. All the prescriptions were collected and obtained necessary information needed for the study. The category of drugs were referred from Drugs in pregnancy and lactation: A reference guide to fetal and neonatal risk.

RESULTS

In total of 247 cases 61.95 % population was from third trimester. This followed by women from second trimester (25.9%), and only (12.1%) from the first trimester. Majority of the patients in the study were from the age group of 23-27 (44.53%), which were followed by 18-22 (31.98%), 28-32(19.03%), 33-37 (3.64%), and 38-43 (0.8%) respectively. Consanguinity was seen in 41 (16.5%) cases, and 206(83.4%) cases were without consanguinity. Majority of pregnant women visiting the hospital are of primary gravida (39.2%) and followed by secondary gravid (32.3%), tertiary garvida (19.02%) and multi gravida (9.31%). One of the major complication identified in the pregnant women is "miscarriage". The majority of women are present with single miscarriage (21.45%), followed by double miscarriage (11.33%), triple miscarriage(2.83%), and greater than three miscarriage are seen in 2.83%. There were no miscarriage seen in (61.53%) of pregnant women. Among the most of the cases collected miscarriage and hypothyroidism was seen in higher number with the percentage of 30.92%, 10.9% respectively, and least percentage was included in others i.e. down's risk, hepatitis B, hypotension, placenta previa, pre eclampsia of percentage 1.71% as shown in table no.1. The highest percentage of complications was observed in age interval of 23-27 with the percentage of 36.28% followed by 18-22, 33-37,28-32, and 38-43 age groups with the percentages of 24.89%, 18.98%, 18.98%, 0.84% respectively. Women with single complication were more in number, 99(40.08%) when compared with double, triple and multiple complications i.e. 36(14.57%), 6(2.42%), 1(0.4%). Second majorly identified condition was vomiting in the percentage of 11.96%. 37.24% cases were with pain, and all type of pains was included and remaining conditions were shown in table 2.

Women with multiple conditions (>4) are also observed in our study in a percentage of 7.28%. Women with one condition were more in number with percentage 26.72%, followed by women with two conditions (21.45%) and three conditions (11.33%).V itamins supplements were highly prescribed drugs in all the three trimesters. Iron, mineral, calcium supplements are frequent prescribed drugs in third trimester followed by second and first trimester. Sex hormones are highly prescribed in first trimester followed by second and third as shown in the table no.3. Prescribing of antibiotics was gradually increased from 1st to 3rd trimester due to patient conditions and complications.

More number of A, B, C category drugs were given in second trimester when compared to first and third trimester. Equal number of drugs were given in D category and X category drugs are mostly prescribed in first trimester. Overall percent of drugs in C category was more 39.84% followed by A category drugs 31.82%, B category drugs 26.62%, X category drugs were given in the percentage of 0.82% followed by D category drugs 0.45%. HCG was the mostly prescribed drugs in1st trimester, which helps in maintenance of corpus luteum which helps in secretion of progesterone in first trimester. Misoprostol was the second most prescribed drug shown in table 4. Use of X drugs causes certain consequences such as birth defects, fetal abnormalities, premature birth, uterine rupture, abortions etc.

DISCUSSION

Periconception care is very much needed to avoid exposure to harmful substances that cause teratogenic effects.[2] that is why, for the safe prescribing of drugs in pregnancy USA - Food and Drug Administration has classified drugs into different categories. They are A, B, C, D and X drugs. Complications in prenatal women are common, like Anemia, UTI, Thyroid dysfunction, Hypertension, Diabetes, Eclampsia, Loss of pregnancy, other conditions like GERD, constipation, diarrhoea, nausea, vomiting, itching, PV discharge and bleeding, headache, fever, and pains. In our study there are total 247 pregnant women. The dominant age group involved is 23-27(44.53%) years age group followed by 18-22(31.98%), 28-32(19.03%), and 33-37 (3.64%), 38-43 (0.8%) years' age group. Study by Fantahun Molla et al., showed that age group of 18-25 was higher in percentage and lowest was 36-40 years of age.[6] Study by SW Wen et al., stated in their study that age group was dominant in 25-29 years, and least was less 20 maternal age.[19] The selection of patients was not biased in terms of trimester. Majority of the sampled women belonged to the third trimester; it gives us the idea that the pregnant woman frequently visits the hospital during their late trimesters. Trimester distribution in our study was more in third trimester(61.9%) and least in first trimester(12.1%). study conducted by Mesfin Fikadu et al., stated that majority of women visited ANC are from first trimester followed by second and third.[20]Regular visits are increased due to much awareness regarding checkups during pregnancy. In our study we conducted percentage distribution of pregnancies which showed higher percentage in primary gravida of 39.2%, followed by secondary, tertiary and multiple gravida. Miscarriage in pregnancies who visited the hospital showed 21.45% of single miscarriage followed by double with 11.33%, triple and multiple with equal percentage of 2.83%. Women with no miscarriages are in higher percentage of 61.53%. In our study consanguinity was less in percentage with 83.4% compared to women with consanguinity with percentage of 16.5%. This shows that there is a less chance of genetic disorders in offspring in our study. In the review article done by Hanan Hamamy the mounting public awareness on prevention of congenital and genetic disorders in offspring is driving an increasing number of couples

contemplating marriage and reproduction in highly consanguineous communities to seek counselling on consanguinity. Preconception and premarital counselling on consanguinity should be part of the training of health care providers particularly in highly consanguineous populations.[21] Pregnant women often suffer from different types of complications. In our study miscarriages are of higher percentage (30.92%) followed and hypothyroidism (10.9%) and oligohydramnios (8.93%). and we included least number of complications in others of percentage (1.71%), other complications include down's risk, hepatitis B, hypotension, placenta previa, pre eclampsia. Loss of pregnancy was less in the study conducted by Devkota R et al., hypothyroidism and oligo hydramnios was also less in number than miscarriage.[7] In our study women with single complication was more in number when compared to double and triple that is in the percentage of 40.08%, 14.57%, and 2.42%. Women with multiple complications are in the percentage of 0.4%. Majority of the women suffered from pain which is in the percentage of 37.24% among all the conditions in antenatal women, we included all the types of pains which are back pain, abdomen pain, stomach pain, leg pain, epigastric pain, body pains, chest pain, knee pain. Second mostly condition was vomiting (11.96%) which is common in all the pregnant women. And other mostly observed conditions include cough, cold, fever, headache, nausea, acid re-flux. PV bleeding and pv discharge was observed in few pregnant women. In the study done by Devakota R et al., most of the cases are presented with pain followed by nausea and vomiting.[7]. In the study conducted Diego F Wyszynski et al., highest percentage was observed in nausea followed by pain.[5] In our study most of the pregnant women were presented with one condition I.e. in the percentage of 26.72% followed by two conditions(21.45%), three conditions(11.33%) and four conditions with the percentage of 8.09%. pregnant women with multiple conditions were in the percentage of 7.28%. C category drugs were most prescribed drugs in our study with the percentage of 39.84%, A category drugs were next most prescribed drugs with the percentage of 31.82% and B category drugs were prescribed in the percentage of 26.62%. D and X category drugs were prescribed in the percentage of 0.45% and 0.82% respectively. Non FDA categorized drugs were prescribed in the least percentage of 0.42%. In the study conducted by Chaine Admasie et al., showed more number of A category drugs was prescribed followed by B, C, D or X.[22] the study conducted by Mesfin Fikadu et al., majority of drugs prescribed are from B category followed by C and A. D category were also more in number when compared to our study. X category drugs are more in percentage (1.09%) compared to ours. Non FDA categorized drugs accounts for 5.5% where as our study shows 0.42%.[20] This difference is due to variation in subjects complications, conditions and different drugs used to treat them in respective studies. Most commonly prescribed X category drugs were HCG(21) in the percentage of 0.63%, followed by misoprostol (3) in the percentage of 0.06% and the other drugs include oxytocin and estradiol, leuproreline i.e. 0.03% percentage. In the study conducted by Mesfin Fikadu et al., shows mesoprostol prescribed in the frequency of 5.[7]

Table 1: Types of complications in antenatal women

Types of complications	Frequency of total Pregnant women (%)
Miscarriage	90 (30.92)
Hypothyroidism	32 (10.9)
Oligo Hydramnios	26 (8.93)
Hypertension	16 (5.49)
Diabetes	10 (3.43)
Anemia	8 (2.74)
UTI	6 (2.06)
Poly Hydramnios	5 (1.71)
Asthma	2 (0.68)
Depression	2 (0.68)
Candid Vaginitis	2 (0.68)
Others	5 (1.71)
Nil	87 (29.89)

Table 2: Types of conditions among antenatal women

Type of Conditions	Frequency (%)
Acid Reflux	12(2.7)
Gastritis	4(0.9)
Abdomen Discomfort	11(2.48)
Nausea	18(4.06)
Vomiting	53(11.96)
Constipation	12(2.7)
Diarrhoea	11(2.48)
Pains	92(37.24)
Fever	26(5.86)
Cold	38(8.57)
Cough	39(8.8)
Edema	17(3.83)
Giddiness	11(2.48)
Headache	20(4.51)
Insomnia	6(1.35)
Itching	11(2.48)
Shortness of breath	14(3.16)
PV Bleeding	16(3.61)
PV Discharge	13(2.93)
Weakness	5(1.12)
Others	14(3.16)

Table 3: Most frequently used drugs in each trimester

Class	Drugs In First Trimester	Drugs in second Trimester	Drugs In Third Trimester
Vitamin	327(43.65%)	489(35.46%)	367(30.6%)
Sex Hormones	73(9.74%)	38(2.75%)	15(1.25%)
Iron	24(3.2%)	113(8.19%)	119(9.92%)
Mineral	54(7.2%)	143(10.36%)	163(13.59%)
Calcium	26(3.47%)	122(8.84%)	132(11%)
Anti platelet	35(4.67%)	66(4.78%)	29(2.41%)
Anti emetic	36(4.8%)	29(2.1%)	14(1.16%)
Antihistamine	28(3.78%)	28(2.03%)	25(2.08%)
Protein	20(2.67%)	58(4.2%)	58(4.83%)
Amino Acids	24(3.2%)	39(2.82%)	32(2.66%)
Antibiotics	16(2.13%)	50(3.62%)	55(4.58%)

Table 4: X category drugs prescribed in antenatal women

X Drugs	Frequency	Possible consequences
Misoprostol	**3 (**0.06%**)**	Birth defects, premature birth, uterine rupture, miscarriage
HCG	**21 (**0.63%**)**	Ovarian hyper – stimulation syndrome, edema or inflammation
Estradiol	**1 (**0.03%**)**	Birth defects
Leuproreline	**1 (**0.03%**)**	Spontaneous abortion, fetal abnormalities
Oxytocin	**1 (**0.03%**)**	Neonatal jaundice, neonatal retinal hemorrage

As our study is observational we did not conduct any interventions but the interventions are necessary to eradicate possible consequences. Though X category drugs are prescribed the perception of the prescriber to treat the patient special conditions where there is no other choice of drugs. In the study conducted by Diego F Wyszynski et al., HCG was given in the percentage of 0.6% whereas in our study 0.63%.[5]

In the study conducted by RAEBEL et al., X category drugs were given in the percentage of 30.3% in interventional group and 22.4% in usual group.[3] In our study we differentiated top 11 prescribed class of drugs according to their trimesters. Vitamins supplements were highly prescribed drugs in all the three trimesters. Iron, mineral, calcium supplements are frequent prescribed drugs in third trimester followed by second and first trimester. Sex hormones are highly prescribed in first trimester followed by second and third. Prescribing of antibiotics was gradually increased from 1st to 3rd trimester due to patient conditions and complications in our study. In the study conducted by Dileep K Rohar et al., percentage of multivitamin (79.4%) was high in all the three trimesters.[23] In the study conducted by J.Z. AL-Hamimi et al., showed highest percentage of multivitamin tablets, followed by Paracetamol and aspirin.[24] In the study conducted by Uchenna I. EZE et al., showed highest distribution of medicines were mineral and vitamin supplements followed by analgesics.[25] Assessment of complications according to age in our study was highest in age group of 23-27 and was least in the age group of 38-43 with the sample size of 2. In the study conducted by Devkota R showed highest frequency of complications in the age group of 20-24 years and least number of complications were observed in the age group of 40-44.[7]

CONCLUSION

A large number of complications and conditions during pregnancy were observed. Miscarriages were observed in highest percentage. X category drugs also were prescribed in pregnant women. This study reveals that keen observation is needed during prescribing drugs to pregnant women so as to avoid risk. Both physician and clinical pharmacist should be well aware of the drugs which are causes risk.

ABBREVIATIONS

UTI: Urinary tract infection
FDA: Food and drug administration
GERD: Gastroesophageal reflux disease
HCG: Human chorionic gonadotropine

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