

Medication Safety in Obstetrics and Gynecology Ward in Jayanagar General Hospital, Bangalore, India

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ABSTRACT

Objective: The present study is aimed at Medication Safety in Obstetrics and Gynecology Ward in Jayanagar General Hospital, Bangalore, India

Methodology: It is a prospective observational study, conducted in the inpatient obstetrics and gynecology ward in Jayanagar General Hospital. The study was conducted for 6 months. CRF (Case record form) was designed to record the clinical profile and treatment pattern which contains patient demography, family history, past medication history, obstetric history and follow up and further medication safety was assessed in the patient according to WHO and US-FDA guidelines. The patient demographics and all medically relevant information were noted in a predefined data collection form. Alternatively, these case charts were reviewed for prescription legibility and completeness, unaccepted abbreviations, the capture of relevant information in case sheets, contraindication, drug interactions, and adverse drug events.

Result: The data of 150 pregnant women admitted to obstetrics and gynecology ward for delivery related care during the period October 2018 to April 2019 were analyzed. It was observed that 20.67% had Hypertension, 14.67% had Gestational diabetes mellitus, and 8.67% had urinary tract infections as major comorbidities. Among the study population most of them 20.67% had oligohydramnios as a major pregnancy risk factor followed by 12% of preeclampsia and 3.33% of small for gestational age. A total of 1950 drugs were prescribed, and thus the average number of drugs per patient was 13.28. Iron, folic acid, calcium, and vitamins were the most frequently used drugs during the pregnancy. Category A drug constituted 623(54.50%) followed by category B drug 398(34.82%) out of 1950 drugs used in pregnant subjects. Another category C, D and X were 6.99%, 3.5% and 0.1% respectively. The most common drug interaction was found to be between Metronidazole and ondansetron, which may be due to high usage of tramadol and metoclopramide in pregnancy.

Conclusion: Among the study patients most them 75.33% were in the age group of 21-30 years. Most of the 20.67% and 14.67% had hypertension and gestational diabetes mellitus as co- morbidities. On the review of 150 prescriptions, the average number of drugs prescribed was found to be 7.62. Iron, folic acid, calcium, and vitamins were the most frequently used drugs during the pregnancy. Most of the used drugs were from Category A (54.50%). Only 0.1% of the drug were from Category X. There were 183 possible risks of major potential drug interactions. The most common interaction was between Metronidazole and ondansetron. The majority of the drugs were prescribed as per FDA category A, the safest category during pregnancy.

Keywords: Medication Safety, Obstetrics, Gynecology, pregnancy

INTRODUCTION

Medication safety during pregnancy has drawn constant attention globally since the thalidomide disaster in the 1960s [1]. Information on prenatal medication safety is truly missing since pregnant ladies are generally avoided from pre-promoting clinical preliminaries out of moral concerns. Creature concentrates as a wellspring of reference likewise have huge restrictions and ought to be deciphered with alerts [2, 3]. The FDA pregnancy risk category was developed in 1979, consisting of five categories (A, B, C, D, and X) based on published evidence of the risks and benefits of medication use during pregnancy [3]. As per the Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products (21 CFR Part 201) gave in 1979, there were two subsections under the "Pregnancy" part: (I) Teratogenic impacts which allude fundamentally to the danger of fetal irregularities identified with medication use; (ii) Nonteratogenic impacts which allude primarily to the drug's consequences for proliferation or nonteratogenic impacts in the hatchling or baby, for example, withdrawal side effects or hypoglycemia [4].

The unique physiologic changes of pregnancy affect the pharmacokinetics of medications used by pregnant women. During pregnancy, a woman's plasma volume increases by 30-50%, and cardiac output and glomerular filtration rate also increase in a similar proportion. These components add to bring down coursing centralization of certain drugs (particularly those discharged by the kidney) in a pregnant lady and conceivably to sub restorative drug levels. Likewise, there is an increment in body fat during pregnancy; which expands the volume of circulation of fat-soluble drugs. A reduction in plasma egg whites focus during pregnancy builds the volume of circulation for profoundly protein-bound drugs for example anticonvulsants. Be that as it may, the unbound drugs are discharged out more quickly by the kidney and liver; and this balances the impact of an increased volume of conveyance. Because of the impact of progesterone, gastric discharging time is diminished especially in the third trimester hence deferring the beginning of the impact of the drug [5]. Simultaneous utilization of other regular medications during pregnancy, for example, acid neutralizers, iron, and nutrients could likewise tie and

inactivate a few drugs. Intramuscular retention of the drug is by and large more quickly because of increased bloodstream; which improves fundamental drug assimilation and the pace of the beginning of the activity. Ultimately estrogen and progesterone adjust hepatic compound movement; which can expand drug aggregation or reduce the disposal of some drugs⁴. The placenta; the result of origination is the practical unit between fetal blood and maternal blood. The elements of the placenta incorporate sustenance, breath, digestion, discharge, and endocrine action to keep up fetal and maternal prosperity. All together for a drug to cause a teratogenic or pharmacological impact on the fetus, it should cross from maternal course to fetal flow through the placenta by diffusion⁵. The pace of move relies upon the compound properties of the drug, for example, protein official, pH contrast, lipid dissolvability, and an atomic load of the drug [6]. Drugs assume a significant part in improving human wellbeing and advancing prosperity. In any case, to create the ideal impact, they must be protected, effective, and must be utilized sanely [7]. All in all, drugs except if totally important ought not to be utilized during pregnancy since drugs taken by a pregnant lady can arrive at the fetus and mischief it by intersection the placenta, a similar course taken by oxygen and supplements, which are required for the development and improvement of the fetus [8].

Drug-Drug Interactions (DDIs) are defined as pharmacokinetic or pharmacodynamics influences of drugs on each other, which may result in undesired effects, reduced efficacy, or increased toxicity. DDIs result in many adverse clinical outcomes; they are responsible for 5% of all hospital admissions [9]. Approximately 37–60% of patients admitted to the medical clinic may have at least one conceivably interacting drug mixes at admission. In inpatients, the risk of having conceivably interacting drug blends can also increment because new drugs are regularly added to the current drug therapy [10]. The risk of drug teratogenicity is reliant on the level of fetal openness, which is managed somewhat by the carrier proteins in the placenta. Perhaps the most plentiful carrier proteins is P-glycoprotein (P-GP), an efflux carrier communicated in the maternal-confronting surface of the placental tissue. P-GP goes about as an obstruction to keeping some possibly hurtful drugs from entering the fetal dissemination, and its capacity can be tweaked by inhibitors and inducers. Numerous drugs are known to be substrates of P-GP, some of which may likewise restrain or initiate this carrier. The utilization of P-GP inhibitors or inducers in blend with a substrate alluded to as 'P-GP-interceded drug connections', may influence the P-GP boundary work in the placenta and accordingly fetal openness to this substrate [11].

Barely any endeavors were made to distinguish the socio-demographic attributes of pregnant ladies related to mentalities and convictions concerning medications. Among these, education, socioeconomic level, age, occupation, way of life, normal convictions just as the seriousness of ailment were accounted for. A patient's information and ability to get information are significant in the advancement of convictions. Albeit some pregnant ladies may have adequate information about high-risk medication in pregnancy, there is a "general fear" from medications [12].

MATERIALS AND METHODS

It was a prospective observational study conducted in Obstetrics and Gynecology ward at Jayanagar General Hospital. The study was conducted for 6 months. CRF (Case record form) was designed to record the clinical profile and treatment pattern which contains patient demography, family history, past medication history, obstetric history and follow up and further medication safety was assessed in the patient according to WHO and US-FDA guidelines. The patient demographics and all medically relevant information were noted in a predefined data collection form. Alternatively, these case charts were reviewed for prescription legibility and completeness, unaccepted abbreviations, the capture of relevant information in case sheets, contraindication, drug interactions, and adverse drug events. The changes and the daily notes in the case sheets were followed until the patient was discharged or shifted to other wards. The prescription guidelines, Micromedex, Medscape, and reference books were used as tools to review the prescription and case charts. The patient interview was done using predefined questionnaires with their consent to assess the usage, attitude, and beliefs about medication used during pregnancy. The data were stored confidentially and subjected to further analysis using appropriate software. The data were subjected to descriptive analysis using statistical tool IBM SPSS version 23.0 and data was entered in Microsoft Excel version 19. And statistical Results were expressed in percentages and mean-standard deviation (SD). Figure 1.

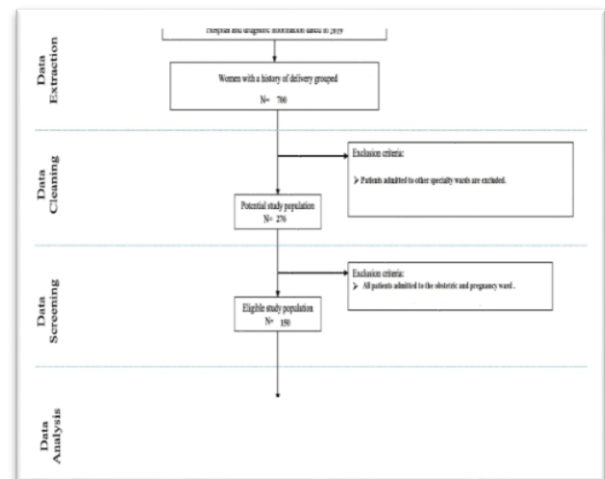


Figure 1: Allocation sequence of participants.

RESULT AND DISCUSSION

The data of 150 pregnant women admitted to the obstetrics and gynecology ward for delivery related care during the period October 2018 to April 2019 were analyzed. The mean age of pregnant patients was 26.38 (± 4.39) which is in agreement with the study by Abubakar K et al. [13] The demographic result of the study revealed a preponderance of pregnant subject in the age group of 21-30 year which is similar to study conducted in North India⁷. Most of the women were multiparous which is similar to a study carried

out by Zaki NM et al. [12] It could probably due to the marriage of women in lower age in India. Also, this could be due to the increased awareness from organizations that are campaigning to ensure reduced maternal mortality and safe motherhood. **Table 1.**

Table 1: Socio-Demographic Characteristic of Pregnant Women

Characteristics	Number of Subjects	Percentage of Subjects
Maternal Age (Years)		
≤20	14	9.33
21 - 30	113	75.33
≥31	23	15.4
Education Status		
Illiterate	22	14.67
Primary	14	27.33
Secondary	55	36.67
University	32	21.33
Parity		
First-time pregnancy	57	38
1-3 previous children	70	46.66
More than 3 previous children	23	15.34
Previous abnormal child		
Yes	12	8
No	138	92

It was observed that 20.67% had Hypertension, 14.67% had Gestational diabetes mellitus, and 8.67% had urinary tract infections as major comorbidities. Similarly, another study conducted in Canada reported Diabetes and Hypertension as major comorbidities. Comorbidity increases the total burden of the illness in a patient and also contributes to clinical outcomes as well as to economic outcomes. The majority 20.67% had oligohydramnios as a major pregnancy risk factor followed by 12% of preeclampsia and 3.33% of small for gestational age. This finding is in agreement with the study conducted by Wenman WM et al. [14] Table 2.

Table 2: Co-morbidities associated with study patients

Comorbidities	Number of subjects	Percentage of subjects
Hypertension	31	20.67
Diabetes Mellitus (Gestational)	22	14.67
Urinary Tract Infection	13	8.67
Asthma	9	6
Epilepsy	5	3.33
Hepatitis	4	2.67

Among the study population most of them 20.67% had oligohydramnios as a major pregnancy risk factor followed by 12% of preeclampsia and 3.33% of small for gestational age. The prevalence of pregnancy risk factors was shown in **Figure 2.**

A total of 1950 drugs were prescribed, and thus the average number of drugs per patient was 13.28. Iron, folic acid, calcium, and vitamins were the most frequently used drugs during the pregnancy. NSAIDs, prostaglandin analogs, antibiotics, and H2 receptor blockers were other commonly used drugs during pregnancy. Alprazolam and Diazepam were the most commonly used anxiolytic drugs. Nifedipine and methyldopa were the most commonly used antihypertensive. Promethazine was the most commonly used antihistaminic drug. Methyldopa was the most

commonly used vasodilator in pregnancy. The details of the medication used is shown in Table 3.

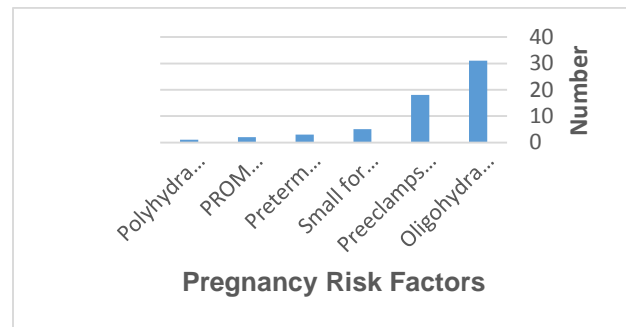


Figure 2: Prevalence of Pregnancy risk factors

Table 3: Pattern of Drug Use during Pregnancy

Parameters	Number of Subjects	Percentage of Subjects
Iron	112	5.7
Folic Acid	150	7.7
Calcium	114	5.8
Vitamins	120	6.2
Paracetamol	47	2.4
Tramadol	76	3.9
NSAIDs	141	7.2
Antiemetic	128	6.6
Ranitidine	144	7.4
Calcium Gluconate	32	1.6
Antibiotics	65	3.3
Alprazolam	2	0.1
Diazepam	48	2.5
Prostaglandin Analogs	82	4.2
Antispasmodics	58	3.0
Cefixime	138	7.1
Enoxaparin	3	0.2
Progesterone	2	0.1
Antimalarial	1	0.1
Methyldopa	6	0.3
Oxytocin	60	3.1
Nifedipine	14	0.7
Promethazine	119	6.1
Metronidazole	138	7.1
Pantoprazole	72	3.7
Ciprofloxacin	27	1.4
Ceftriaxone	38	1.9
Drotaverine	13	0.7

Generic prescribing was less compared to other studies by Rohra DK et al.[15] The use of generic drugs is becoming more popular in the world and it is commonly used as an option to reduce the higher costs of treatments with originals. Generic prescribing is considered as a safety precaution for the patients as it gives clear identification and enables easy information exchange and allows better communication between health care providers. The use of brand names may lead to the increased cost of drugs for these women. Factors that may be responsible for this trend include the influence of drug promotional activities, pressures of pharmaceutical detail men, lack of continuing education on the principles of rational prescribing and non-familiarity with generic names among the prescribers. In my study, iron, folic acid, calcium, and vitamins were the most

as often as possible utilized drugs in pregnancy. Isoxsuprine, progesterone, paracetamol, NSAIDs, anti-infection agents, enemies of emetics, proton siphon inhibitors/H2 blockers, antacids, and antihypertensive drugs (nifedipine, methyldopa) were the other normally utilized drugs.

In a prospective study in Southwestern Finland, iron and vitamin supplementation were the most as often as possible utilized drugs, trailed by analgesics, tocolytic specialists, and drugs for persistent conditions and basic pregnancy indications. [16] In another study from Australia, folate (70%), iron (38%), and multivitamins (27%) were the most frequently taken drugs by pregnant women; along with herbal drugs like ginger (20%) and raspberry leaf (9%). [17]

Periconceptional folic acid supplementation can prevent most neural tube defects and other congenital abnormalities of the cardiovascular system, urinary tract, and limb deficiencies. Moreover, folic-acid supplementation in pregnancy is associated with the decreased incidence of habitual spontaneous abortion and pregnancy complications (e.g., placental abruption and preeclampsia) [36]. Percentage encounter with antibiotics was found to be 43.33%, this is higher than the recommended value of 20%. Antibiotics are usually prescribed with caution due to the problem of drug resistance, bearing this in mind the higher percentage of antibiotics prescribed in the study could be due to opportunistic infections, respiratory and urinary tract infection which occur commonly among pregnant women. A similar result (43.5%) was reported by Reddy BR37 et al. Paracetamol was the most prescribed analgesic during pregnancy (>31.33%), this may be due to its affordability, tolerability, and lack of the adverse effect of the NSAIDs.

Category A drug constituted 623(54.50%) followed by category B drug 398(34.82%) out of 1950 drugs used in pregnant subjects. Another category C, D and X were 6.99%, 3.5% and 0.1% respectively. Category A drugs were multivitamins, iron, folic acid, calcium, thyroxin. Category B drugs were paracetamol, diclofenac sodium, antacids, ranitidine, ampicillin, amoxicillin, cephalosporins, metronidazole, insulin, methyldopa. Category C drugs were Nifedipine, pantoprazole. Category D was antiepileptic. The Category X drug was progesterone. US FDA pregnancy risk categories of drugs used in pregnancy were shown in Figure 3.

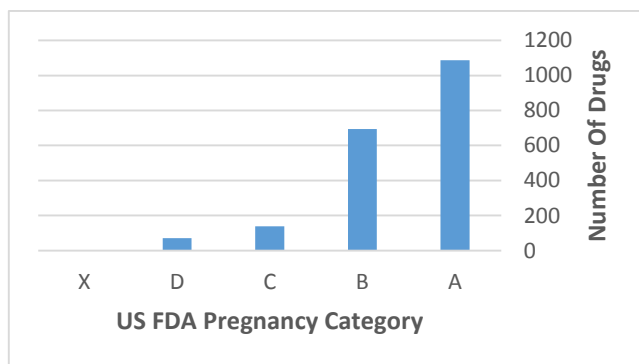


Figure 3: US FDA Pregnancy Risk Category of Drugs used

The normal number of drugs per prescription is a significant record of a prescription review. It is desirable to keep the number of drugs per prescription as low as conceivable to limit the risk of drug cooperations and clinic costs. The mean number of drugs received by patients in the present study (7.62) was higher compared to a report from another study in 2014 which recorded a mean of 3.1 drugs. [26] This may be related to the physician's tendency to polypharmacy and also multiwindowed prescriptions written for some patients. Polypharmacy is characterized as the corresponding utilization of at least five drugs and it could upgrade drug associations and drug-related issues. Extensive polypharmacy (81%) that is more than five drugs were prescribed in all the patients. Polypharmacy in some instances becomes necessary especially when the patient has some co-morbid conditions associated with the pregnancy. Moreover, most pregnant women take hematinic and vitamins such as Iron preparations, folic acid, ascorbic acid, and vitamin B complex tablets.

The majority of the drugs used during pregnancy in the present study, were from category-A, followed by Category-B and category-D whereas category-X was 0.1%. There are reports of the use of potentially harmful drugs (category D drugs-1.5% to 4.8% and category X drugs-2.3 to 4.6%) during pregnancy from other developed and underdeveloped countries of the world.

In a retrospective, register-based cohort study in Finland, it was found that 20.4% of women purchased at least one drug classified as potentially harmful during pregnancy and 3.4% purchased at least one drug classified as clearly harmful. [18] According to the HIMAGE study from France, 4.6% of women were exposed to drugs (mainly NSAIDs), involved in risk during pregnancy. In a study from Bratislava and Nitra, it was reported that a vast majority of prescribed drugs during pregnancy, belonged to Category-C. [20]

The study prescriptions comprised 179(49.72%) pharmacodynamics drug interaction, 92(25.56%) were by an unknown mechanism and 89(24.72%) were pharmacokinetic drug interaction. These findings were different from another study reported in the literature where the pharmacokinetic drug interaction was dominant. [10] The severity assessment of drug interaction in the present study showed that most of the interactions were major (183) followed by moderate (173) and contraindicated (4). This trend is different from that found in another report. [21] The most common drug interaction was found to be between Metronidazole and ondansetron, which may be due to high usage of tramadol and metoclopramide in pregnancy. The most common management plan found in the present study for most of the drug interaction was monitoring and time spacing; this is similar to the results reported by Bergk, V., and colleagues. [22] The result obtained in the present study was based on the classification as minor, moderate, or major according to the Micromedex-2 drug interaction checker. Sepehri and colleagues used a similar software detection approach and found the occurrence of drug interaction in 20% of patients which is lower compared to this study. [23] Table 4

Table 4: Potential Drug-drug Interactions

Parameters		Total N
Severity	Major	183
	Moderate	173
	Contraindicated	4
	Total	360
Pharmacokinetic Interaction	Absorption	89
	Synergism	127
Pharmacodynamics Interaction	Antagonism	52
	Total	179
Unknown Mechanism		92

CONCLUSION

Pregnancy is a special physiological condition where drug treatment presents an extraordinary concern because the physiology of pregnancy influences the pharmacokinetics of medications utilized and certain medications can arrive at the fetus and cause hurt. The extraordinary physiologic changes of pregnancy influence the pharmacokinetics of medications utilized by pregnant ladies. During pregnancy, a lady's plasma volume increments by 30-half, and cardiovascular yield and glomerular filtration rate additionally increment incomparable extent. Among the investigation patients, the greater part of the 75.33% was in the age gathering of long term. Most of the 20.67% and 14.67% had hypertension and gestational diabetes mellitus as co-morbidities. On the review of 150 prescriptions, the average number of drugs prescribed was found to be 7.62. Iron, folic acid, calcium, and vitamins were the most frequently used drugs during the pregnancy. Other drugs include paracetamol, prostaglandin analogs, antibiotics, and H2 receptor blocker. Most of the used drugs were from Category A (54.50%). Only 0.1% of the drug were from Category X. There were 183 possible risks of major potential drug interactions. The most common interaction was between Metronidazole and ondansetron. The management for most adverse drug interactions was monitoring and time spacing. Most women had an inspirational mentality toward medications in general however they accepted pregnant ladies ought to be more mindful concerning drug-use during pregnancy. About 32.67% of the participants were able, individually, to name some medications to be avoided during pregnancy. The primary information sources were from gynecologists followed by general practitioners and pharmacists. Overall drug use pattern is rational with few exceptions. A larger part of the drugs was endorsed according to FDA class A, the most secure classification during pregnancy. Short of what one percent of the pregnant ladies going to tertiary consideration medical clinics in Bangalore are endorsed teratogenic drugs. The average number of prescriptions per encounter was much higher than the WHO standard, indicating the occurrence of polypharmacy. Generic drug prescribing was low. The drug interaction was found to be potentially harmful so monitoring should be required for appropriate management. The insufficient information regarding drugs in pregnancy is a territory that requires further improvement future. Drug specialists, with skill in furnishing ladies with positive convictions about medications during pregnancy and in enhancing drug therapy results, are important segments of the medical care

group and ought to be progressively engaged with general wellbeing endeavors. Medical services experts ought to know about ladies' mentalities while encouraging them to take medication during pregnancy. This kind of study can help in assessing the current drug use pattern and in planning appropriate interventions to ensure rational drug therapy. The insufficient information regarding drugs in pregnancy

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