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# The Study of Drug use and Drug-Drug Interactions in Hospitalized Pregnant Women at Hayatabad Medical Complex, Peshawar

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**Abstract:-**
**Introduction: Pregnancy is a unique physiological situation in which medication therapy poses unique challenges. The use of drugs, during pregnancy raises additional concerns because, in this case, the health and life of the woman's fetus are also at danger. Medicines provided to pregnant women for medical reasons may have substantial anatomical and functional consequences for the fetus.**
**Aim: To evaluate drug utilization pattern and Identify drug-drug interactions in pregnant patients' prescriptions at HMC Peshawar.**
**Materials and Methods: Observational study aimed from June 2022 to August 2022 in Gynecology Ward A at Hayatabad Medical Complex Peshawar, KpK, Pakistan. 120 prescriptions in total were collected using the selective sample method.**
**Results: In 120 prescriptions, a total of 328 drugs were prescribed, with an average of 2.73 medications prescribed per case. In all trimesters category A drugs were mostly prescribed comprised of 14 (50%), 42 (52.5%) and 148 (64.9%) drugs, in 1st, 2nd and 3rd trimester respectively. In total 120 prescriptions, 83 (69.1%) interactions were observed among which 82 interactions were reported from 3rd trimester followed by 2nd trimester with only 01 interaction. Majority interactions were of Ketorolac (15 interactions) followed by Tramadol which contributed 9 drug interactions. Types of interactions were classified on the basis of severity among which 30.1% interactions were Minor, 67.4% interactions were Moderate and 2.4% interactions were of Major type.**
**Conclusion: Women of childbearing age need to be informed about the benefits and risks of drug use during pregnancy, with a special focus on alternative therapies and self-medication. Even the medical professionals must be skilled to treat pregnant women rationally.**

***Keywords:-*** *Pregnancy, Drug-Drug Interactions.*

**Abbreviations**
**HMC**- Hayatabad Medical complex
**KPK**-Khyber Pakhtunkhwa
**DDI**- Drug-Drug Interactions
**WHO**-World health Organization
**ADR**-Adverse Drug reaction

## I. INTRODUCTION

Pregnancy is a unique physiological circumstance in which medical therapy confers a particular anxiety. When providing prenatal medical counseling, it is mandatory to conduct a careful analysis of the benefits to the mother and the potential risks to evolving infants [1]. Because in this condition the health and life of the fetus are also at danger in addition to the woman, the use of drugs during pregnancy awakens for special awareness. Pregnant women may experience substantial structural and functional harm from the drugs they are prescribed for medical reasons [2]. Since the thalidomide catastrophe in the 1960s, international attention has been focused on prenatal medicine. Since pregnant women are typically excluded from pre-promoting medical preliminaries due to moral concerns, there is actually little evidence regarding prenatal medication care. [3].In 1979, the FDA created a pregnancy risk category consisting of five categories (A, B, C, D, and X) based on available research on the disadvantages and benefits of drug usage during pregnancy.

Drug-Drug interactions occur when two drugs are used concurrently and the impact or effects of one drug are altered by the presence of another [4]. When a patient uses OTC (Over the counter) medications and multiple medications, interactions and other problems based on interactions become more challenging [5]. Numerous drug therapies or the use of numerous medications is closely associated with an increased risk of hospitalization, adverse drug events or drug reactions, pharmaceutical errors such as prescription, dispensing, dose error, and drug-drug interactions [1]. Many surveys have also revealed that approximately 3% of all hospital admissions are related to drug-drug interactions [6]. The most crucial procedure now used by pharmacists to identify and detect drug-drug interactions in prescriptions is manual review, however the accuracy and efficacy vary from prescription to prescription depending on the number of drugs dispensed. The accuracy and effectiveness of prescriptions with only 2 medications in them for drug-drug interactions is determined to be only 70%, and the percentage rapidly decreases as the number of medications rises [7]. Computerized drug-drug interaction screening methods, which can identify harmful drug-drug interactions more quickly and accurately than can be done with manual review alone, are the most sophisticated way of drug-drug interaction identification and detection [8].

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Drug-drug interactions are broadly classified into two categories i.e basis of mechanism of action and basis of severity. a. Typically, three broad categories of underlying mechanisms are used to describe drug interactions. i. Pharmacokinetic interactions occur when the absorption, distribution, metabolism, or excretion of one medication is altered by another [6]. ii. When one drug alters the pharmacological activity or effects of another, this is referred to as a pharmacodynamics drug interaction [9]. iii. Pharmaceutical interactions occur when two substances or medications that are physically or chemically incompatible interact with one another. [10]. b. As per facts Compendia of drug interactions, Drug interactions are classified as follows on the basis of severity: (a) Major: The implications of Major types of interactions are either fatal or capable of causing lasting alterations. These alterations are irreversible, and permanent damage may result. There is no cure for such medication interactions. (b) Moderate: The Effects of Moderate interactions may aggravate a patient's clinical condition. Such interactions result in manageable outcomes. The patient's condition may be critical, yet it is manageable. (c) Minor: Minor interactions usually have minor effects. The results could be tedious or unimpressive. These kinds of interactions-related effects are not discernible [11].

## II. MATERIALS AND METHODS

From June 2022 to August 2022, an observational study was carried out in the gynecology ward A of the Hayatabad Medical Complex in Peshawar, Pakistan. For the study, a total of 120 prescriptions were reviewed, and three prescriptions each day were assessed.

### *A. Study Design*

Inpatients prescriptions were included for the study. Patients between the ages of 20 years and 45 years were included in the study, whereas those older than 45 were not. The study did not include a prescription that just contains one drug. Patients who did not have pregnancies but had any other gynecological problems were also excluded from the study. The study omitted all patients who did not meet the inclusion criteria. We strictly followed the inclusion and exclusion criteria and selected 120 prescriptions and patient histories for evaluation.

### *B. Collection of Data*

Only data from hospitalized pregnant women were collected, using a selective sampling technique. The data collected included the patient's age, diagnosis, previous medical or medication history, and prescribed drugs. Data was gathered using patient case sheets and medical records. On a pre-designed data sheet, patients' demographic information, past histories of chronic diseases, and medications data were recorded, which was standardized as per requirement of the project. The complaints associated with gynecological issues and diagnosed diseases, Lab findings or Biochemical tests for diagnosis, Dose, mode of administration of drug, dose form, frequency, drug generic name, and drug-related issues were also recorded.

### *C. Analysis of Data*

Spreadsheet 2010 of Microsoft Excel was used to record all the data. Age of patients and prescribed medications were represented using percentages and frequencies. As needed, the terms mean and median were employed. Pie charts and tables were used accordingly.

### *D. Evaluation of Data*

Drug Interactions Checker, Medscap's online drug interaction checker, and the handbook of drug interactions were used to identify drug-drug interactions.

## III. RESULTS

According to the findings of this survey, majority of pregnant patients who visited the hospital were between the ages of 20 years and 25years, accounting for approximately 54.16% of all patients, followed by those between the ages of 26 years and 30 years (29.16%). The percentage of patients aged 31-35 years was 10.83%, 36-40 years was 4.16%, and 41-45 years was 1.66%. It is evident that maximum patients of study population who visited hospitals were in 3rd trimester (79.1%) followed by 2nd and 1st trimester (12.6%) and (8.3%) respectively. (Table 1)

Table 1: Trimester wise Distribution

| Trimester | No. (%) |
|---|---|
| First Trimester | 10 (8.3%) |
| Second Trimester | 15 (12.6%) |
| Third Trimester | 95 (79.1%) |

In all trimesters category A drugs were mostly prescribed comprised of 14 (50%), 42 (52.5%) and 148 (64.9%) drugs, in 1st, 2nd and 3rd trimester respectively. The category B, C and D drugs were mostly prescribed in 3rd trimester comprised of 18 (7.89%), 26 (11.4%) and 28 (12.28%) respectively. Following the Pearson Chi-square test no significant relationship was observed between the drug categories and their prescription frequencies in all three trimesters. Overall the Chi-square value X2 (13.8) is less than critical value at degree of freedom of 8 as per distribution chart (X2 = 15.51). (Table 2).

ISSN No:-2456-2165

Table 2: Different categories and classes of drugs used during different trimesters.

| Category | 1st Trimester n=28 (%) | 2nd Trimester n=80 (%) | 3rd Trimester n=228 (%) | P-value |
|---|---|---|---|---|
| A (Vitamins or vitamin complex, Antibiotics, Calcium/Calcium complex) | 14 (50) | 42 (52.5) | 148 (64.9) | 0.199 |
| B (Antihistamines, Folic Acid, NSAIDS) | 07 (25) | 14 (17.5) | 18 (7.89) | 0.199 |
| C (proton-pump inhibitors, Tranexamic acid, Cranberry fruit concentrate), (Tramadol, Beta blockers, Ondansetron) | 02 (7.14) | 12 (15) | 26 (11.4) | 0.199 |
| D (Iron and iron complex, L-methylfolate, Insulin), Alginate compound, Amlodipine, Cefoperazone/ Sulbactam Dextrose 5%, Furosemide Heparin,l-ornithine-l-aspartate Phloroglucinol /Trimethylphloroglucinol Oxytocin | 04 (14.29) | 11 (13.75) | 28 (12.28) | 0.199 |

A total of 328 medicines were prescribed, with an average of 2.73 being prescribed per prescription. Vitamin and vitamin complex were frequently prescribed in all three trimesters followed by antibiotics. Drug use pattern in study population. (Table 3).

Table 3: Drug Use pattern in Study population

| Name/class of drug | Total number (328) | Distribution in first trimester (n=28) | Distribution second trimester (n=79) | Distribution third trimester (n=221) |
|---|---|---|---|---|
| Vitamins or vitamin complex | 124 | 12 (12.8%) | 27 (34.1%) | 85 (38.4%) |
| Antibiotics | 53 | 02 (7.1%) | 09 (11.3%) | 42 (19.0%) |
| Calcium/Calcium complex | 27 | - | 06 (7.5%) | 21 (9.5%) |
| Antihistamines | 13 | 02 (7.1%) | 07 (8.8%) | 04 (1.8%) |
| Folic Acid | 13 | 04 (14.2%) | 03 (3.7%) | 06 (2.7%) |
| NSAIDS | 13 | 01 (3.5%) | 04 (5.0%) | 08 (3.6%) |
| proton-pump inhibitors | 12 | 01 (3.5%) | 08 (10.1%) | 03 (1.3%) |
| Tranexamic acid | 11 | - | - | 11 (4.9%) |
| Cranberry fruit concentrate | 10 | - | 04 (5.0%) | 06 (2.7%) |
| Iron and iron complex | 06 | - | 06 (7.5%) | - |
| L-methylfolate | 05 | - | 05 (5.0%) | - |
| Insulin | 04 | - | - | 04 (1.8%) |
| Tramadol | 04 | 01 (3.5%) | - | 03 (1.3%) |
| Beta blockers | 03 | - | - | 03 (1.3%) |
| Ondansetron | 03 | - | - | 03 (1.3%) |
| Alginate compound | 02 | 02 (7.1%) | - | - |
| Amlodipine | 02 | - | - | 02 (0.9%) |
| Cefoperazone/ Sulbactam | 02 | - | - | 02 (0.9%) |
| Dextrose 5% in Water | 02 | - | - | 02 (0.9%) |
| Furosemide | 02 | - | - | 02 (0.9%) |
| Heparin | 02 | | | 02 (0.9%) |
| l-ornithine-l-aspartate | 02 | 02 (7.1%) | - | - |

Out of 120 prescriptions, 83 drug-drug interactions were reported. More than two drug-drug interactions have been documented in some prescriptions. In 83 interactions 82 were reported in third trimester. Nearly 69% of interactions between drugs were observed. The most common type of drug-drug interaction (DDI) was the moderate type, which made up roughly 67.4% of all DDIs, then type minor and type major. Minor and Major type of DDIs percentage was 30.1 % and 2.4% respectively. (Table 4)

Table 4:Classes of Drug-Drug Interactions

| Total drug-drug interaction | | 83 |
|---|---|---|
| **Class of DDIs** | **No. of interactions** | **Percentage** |
| Minor | 25 | 30.1% |
| Moderate | 56 | 67.4% |
| Major | 02 | 2.4% |

Each prescription was assessed for Drug-drug interactions. As most of drug interactions were of Moderate and Minor type, except two which were severe type, therefore effect of drug is not so dangerous. The effect is either a decrease in one medication's metabolism or an increase in the serum levels of another drug as in case of Metronidazole+Ketorolac and Tramadol+ Omeprazole respectively. Total of 83 drug-drug interaction has been identified. Interactions that occur frequently, as well as the type of interaction and the effect mentioned. (Table 5)

Table 5:Classes and Effects of Drug-Drug Interactions

| Interacting Drug | Severity/ nature of Interaction | Effect |
|---|---|---|
| Metronidazole+Ketorolac | Moderate/ Pharmacokinetics | Ketorolac metabolism is reduced when Ketorolac and Metronidazole are used together. [12]. |
| Omeprazole+Ketorolac | Moderate/ Pharmacokinetics | Combination of Ketorolac with Omeprazole reduced metabolism of Ketorolac [12] |
| Ketorolac+Ceftriaxone | Moderate/ Pharmacodynamics | The chance of nephrotoxicity can be amplified when Ketorolac is used in combination with Ceftriaxone. [13] |
| Ibuprofen+ Ketorolac | Major/ Pharmacodynamics | The risk or severity of adverse effects can be increased when Ketorolac is combined with Ibuprofen. Concomitant use of ketorolac with other non-steroidal anti-inflammatory agents is contraindicated due to a lack of synergistic effect and an increased risk of adverse effects such as bleeding. |
| Tramadol+ Metronidazole | Moderate/ Pharmacokinetics | Metronidazole reduced metabolism of Tramadol. |
| Sucralfate+Vitamin D3 | Major/ Pharmacokinetics | The serum concentration of Sucralfate can be increased when it is combined with Cholecalciferol. Vitamin D/analogs are known to increase aluminum absorption and retention and therefore, may influence the absorption Sulcralfate, an aluminum-containing complex. Concomitant use of these two compounds may be associated with increased exposure to aluminum potentially cause aluminum toxicity [14]. |
| Tramadol+ Omeprazole | Moderate/ Pharmacokinetics | Ceftriaxone may decrease Tramadol excretion, resulting in a higher Tramadol serum level. |

## IV. DISCUSSION

According to this study, majority of pregnant patients who visited the hospital were between the ages of 20 years and 25 years, accounting for around 54.16% of all patients, followed by those between the ages of 26 years and 30 years (29.16%). The proportion of patients aged 31-35 years was 10.83%, 36-40 years was 4.16%, and 41-45 years was 1.66%. In total, 328 drugs were prescribed in 120 prescriptions, with an average of 2.73 medications prescribed each case. As per World Health Organization, the term polypharmacy is defined as the Concurrent use of three or more medicines results in a significant increase in undesirable effects and drug interactions and ADR, and in return quality of life of the patient is compromised [15], the average number of medicines recommended in a prescription in these clinical investigations is 2.73. So as per number of prescribed medication, all prescriptions are rational. In this study it was found that patients in third trimester mostly visited the hospital in a similar study it was found that majority of women in third trimester visited clinics and ration of first trimester patient is smaller as compared to that of second and third trimester [16] According to the findings of the study, the percentage of drug-drug interactions in pregnant patients is high. Out of 120 prescriptions, 83 drug-drug interactions were reported in this study. More than two drug-drug interactions have been documented in some prescriptions. Drug-drug interactions accounted for about 69% of all interactions. The most common form of drug-drug interaction (DDI) was moderate, accounting for approximately 67.4% of total DDIs, followed by Minor and Major. The percentages of Minor and Major DDIs are 30.1% and 2.4%, respectively. According to a study, moderate-type DDIs are the most common type [17].

## V. CONCLUSION

It is concluded that the usage of numerous drugs increases during pregnancy, but if it's not carefully controlled, it can turn into a nightmare. The patient's reaction to the medications as well as a quick response and proactive approaches from medical personnel to any drug-related issues is crucial to managing numerous medications during pregnancy. This study suggests that there is a need to educate and counsel women of child-bearing age about the pros and

cons of drug use during pregnancy, with a special emphasis on alternative therapies and self-medication. Even the medical professionals must be skilled to treat pregnant women rationally.

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## REFERENCES

[1]. Bjerrum, L., Andersen, M., Petersen, G., & Kragstrup, J.(2003). Exposure to potential drug interactions in primary health care. Scandinavian. Journal of primary health care, 21(3), 153-158.
[2]. PJ., M. (1994). Maternal Physiology during Pregnancy. In: De Cherney AH, Pernoll ML, editors. Current obstetrics and gynaecological diagnosis and treatment. 8th ed. New York: McGraw-Hill; p. 146-54.
[3]. Daud, A. N., Bergman, J. E., Bakker, M. K., Wang, H., Kerstjens-Frederikse, W. S., de Walle, H. E., Wilffert, B. J. (2015). P-glycoprotein-mediated drug interactions in pregnancy and changes in the risk of congenital anomalies: a case-reference study. Drug safety, 38(7), 651-659.
[4]. Edwards, I. R., & Aronson, J. K. (2000). Adverse drug reactions: definitions, diagnosis, and management. Lancet, 356(9237), 1255-1259.
[5]. Linnarsson, R. (1993). Drug interactions in primary health care: a retrospective database study and its implications for the design of a computerized decision support system. Scandinavian journal of primary health care, 11(3), 181-186
[6]. Huic, M., Mucolic, V., Vrhovac, B., Francetic, I., Bakran, I., Giljanovic, S. (1994). Adverse drug reactions resulting in hospital admission. International journal of clinical pharmacology and therapeutics. 32(12), 675-682.
[7]. Weideman, R. A., Bernstein, I. H., & McKinney, W. P. (1999). Pharmacist recognition of potential drug interactions. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists, 56(15), 1524-1529.
[8]. Glassman, P. A., Simon, B., Belperio, P., & Lanto, A. (2002). Improving recognition of drug interactions: benefits and barriers to using automated drug alerts. Journal of Medical care 40(12), 1161-1171.
[9]. Mallet, L., Spinewine, A., & Huang, A. J. T. L. (2007). The challenge of managing drug interactions in elderly people. 370(9582), 185-191.
[10]. Verschraagen, M., Kedde, M. A., Hausheer, F. H., Van Der Vijgh, W. J. J. C. c., & pharmacology. (2003). The chemical reactivity of BNP7787 and its metabolite mesna with the cytostatic agent cisplatin: comparison with the nucleophiles thiosulfate, DDTC, glutathione and its disulfide GSSG. 51(6), 499-504
[11]. Davis.S Tatro,(2008). Wolters Kluwer Health/Facts & Comparisons, St. Louis, Missouri.
[12]. Backman, J. T., Filppula, A. M., Niemi, M., & Neuvonen, P. J. J.. (2016). Role of cytochrome P450 2C8 in drug metabolism and interactions. Pharmacological reviews, 68(1), 168-241.
[13]. Ranpuria, R., Hall, M., Chan, C. T., & Unruh, M. (2008). Heart rate variability (HRV) in kidney failure: measurement and consequences of reduced HRV. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 23(2), 444-449.
[14]. Moon, J., Davison, A., & Bandy, B. (1992). Vitamin D and aluminum absorption. Canadian Medical Association Journal, 147(9), 1308
[15]. Maria Alcira. (2011). Organización Mundial de la Salud. Los adultos mayores y el consumo de medicamentos. Recomendaciones para mayores, sus cuidadores y profesionales delasalud.OMS-OPS. http://new.paho.org/hq/index.php?option=com_content&view=article&id=6623&Itemid= 259&lang=es.
[16]. Rohra D, et al. (2007). Drug-prescribing patterns during pregnancy in the tertiary care hospitals of Pakistan: a cross sectional study. BMC Pregnancy and Childbirth, 8(24),1-5
[17]. Ferracini, A. C., Rodrigues, A. T., Visacri, M. B., Stahlschmidt, R., Silva, N. M. O. d., Surita, F. G., & Mazzola, P. G. (2017). Potential drug interactions and drug risk during pregnancy and breastfeeding: an observational study in a women's health intensive care unit. Journal of Revista Brasileira de Ginecologia e Obstetrícia, 39, 258-264.