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A PROSPECTIVE COHORT STUDY ON USE OF MEDICATIONS PRESCRIBING DURING PREGNANCY AND LACTATION

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ABSTRACT

Despite lack of scientific evidence about the safety of some medications, the reported use of medications during pregnancy has increased leading to adverse reproductive outcomes, due to potential risk to the mother and foetus. This study aimed to evaluate the pattern of medicines prescribed and their risk categories during pregnancy, child birth and lactation. A prospective – observational cohort study was carried out in 412 pregnant women for six months in an OB&G department of a tertiary care teaching hospital. Prescriptions were analyzed for rationality using WHO prescribing indicators and for risk drugs prescribed during pregnancy and lactation using US FDA and Dr. Hale's lactation risk category. In this study ATC group J (31.26%) were most frequently prescribed drug during pregnancy followed by group M (15.68%) and group B (13.36%).The average no of drugs per encounter was 4.66. Drugs prescribed by generic name were 38% and 33% were prescribed from EDL. Use of antibiotics was frequent (26.10%) and injections prescribed was also high (23.4%). The result indicate major drugs from category B (56.73%) followed by category C (16.64%) and category A(16.58%) as per FDA risk category. According to Dr. Hale's lactation risk category, majority of the drugs belong to L2 (83.61%) followed by L1(15.38%) and L3(1%).The study shows considerable medication use during pregnancy, childbirth and lactation. It is suggested that medicine use during pregnancy and lactation should be monitored regularly by analyzing prescription data.

KEYWORDS: Childbirth, FDA, Lactation, Medication, Pregnancy, WHO.

INTRODUCTION

Pregnant women requiring prescription drugs pose a challenge to physicians to avoid any risk to the mother and to the fetus. Thalidomide crisis in the 1960's and the teratogenic effects of use of diethylstilboestrol in 1971 led the US Food and Drug Administration [US FDA] to demonstrate safety and efficacy of any drug before it is marketed. However, pregnant women are generally excluded from clinical trials on ethical grounds. Safety information regarding drug use in pregnancy is gathered through case reports, epidemiological studies and animal studies, all of which have limitations. Results related to effect of drug on pregnant animals cannot always be extrapolated in human population. Regardless of the limited information on the safety of drugs in pregnancy, drug use in pregnancy is common.[1]

Drugs that a pregnant woman takes can affect the fetus in several ways. They can act directly on the fetus causing damage or abnormal development leading to birth defects or death. Drugs can also alter the function of the placenta usually by constricting blood vessels and reducing the blood supply of oxygen and nutrients to the fetus from mother and thus resulting in a baby that is underweight and underdeveloped. Moreover they can cause the muscles of the uterus to contract forcefully; indirectly injuring the fetus by reducing the blood supply or triggering pre-term labor and delivery.[2]

Pregnancy management using medications has been challenging to both health care providers and pregnant women, given the fear of teratogenic effects and the potential for fetal harm. This increased burden of risk assessment for providers, when treating pregnant women, can significantly impact therapeutic decision making. The teratogenic outcome of a drug depends on the dose taken, the timing of exposure, maternal disease and abnormality, and drug characteristics.[3]

Breast-feeding is beneficial for the health of a mother and her child. However, many medicines can be transferred into breast milk causing the risk of breast-feeding to exceed its benefit to the infant, mother, or both. Although, a study had reported that the majority of prescription and non-prescription medicines are not found in breast milk after ingestion, there is limited evidence-based data regarding the actual safety of many of these medicines, this therefore calls for caution on medicine use during lactation.[4]

The potential harm that can come to a fetus from exposure to pharmacologic drugs validates the need for an effective study that will provide indispensable information to health care

professionals on the effects of specific drug therapies on the developing fetus. One large US study estimated that 64% of women are being prescribed one or more drugs, not including vitamins and minerals, during pregnancy.[5]

Therefore judiciary use of drugs, adequate knowledge, positive approach and awareness towards the drug use are mandatory prerequisites for gynecological, maternal and child health. It becomes essential to assess the drug utilization pattern in pregnancy to see what extent there may be scope for improvement of current prescribing pattern. Since there are numerous gaps in knowledge about deleterious consequences for the fetus, prescribing drugs to pregnant women should be viewed as a public health issue. By keeping all of these issues in mind, the department of pharmacy practice has planned to conduct this study.[6]

MATERIALS AND METHODS

A prospective-Observational Cohort Study was carried out for a period of 6 months from March 2014 to August 2014 in OB&G department of Navodaya Medical College Hospital & Research Center, Raichur. A total of 412 pregnant inpatient's data were collected in structured data entry format. Pregnant woman who receiving antenatal care , delivered their babies, and followed up post-natal for the period of 6 week in in-patient department of obstetrics and gynecology and pregnant women who were seen over a 6 month period of study were included. However, pregnant women who had incomplete or unavailable medical records for review and visiting outpatient antenatal clinic were excluded. The study was approved by Institutional Ethical Committee by issuing Ethical clearance certificate.

Items Monitored in the study include

1. Socio-economic status of study population.
2. Duration of pregnancy.
3. Prescribing pattern according to WHO prescribing indicators.
4. ATC classification of medicine during pregnancy.
5. Categorization of Drugs according to US-FDA.
6. Drugs prescribed during lactation-Dr Hale's risk category.

Materials Used

1. Patients/Pregnant women case files.
2. Structured Data Entry Format.
3. WHO Drug Use Indicators – Prescribing Indicators.

4. US-FDA risk classification for pregnancy.
5. Dr. Hale's lactation risk category.

Table 1: FDA Classification of drug safety during pregnancy [6]

CATEGORY	DESCRIPTION
Category A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of risk in later trimesters), and the possibility of foetal harmappearsremot
Category B	Either animal reproduction studies have not demonstrated a foetal risk but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of risk in later trimesters).
Category C	Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
Category D	There is positive evidence of human foetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease in which safer drugs cannot be used or are ineffective).
Category X	Studies in animals or human beings have demonstrated foetal abnormalities or there is evidence of foetal risk based on human experience, and the risk of the use of the drug in pregnant. Womens clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

Table 2: Dr.Hale's lactation risk category [7]

Category	Description
L1	**Safest:** Drug which has been taken by a large number of breastfeeding moth-ers without any observed increase in adverse effects in the infant. Controlled studies in breastfeeding women fail to demonstrate a risk to the infant and the possibility of harm to the breastfeeding infant is remote; or the product is not orally bioavailable in an infant.
L2	**Safer:** Drug which has been studied in a limited number of breastfeeding women without an increase in adverse effects in the infant; And/or, the evidence of a demonstrated risk which is likely to follow use of this medication in a breastfeeding woman is remote.
L3	**Moderately Safe:** There are no controlled studies in breastfeeding women, however the risk of untoward effects to a breastfed infant is possible; or, con-trolled studies show only minimal non-threatening adverse effects. Drugs should be given only if the potential benefit justifies the potential risk to the infant.
L4	**Possibly Hazardous:** There is positive evidence of risk to a breastfed infant or to breast-milk production, but the benefits of use in breastfeeding mothers may be acceptable despite the risk to the infant (e.g. if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
L5	**Contraindicated:** Studies in breastfeeding mothers have demonstrated that there is significant and documented risk to the infant based on human experience, or it is a medication that has a high risk of causing significant damage to an infant. The risk of using the drug in breastfeeding women clearly outweighs any possible benefit from breastfeeding.The drug is contraindicated in women who are breastfeeding an infant.

Assessing Prescribing Indicators

WHO Prescribing indicators were calculated based on the following ratios

1. Average number of drugs per encounter = Total number of drugs prescribed / total number of encounters surveyed.
2. Percentage of drugs prescribed by generic name = (number of drugs prescribed by generic name / total number of drugs prescribed) x 100.
3. Percentage of encounters with an antibiotic prescribed = (number of patient encounters during which an antibiotic was prescribed / total number of encounters surveyed) x 100.
4. Percentage of encounters with an injection prescribed = (number of patient encounters during which an injection was prescribed / total number of encounters surveyed) x 100.
5. Percentage of drugs prescribed from essential drugs list = (number of drugs prescribed from essential drugs list / total number of prescribed drugs) x 100.[8]

Statistical Analysis

Statistical analysis was done by using descriptive statistics. Data were collected in predesigned Microsoft(R) Excel 2007. Continue variables were presented as mean values ± standard deviation (SD), and categorized variables were prescribed as percentages.

RESULTS AND DISCUSSION

Details of patients enrolled into the study: During the six month study period, total of 412 pregnant patients from the department of OB&G were enrolled as per our inclusion and exclusion criteria. Characteristics of study population are shown in Table 3.

Table 3: Characteristics of study population

Parameter	**No. of Subjects**			
Age (years)	**18-20 (16.32%)**	**21-25 (52.04%)**	**26-30 (28.91%)**	**31-35 (1.70%)**
Duration of Pregnancy	First Trimester (45) 10.9%	Second Trimester (73) 17.71%	Third Trimester (294) 71.35%	
Type of family	Nuclear (107) 25.97%	Joint (236) 57.28%	Third generation (69) 16.74%	
Education Status	Literate (109) 26.46%	Illiterate (303) 73.54%		
Gravida	Primigravida (201) 48.78%	Multigravida (211) 51.21%		

Demographic data obtained showed that a mean age was 23.87± 3.31 years. The average maternal age obtained in this study was similar to that obtained in a study done in Nigeria.[4]

Analysis of Prescription: The prescriptions were analysed for rationality. Number of drugs per prescription were analysed and which shows that more patients (26.94%) were given 3

drugs followed by 2 drugs (22.33%) and more than 6 drugs (22.33%) which is shown in table.4

Table 4: Number of drugs prescribed per prescription (n=412)

No of drugs per prescription	No of patients	Percentage (%)
Single	12	2.91
Two	92	22.33
Three	111	26.94
Four	66	16.01
Five	39	9.46
>Six	92	22.33

In this study ATC group J (Anti-infective) (31.26%) were most frequently prescribed during pregnancy. The reason may be to avoid the systemic infections, followed by group M (Musculoskeletal system) (15.68%) and group B (Medicines for blood and blood forming organs) (13.36%) shown in Table 5.

Table 5: Anatomical therapeutic chemical (ATC) classification of medicine prescribed during pregnancy (n=1923)

ATC group	Frequency of prescription	Percentage (%)
A)Alimentary tract and metabolism`	32	1.66
B)Blood and blood forming organs	257	13.36
C)Cardiovascular system	0	0
H) Genitourinary system and sex hormones	0	0
J) Anti infective	602	31.26
M)Musculoskeletal system	302	15.68
N)Nervous system	89	4.62
P) Anti parasitic products	0	0
R) Respiratory system	69	3.58

Hematinics constituted over 90% of these medicines and consistently remaining the most frequently prescribed in similar studies [9,11,12,13,14]. Thus it seems that hematinic were prescribed as prophylaxis against anemia in pregnancy, a problem thus more common in developing countries.[15]

Antibiotics (26.10%) were the most prescribed drugs followed by antiulcer 423(23.06%) and analgesics 354(18.51%). Minerals and vitamins were prescribed only for 14.92%. Among minerals and vitamins folic acid 120(6.24%) was mostly used followed by iron sulphate and calcium which is in accordance with earlier study done in North India.[9] Folic acid supplementation in pregnancy associated with the decrease incidence of habitual spontaneous

abortion and pregnancy complications.[16] From antibiotics group chloramphenicol 302(15.70%) was highly prescribed followed by ceftrixone 78(4.05%). Diclofenac was the most frequently prescribed analgesic. Frequency distributions of the prescribed medicines in these patients were showed in Fig 1.

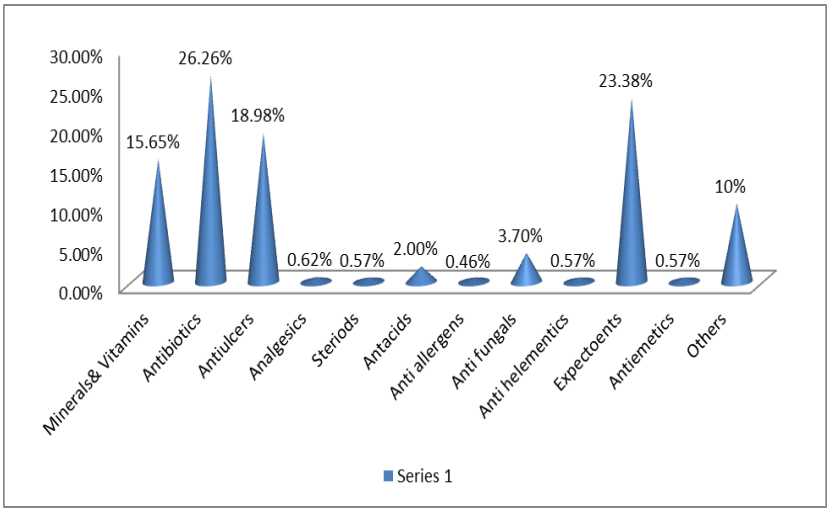

Fig 1: Frequency distribution of the medicines prescribed (n=1923)

World Health Organisation (WHO) has given 3 types of indicators, namely prescribing indicators, patient core indicators, and facility indicators as determinant of rational prescribing. Out of these, in the present study only prescribing indicators were used. The average number of drugs per encounters was found to be 4.66. Table 6 shows the WHO prescribing indicators that were evaluated.

Table 6: WHO prescribing indicators for pregnant women

Prescribing indicators	Value obtained	Who standard
Average no of drugs per prescription	4.66	<2
Percentage of drugs prescribed by generic name	38	100%
Percentage of prescriptions with an antibiotics prescribed	26.10	<30%
Percentage of prescriptions with an injections prescribed	23.4	<10%
Percentage of drugs prescribed from EDL	33	100%

Despite the general concern or safety of medicines used during pregnancy several studies are reported that most pregnant women used more than 1 medicine over the course of gestation. The average number of drugs prescribed per encounter differ from the standard set by WHO i.e 4.66, however similar values obtained in Kumar TN et al.[11] Similar study conducted by Belay et al[12] showed an average number of 1.72. Most of the medicines prescribed in brand names irrespective of type and this pattern is common in country. The low value obtained on

generic name indicates that irrational prescription. However value obtained by Joshi H et al[13] was even lower than our result. The percentage encounter of antibiotics was lower than that prescribed by WHO and this is encouraging. Similar values were also obtained in previous studies.[9,11,12,13,14]

Although a number of similar studies are used various methods to classify medicine risk in pregnancy, the US-FDA risk classification remains the most widely used.[17-18] In the present study majority of drugs were category –B(53.73%) which is the safe category followed by category C (16.64) and category A followed by category D. Our study shows that 1.24% of categories X drugs are also prescribed as shown in Fig 2.

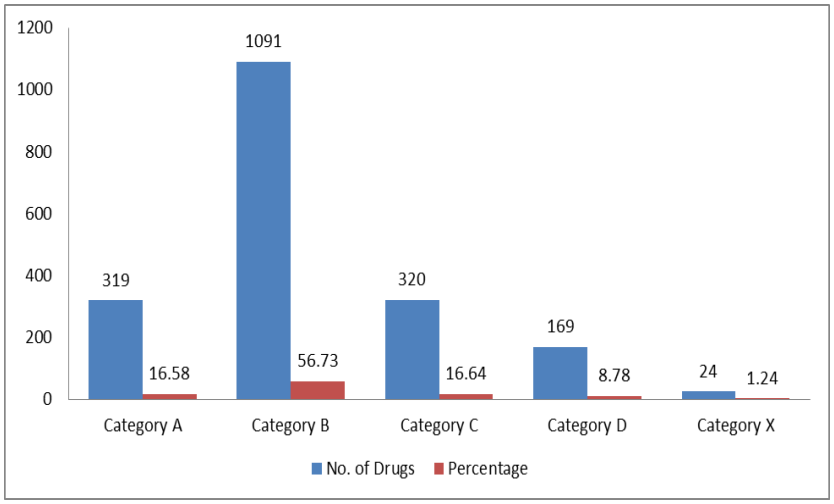

Fig.2: FDA category of drugs prescribed during pregnancy (n=1923)

Although, a category X medicine, which is absolutely contraindicated in pregnancy, was prescribed in this study, the prescribing of a medicine with unavailable safety data in pregnancy (Misoprostol), is however of a great concern. Other studies from Nigeria also have shown that categories A and B medicines are prescribed more frequently than category C or D medicines.[19] Our results were however at variance with those reported from other developing and developed countries where a low proportion of women were exposed to category X medicines during pregnancy, thus suggesting that, between countries, there are variations in disease pattern and medicine exposure during pregnancy.[20-21]

The risk category of medicines prescribed during lactation is shown in Table 7.

According to the Dr. Hale's lactation risk category, the majority of the drugs belongs to L2 250(83.61%) and followed by L1 46(15.38%) and L3 3(1.00%).The majority of the

medicines were prescribed during lactation is compatible with breast feeding. Although the proportion of patients who were prescribed with ciprofloxacin were low, potential adverse effects of ciprofloxacin on breast feed infants would require the use of alternative medicine if necessary.

Table 7: Prescribing pattern according to Dr. Hale's lactation risk category (n=299)

Lactation category	No of drugs	Percentage (%)
L1	46	15.38
L2	250	83.61
L3	03	1.00
L4	00	00
L5	00	00
	S. M -59.80	
	S. D -108.10	

CONCLUSIONS

The study shows considerable medication use during pregnancy, child birth and lactation. The moderate exposure during pregnancy to medicines with potential harm to the fetus, and further exposure during lactation to breast feeding infants, of great concern. It is suggested that medicine use during pregnancy and lactation should be monitored regularly by analyzing prescription data.

It is recommended that there should be intensive assessment of pregnant women including the FDA risk category, the gestational period and the risk benefit balance of drug before its prescription. In addition, pharmacists should interact with other members of the healthcare team to develop, implement and monitor a therapeutic plan so as to achieve optimal care for mother and her child.

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REFERENCES

1. Rathod AM, Rathod RM, Jha RK, Gupta VK, Tabish A. Prescribing trends in antenatal care at a tertiary level teaching hospital of Vidarbha Region. Res J Pharm Bio Chem Sci. 2012; 3(3): 865-72.

2. Puranik SB, Khan I, Joshi M, Iran M. Safe drugs during pregnancy and lactation. RGUHS J Pharm Sci. 2013; 3(1): 21-31.
3. Kureshee NI, Dhande PR. Awareness of mothers and doctors about drug utilization pattern for illnesses encountered during pregnancy. J of Clin Diagn Res. 2013 Nov; 7(11): 2470-74.
4. Oshikoya KA, Akionla IO, Senbanjo IO, Ogunleye OO. Medicines used in pregnancy, childbirth and lactation in a teaching hospital Lagos, Nigeria. Sri Lanka J Obstet Gynecol. 2012; 34(3): 84-98.
5. Andrade SE, Gurwitz JH, Davis RL, Chan KA, Finkelstein JA, Fortman K. et.al. Prescription drug use in pregnancy: Am J Obstet Gynecol. 2004; 191(2): 398-407.
6. Briggs GG, Freman RK, Yaffe SJ. Drugs in pregnancy and lactation: A reference guide to fetal and neonatal risk.5thed.Baltimore. Williams & Wilkims. 1988: 577-8,627-8.
7. Hale, Thomas. Medications and Mothers' Milk, 15th ed. Pharmasoft Medical Publishing, 2012-Infant Risk Center (806) 352-2519.
8. How to investigate dug use in health facilities. Selected drug use indicators [online] World Health Organization 1993. Available from: URL: http://www.WHO/DAP/93.1.pdf. Accessed on 26th Apr 2007.
9. Patel KP, Joshi HM, Patel VJ.A study of morbidity and drug utilization pattern in indoor patients of high risk pregnancy at tertiary care hospital. Int J Reprod Contracept Obstet Gynecol. 2013; 2(3): 372-76.
10. Mohammed MA, Ahmed JH, Bushra AW, Aljadhey HS. Medications use among pregnant women in Ethiopia: A cross sectional study. J App Pharm Sci. 2013 Apr; 3(4): 116-23.
11. Kumar TN, Tadvi NA, Kaul R. Prescription pattern of drugs in pregnancy induced hypertension in a tertiary care hospital. Int J Basic Clin Pharmacol. 2013 Dec; 2(6): 783-87.
12. Belay M, Kahaliw W, Ergetie Z. Assessment of drug utilization pattern during pregnancy in adama referral hospital,Oromia region, Ethiopia. Int J Pharm Sci Res. 2013; 4(5): 1905-11.
13. Joshi H, Patel S, Patel K, Patel V. Drug use pattern during pregnancy: A prospective study at tertiary care teaching hospital. NHL J of Med Sci. 2012 Jul; 1(1): 14-17.
14. Eze UI, Eferakeya AE, Oparah AC, Enato EF. Assessment of prescription profile of pregnant women visiting antenatal clinics.pharmacy practice. 2007; 5(3): 135-39.

15. World Health Organization. The prevalence of anaemia in women: a tabulation of available information. Geneva: Maternal Health and Safe Motherhood Programme, World Health Organization. 1992; 100.
16. Inamdar IF, Aswar NR, Sonkar VK, Doibale MK. Drug utilization pattern during pregnancy. Ind Med Gazette. 2012 Aug: 305-11.
17. Kebede B, Gedif T, Gatechew A. Assessment of drug use among pregnant women in Addis Ababa, Ethiopia. Pharmacopidemiol Drug Saf. 2009; 18: 462-8.
18. Olesen C, Steffensen HF, Nielsen GL, de Jong-van den Berg L, Olsen J, Sorensen HT, The Euromap Group. Drug use in first pregnancy and lactation: a population-based survey among Danish women. Eur J Clin Pharmacol. 1999; 55: 139-44.
19. Gharoro EP, Igbafe AA. Pattern of drug use amongst antenatal patients in Benin City, Nigeria. Med Sci Monit. 2000; 6: 84-7.
20. Gagne JJ, Maio V, Berghella V, Louis DZ, GonnellaJS. Prescription drug use in pregnancy: a population-basedstudy in Regione Emilia-Romagna, Italy. Eur J ClinPharmacol. 2008; 64: 1125-32.
21. World Health Organization. Breast feeding and maternal medication: Recommendations for drug in the eleventh WHO Model List of Essential Drugs, 2002. Available at http://whqlibdoc.who.int/hq/2002/55732.pdf (Accessed 31 August, 2011).