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DRUG UTILIZATION PATTERN AND POTENTIAL TERATOGENESITY RISK AMONG PREGNANT WOMEN; THE CASE OF AYDER REFERRAL HOSPITAL, TIGRAY - ETHIOPIA

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ABSTRACT

It is important to treat the mother whenever needed while protecting the unborn from any side effects to the greatest possible extent. Objective of this study is to assess the utilization pattern and the teratogenesity risk of the drugs prescribed among pregnant women in Ayder referral hospital, Mekelle, Ethiopia. Retrospective study was employed to assess drug utilization pattern and teratogenesity risk among pregnant women who were admitted to and/or visited Ayder referral hospital from 11 September 2010 to 9 March 2011. From Patient medical record, FDA pregnancy drug category of prescribed drugs was identified. The total number of pregnant women who were admitted to and/or visited Ayder referral hospital during the study period were 570. Only 217 (41.02%) of them have medication history. The rates of first trimester, second trimester and third trimester pregnancy term were 18 (8.30%), 20 (9.20%) and 179 (82.5%), respectively. According to FDA drug category, our finding reveals that there were few drugs prescribed inappropriately. In conclusion, medication practice during pregnancy in the hospital is encouraging except few drugs. However, hematinics prescription habit is very low for pregnant women who came to the Hospital for their ANC follow up. Hence, the hospital have to develop a system so that medication error during pregnancy can be minimized. And anemia during pregnancy should be addressed by hematinics.

INTRODUCTION: Pregnancy care is one of the great challenges in medicine. Drug therapies and protocols may affect the life of mothers and babies. Diseases occurring during pregnancy are even more dangerous, because of the difficulties in their treatment strategy. Prevention must be emphasized using safe and natural drugs [1].

Medication use during pregnancy has been an issue of concern since the discovery of birth defects resulting from Thalidomide use in early pregnancy during the 1960s.

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 [2, 3]. To guide safe drug use during pregnancy, the U.S.A. Food and Drug Administration (FDA) classified drugs into the following major categories; A, B, C, D, and X with categories D and X indicating evidence of risk in pregnancy [4, 5].

Hence, the authors used the FDA drug category for pregnant women, FDA currently uses a system of pregnancy categories based on the degree to which available information has ruled out risk to the fetus, balanced against the drug's potential benefits to the patient [4, 6, 7].

The teratogenic outcome of a drug depends on the dose taken, the timing of exposure, maternal disease and abnormality, and drug characteristics (metabolic activity half life and lipid solubility) [8].

In Ayder Referral Hospital (ARH), there is no such study before for the safety and effectiveness of drug use during pregnancy. Hence, these reports underscore the need to understand drug utilization patterns for pregnant women and investigate safety of drugs taken by the target population.

MATERIALS AND METHODS: In this work, a retrospective study on drug utilization pattern and teratogenesity risk among pregnant women in ARH was conducted by reviewing the medical record of each pregnant woman admitted to and or visited ARH, Mekelle, from September 11, 2010 up to March 9, 2011. Registration book of gynecology/obstetrics (GYN/OBS) ward/ OPD was used so that the Patient medical record (PMR) of all pregnant women who were admitted to/visited ARH in the specified period was easily accessed in the card room. Required information was collected using a structured data collection sheet. Drugs prescribed, dose, dosage form, route of administration, the nature of the service delivered, the trimester and the gestational age during drug administration, and other related issues were collected from the PMR. The collected data were checked manually for completeness and then they were coded and analyzed using the FDA pregnancy drug category.

Ethical Consideration: Research on pregnant women raises a unique set of ethical concerns. Therefore, before starting to collect data and sample for the study, a formal letter was obtained from the department of pharmacy and medical director of the hospital. Ethical clearance was obtained from ethical clearance committee of College of Health Sciences (CHS), Mekelle University. The issue of assuring privacy and confidentiality had been given more attention in the study.

RESULTS: A total of 570 pregnant women were admitted to/visited ARH in the specified study period. As per the registration book in each ward and OPD, 162, 13, and 395 of them have attended GYN/OBS OPD (for antenatal care, ANC), GYN ward, and OBS ward of ARH respectively. PMR of 41 pregnant women were missed from the archive room. Hence, 529 PMRs were reviewed and only 217 (41.02%) of them have records that show prescription for medication(s) (**Table 1a**). Among the 217 pregnant women who got at least one medication during their visit, 18 (8.30%) were in their first trimester; 20 (9.20%) in their second trimester and 179 (82.5%) in their third trimester (Table 2b).

TABLE 1A: PMR OF PREGNANT WOMEN ATTENDING AT ARH

	Pregnant women registered in the registration book of the respective wards or OPD	PMR actually obtained in card room	PMR not found in card room	PMR with prescribed drugs
ANC	162	147	15	46(31.3%)
OBS	395	369	26	160(40.5%)
GYN	13	13	0	11(84.6%)
Total	570	529	41	217(41.02%)

IM = intramuscular, IV= intravenous, IT= intrateccal, PO= oral route and SC= subcutaneous

TABLE 1B: TRIMESTERS OF PREGNANT WOMEN WITH A RECORD OF DRUG(S) IN THE STUDY PERIOD

Trimester	1st trimester	2nd trimester	3rd trimester
Frequency	28	20	169

Among the 100 drugs prescribed during ANC, most of them (43%) were prescribed in tablet form. The rest were capsules (29%) and injection (17%). In addition, 79% (43% Tablets, 29% capsules, 5% syrup, 1% suspension) of all the drugs were taken orally and the injectables that have been prescribed during ANC included Anti D, Insulin and other antibiotics. However, in the Gyn/OBS wards 70% and 86% of drugs used were injectables (**Table 2a and 2b**).

TABLE 2A: DOSAGE FORM OF DRUGS PRESCRIBED TO PREGNANT WOMEN

Dosage form	ANC	GYN	OBS
Injection	17(17%)	42(70%)	361(86%)
Tablet	43(43%)	12(20%)	38(9%)
Capsule	29(29%)	4(6.7%)	9(2.1%)
Syrup	5(5%)	2(3.3%)	0
Pessary	1(1%)	0	12(2.9%)
Suppository	3(3%)	0	0
Gel	1(1%)	0	0
Suspension	1(1%)	0	0
TOTAL	100	60	420

A total of 46 pregnant women who visited ARH for their ANC follow up got at least one medication and the rest 101 pregnant mothers did not receive any medication (Table 1). Accordingly, 31 drugs with an average of 1.63 drugs per pregnant woman were prescribed in first trimester; 41 drugs with an average of 2.28 drugs per pregnant woman in second trimester; and 28 drugs with an average of 3.1 drugs per pregnant woman in third trimester. Therefore, a total of 100 drugs with an average of 2.17 drugs per pregnant woman following ANC were prescribed (**Table 2a and 3**).

TABLE 2B: ROUTE OF ADMINISTRATION OF PRESCRIBED DRUGS FOR PREGNANT WOMEN IN ARH

Route of administration	ANC			GYN/OBS		
	1st trimester	2nd trimester	3rd trimester	1st trimester	2nd trimester	3rd trimester
Po	23	35	21	15	3	47
IV	4	4	3	30	8	255
IM	1	1	3	3	1	31
Vaginal	0	1	0	0	0	12
Rectal	2	0	1	0	0	0
IT	0	0	0	0	0	74
SC	1	0	0	0	0	1

IM = intramuscular, IV= intravenous, IT= Intrathecal, PO= oral route and SC= subcutaneous

The most frequently prescribed drugs in each trimester were: antibiotics, anti emetics, vitamins, proton pump inhibitors /histamine H_2 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 (**Table 3**). Therefore, antibiotics were the most frequently used drugs during all the trimesters of pregnancy. Category B and C drugs cover the highest percentage of the total FDA pregnancy drug category (**Table 4, Figure 1**).

TABLE 3: DRUGS PRESCRIBED FOR PREGNANT WOMEN DURING THEIR ANC FOLLOW UP

Drug prescribed	1st trimester	2nd trimester	3rd trimester	Total
Vitamins	3	2	0	5
Iron sulfate	1	1	0	2
Folic acid	0	1	0	1
Iron folate	0	4	5	9
Antibiotics	13	14	10	378
Paracetamol	3	0	3	6
NSAID	0	1	0	1
Oxytocin	0	0	1	1
Antacids	0	3	3	6
Metoclopromide	3	2	0	5
PPIs/H_2blocker	3	1	0	4
AZT	1	3	1	5
Insulin	1	0	0	1
Methyl dopa	0	1	0	0
Anti-D	0	0	3	3
Misoprostol	0	1	0	1
Predinisolone	0	1	0	1
Miconazole	0	0	1	1
Cotrimoxazole	0	4	0	4
Anti protozoa	0	2	0	2
Bisacodyl	2	0	1	3
Chlorpromazine	1	0	0	1
Cough syrup	1	0	0	1
Total	31	43	28	100

Antibiotics (amoxicillin, ampicillin, ceftriaxone); IV fluids (dextrose, ringer lactate, normal saline, glucose); NSAIDs (diclofenac); PPIs/antihistamines H_2 blocker (omeprazole /cimetidine); Anti protozoa (tinidazole)

TABLE 4: FDA CATEGORY OF THE DRUG PRESCRIBED DURING ANC FOLLOW UP

FDA drug category	1st trimester	2nd trimester	3rd trimester	Total	Representative drugs
A	1	7	5	13	Iron folate
A/C	3	1	0	4	Vitamin B
B	17	15	14	46	Amoxicillin
B*	0	1	0	1	Metronidazole
B/C/D	0	1	0	1	Diclofenac
C	9	14	8	31	Omeprazole
D	1	1	0	2	Doxycycline
X	0	1	1	2	Misoprostol

A/C stands for manufacturer difference; B/C/D safety differs according to the trimester they are given; B* indicates that the drug is contraindicated in first trimester and is acceptable in second and third trimester

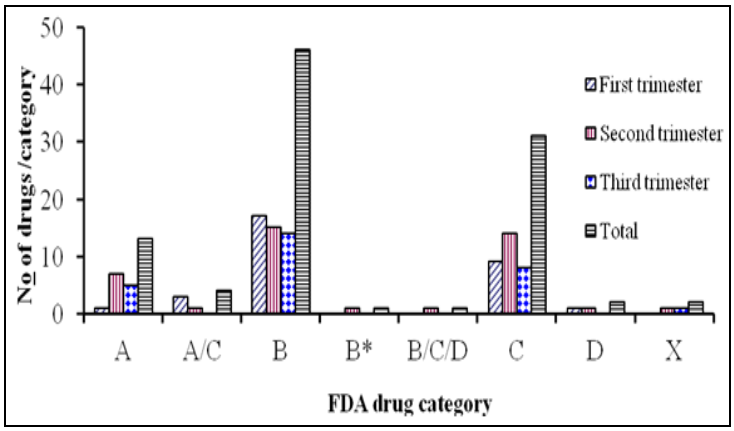

FIGURE 1: FDA CATEGORY OF DRUGS PRESCRIBED IN EACH TRIMESTERS OF PREGNANCY DURING ANC FOLLOW UP

A/C stands for manufacturer difference; B/C/D safety differs according to the trimester they are given

A total of 160 pregnant women were admitted to OBS ward and accordingly some 420 drugs, with an average of 2.63 drugs per pregnant woman were prescribed to them. Antibiotics, lidocaine, oxytocin and IV fluids were the most frequently prescribed drugs. In addition, category X drugs (oxytocin and misopostol) were prescribed 66 times (**Table 5**). As **Figure 2 and Table 6** reveals, the most prescribed drugs were under FDA category "B" and "C".

TABLE 5: DRUGS PRESCRIBED FOR PREGNANT WOMEN AT OBS WARD

Drug prescribed	Frequency	Drug prescribed	Frequency Frequency
Vitamins	1	Insulin	1
Digoxin	4	Metronidazole	14
Anti D	7	Chlorpromazine	1
Iron folate	2	Pethidine	6
Antibiotics	95	Iv fluids	49
Paracetamol	1	Ketamine	7
Diclofenac	2	Hyoscine	5
Oxytocin	53	Atropine	1
Lidocaine	74	Spironolactone	2
Metoclopromide	2	Frusemide	3
PPIs/H_2 blocker	1	Propranalol	3
Zidovudine (AZT)	5	Magnesium	24
Lamuvidine (3TC)	4	Nifedipine	1
Neverapine	4	Hydralazine	7
3TC+AZT	1	Methyldopa	8
Diazepam	14		

Antibiotics (amoxicillin, ampicillin, ceftriaxone); IV fluids (dextrose, ringer lactate, normal saline, glucose); NSAIDs (diclofenac); PPIs/antihistamines H2 blocker (omeprazole /cimetidine); Anti protozoa (tinidazole)

TABLE 6: FDA DRUG CATEGORY OF PRESCRIBED AT OBS WARD

FDA category of the drug	1st trimester	2nd trimester	3rd trimester	Representative drugs
A	0	0	2	Iron folate
A/C	0	0	25	Magnesium
B	0	0	169	Amoxicillin
B*	0	0	14	Metronidazole
B/D	0	0	6	Pethidine
B/C/D	0	0	3	Diclofenac
C	0	0	120	Iv fluids
D	0	0	16	Diazepam
X	0	0	66	Oxytocin

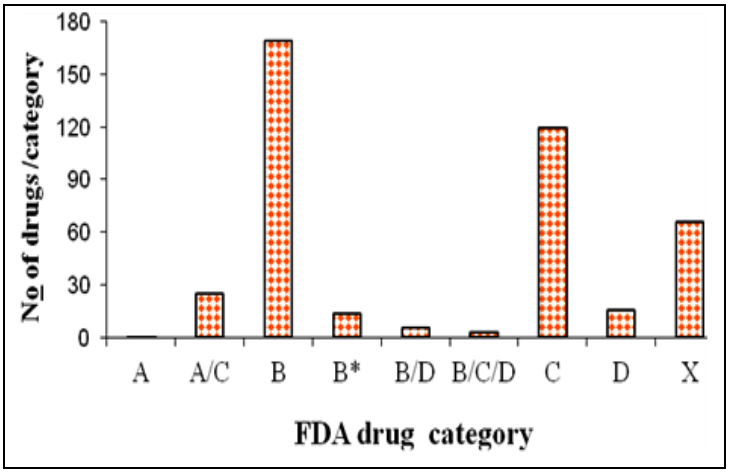

FIGURE 2: FDA DRUG CATEGORIES OF PRESCRIBED DRUGS FOR THIRD TRIMESTER PREGNANT WOMEN IN OBS WARD

A/C stands for manufacturer difference; B/C/D safety differs according to the trimester they are given

On the other hand, a total of 11 pregnant women were admitted to GYN ward. 9 of them were in their first trimester and the remaining 2 in their second trimester. A total of 60 drugs were prescribed to these women and the average number of drugs per pregnant woman was 5.45. According to **Table 7**, Vitamins 16 (26.7%), anti emetics 14(23.3%) and IV fluids 12 (20%) were among the most frequently prescribed drugs in the GYN ward. FDA category of the most prescribed drugs to these women were category B (35%), category C (33.3%) and category A/C (28.3%) (**Table 8 and Figure 3**).

Category D drugs, which are considered to be risky both to pregnant women and fetus, including doxycycline, tetracycline, diazepam, spironolactone and diclofenac were also prescribed in the specified study period. Another risky drug, Cimetidine, was prescribed in GYN ward during first trimester, in ANC during 2nd trimester, and in OBS ward during 3rd trimester for dyspepsia (**Table 9**).

TABLE 7: DRUGS PRESCRIBED FOR PREGNANT WOMEN AT GYN WARD

Drugs used	First trimester	Second trimester	Third trimester	Total
Vitamins	13	3	0	16
Iron folate	1	0	0	1
Antibiotics	4	1	0	5
NSAIDs	0	1	0	1
Ant acids	2	1	0	3
Anti emetics	11	3	0	14
PPIs/H2	3	0	0	3
Chlorpromazine	3	1	0	4
IV fluids	10	2	0	12
Promethazine	1	0	0	1
Total	48	12	0	60

Antibiotics (amoxicillin, ampicillin, ceftriaxone); IV fluids (dextrose, ringer lactate, normal saline, glucose); NSAIDs (diclofenac); PPIs/antihistamines H_2 blocker (omeprazole /cimetidine); Anti protozoa (tinidazole)

TABLE 8: FDA CATEGORY OF THE DRUG PRESCRIBED AT GYN WARD

FDA drug	First trimester	Second trimester	Third trimester	Total	Representative drugs
A	1	0	0	1(1.7%)	Iron folate
A/C	14	3	0	17(28.3%)	Vitamin B
B	17	4	0	21(35%)	Plasil
C	16	4	0	20(33.3%)	Iv fluids
B/C/D	0	1	0	1(1.7%)	Diclofenac

A/C stands for manufacturer difference; B/C/D safety differs according to the trimester they are given

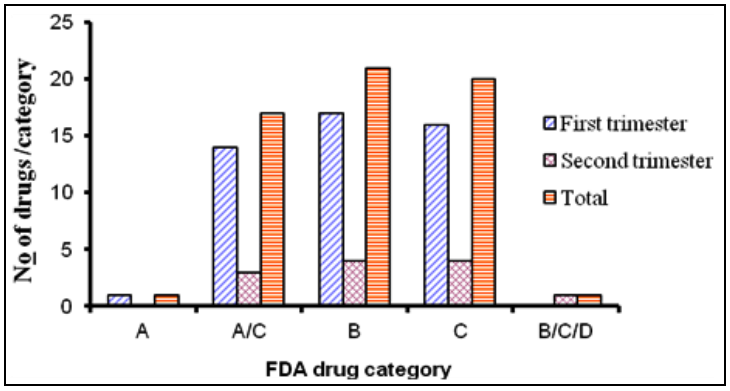

FIGURE 3: FDA CATEGORY OF THE DRUGS PRESCRIBED IN GYN WARD

Nature of the service: Among the 217 patients who were admitted to/ visited ARH, free service was provided for 27 (12.5%) pregnant women and 188 (86.6%) women paid for the service they had received. The nature of the service provided for 2(0.9%) patients was not specified for unknown reasons (**Table 10**). Now according to Ethiopian ministry of health MDG, ANC follow-ups are set free for all pregnant mother visiting any of government owned health facility.

TABLE 9: LIST OF CATEGORY D AND CATEGORY X DRUGS PRESCRIBED AND THEIR INDICATION

Drugs	Site	Trimester	Indication	FDA category
Doxycycline *	ANC	1st	UTI	D
Tetracycline*	ANC	2nd	UTI	D
Diclofenac*	OBS	3rd	Pain in labor	B/C/D
Spironolactone*	OBS	3rd	CHF	D
Diazepam	OBS	3rd	Eclampsia/Pre eclampsia	D
Misoprostol	ANC & OBS	3rd	Labor	X
Oxytocin	OBS	3rd	Labor	X

* The drug was given inappropriately to pregnant women admitted to/visited ARH

Residence: Most of the patients (68.2 %) who attended ARH came from rural area and 31.3% from urban area. But, it was not clearly identified for 0.5% of the patients as to where they came from (**Table 10**).

TABLE 10: NATURE OF THE SERVICE AND RESIDENCE OF PATIENTS ADMITTED TO ARH

	Nature of the service			Residence		
	Free	Paid	US	Rural	Urban	US
ANC	16	30	0	37	8	1
GYN	2	9	0	10	1	0
OBS	9	149	2	101	59	0
Total	27	188	2	148	68	1
	12.5%	86.6%	0.9%	68.2%	31.3%	0.5%

US = unspecified

DISCUSSION: Among the pregnant women who were admitted to or visited ARH and whose records were fully accessed (529), only 41.02% of them had a record for drug (s) and hence analyzed in the study (Table 1). The low percent drug prescription (41.02%) is probably due to most pregnant women (71.7%) came to the hospital for ANC follow up or for pregnancy test. And also some pregnant women who were admitted to OBS ward give birth without taking any medication.

Moreover, the impact of the lost records should not be underestimated. The highest drug utilization recorded in the hospital was during the third trimester, as the number of pregnant women admitted to/visited ARH at this trimester accounts for 77.8 % (169) of all the pregnant women visiting the hospital (Table 1b).

Additionally, the women took many drugs including different IV fluids in OBS ward (the average number of drugs per pregnant woman was 2.62). Our findings also reveal that the highest average number of medications prescribed per pregnant woman was recorded in the GYN ward. This is probably due to, almost all of the pregnant women were admitted for the hyper emesis gravid arum (HG) in which they took different parentral drugs such as anti emetics, anti pain, IV fluids, antibiotics and others per drug encounter.

Among the total drugs prescribed during ANC, 2% were category D, namely tetracycline and doxycycline (Table 4 and 9). These drugs were prescribed for upper respiratory tract infection in the first and second trimester. The prescription was inappropriate as both drugs can cross the placenta and their use late in pregnancy causes permanent discoloration of teeth, enamel hyperplasia and impaired fetal skeletal growth [9]. There were also categories X drugs (2%) prescribed in the second and third trimester. The drugs were misoprostol (to terminate pregnancy) and oxytocin (to induce labor) and this was appropriate.

Number of iron and folate supplements prescribed in this study were only 16 (out of 580 drugs totally prescribed) (Table 3). Globally pregnant women and young children are at high risk of anemia with iron deficiency contributing to 50% of this risk [10]. WHO has estimated that prevalence of anemia during pregnancy in developed countries is 14% and developing countries 51 percent [11]. Nearly all women are to some degree iron deficient and more than half of pregnant women in developing countries suffer from iron deficiency anemia [12]. As Ethiopia is one of the developing countries, result of our study implies that ARH failed to prevent prevalence of anemia during pregnancy. Therefore it is mandatory to consider iron supplement during pregnancy so as to minimize the risks associated with anemia.

Among the 420 drugs prescribed in OBS ward, most of them were under category B (40.23%) category C (28.6%) and category X (15.7%) respectively. A total of 66 Category X labor-inducing drugs (misoprostol and oxytocin) were also prescribed (Table 5 and 6, Figure 2). Moreover, category D drugs like diclofenac (if given for third trimester mother), diazepam, and spironolactone were prescribed in the 3rd trimester.

Diazepam was used for the treatment of mild to severe pre eclampsia. If diazepam is used for long period during pregnancy or at high doses, it might be associated with a high incidence of physiological depression when maternal doses exceed 30 mg, the babies being likely to have a tendency to apnea, reluctance to feed and impaired hermogenesis [13, 14, 15].

Our result had shown that spironolactone (category D) was used for the patients with congestive heart failure. High dose of this drug is contraindicated during pregnancy before determining the sex of the fetus because of its antiandrogenic effects resulting in feminization of male fetuses [16]. The same is true for higher dose of cimetidine (histamine H_2 blocker) prescribed for the patients with dyspepsia, which may lead to gynecomastia in male [17]. These drugs should not be prescribed without determining the sex of the fetus. However, their use may be acceptable if the benefit outweighs the associated risk. Hence, either safe alternatives should be used or close monitoring of the patient is required.

According to our results, diclofenac was used in third trimester for pregnant women in labor; however, this can cause early closure and constriction of ductus arteriosus with subsequent neonatal pulmonary hypertension and transient right-sided hypertrophic cardiomyopathy [18]. Therefore, it is very important to search for other alternatives that could alleviate pain during labor.

Pregnant women who were admitted to the GYN ward in ARH took a total of 60 drugs: (35%) under category B, (33.3%) under category C and (17%) under category A/C. Category A/C includes pyridoxine and vitamin B complex (Table 7 and 8). The A/C stands for manufacturer difference and B/C/D indicates safety differs according to the trimester, Figure 1, 2 and 3 [19], but it was difficult to exactly know the category of such drugs because only generic names were written on the patient medical record. Besides, as it is depicted in Table 7, the most commonly recommended drug for HG, i.e., chlorpromazine, has been used not often. Metoclopromide was highly prescribed in its place.

Most of the drugs in OBS ward were given parentrally (Table 2a and b); this may be due to the nature of the diagnosis in which they can not take drugs orally.

Moreover, most of the patients were admitted to OBS ward for labor and they underwent cesarean section for delivery, in which they took different IV fluids and anesthetics parentrally. The high value for the injectables prescribed in GYN ward may be due to the nature of the diagnosis observed (i.e., hyper emesis gravid arum in which the patient can't take drugs orally), Table 2a and b.

Generally the dosage form of a drug given has its own impact on promoting rational drug use. For instance if a drug given was injectable, the nurse who administer the drug may recall the safety of the drug to pregnant women even though the pescriber makes error. However in case of tablets, capsules and other orally taken drugs (doxycycline and tetracycline) where patients take the drug at home, the risk will be very high. For orally administered drugs the role of pharmacists working at the hospital pharmacy is very crucial to identify medication related problem.

Most of the patients who attend ARH came from rural area (Table 10). This may indicate inadequate health care service provided in rural areas and/or bias by the mothers for being safe when treated in a referral hospital. The fewer number of patients coming from urban areas may be linked to their economic background to be diagnosed in private hospitals and higher clinics in their vicinity.

CONCLUSIONS AND RECOMMENDATIONS: The drug utilization pattern observed among the pregnant women admitted to/visited ARH was good and almost all the teratogenic drugs prescribed to them were labor inducing and they all were prescribed at term and post term. However, there were some category D drugs (diclofenac, if given in third trimester, tetracycline, doxycycline, spironolactone, and others) and category C (cimetidine) drugs prescribed inappropriately to some of the patients.

Such inappropriate prescription of drugs should not be underestimated because it definitely affects the life of both the mother and the fetus. Therefore, 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 a drug before its prescription.

In addition, pharmacists should interact with other members of the health care team to develop, implement and monitor a therapeutic plan so as to achieve optimal care for each pregnant woman.

It is also recommended to strengthen the use of smart care (electronic medical record system), which is already practiced in the hospital, so that every health care provider including the pharmacist can have access to the patient information and understand the contraindication and adverse effect of the drug. Moreover there will be no loss of records and thus any data can be accessed easily. 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 or through the pharmacist working in the drug information centre.

Preparing a check list for commonly prescribed drugs to pregnant women, Continuous education on medication during pregnancy to health care provider working at GYN OPD and ward is also very important. As ARH is teaching hospital, interns (medical students) and other maternity related Msc and Bsc students should be well trained regarding pregnancy related medications. To the extent of revising the curriculum and assessing the quality of the teaching learning process. In addition to this, ANC follow-up service should be monitored on regular base. Strengthening the drug information center in the hospital is the other best possible solutions for medication error during pregnancy.

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REFERENCES:

1. Wacha J and Szijarto A: Probiotics and pregnancy. Orv Hetil 2011;152 (11):420-6.
2. Lee E, Maneno M, Smith L, Weiss S, Zuckerman I, Wutoh A, Xue Z. National Patterns of Medication use during Pregnancy. Pharmacoepidemiology and drug safety 2006;15:537-45.
3. Oren GK, Astuszak AP and Ito S. Drugs in pregnancy. New England Journal of Medicine 1998;338 (16):1128-37.
4. FDA. Pregnancy categories for prescription drugs. FDA Drug Bulletin. 1982;12:24-5.
5. Dı´az H. Prescription of Medications during Pregnancy: Accidents, Compromises, and Uncertainties. Pharmaco-epidemiology and Drug Safety 2006;15:613–7.

6. Andrade SE, Gurwitz JH, Davis RL, Chan KA, Finkelstein JA, Fortman K. Prescription drug use in pregnancy. American Journal of Obstetrics and Gynecology 2004;191:398-407.
7. Gagne JJ, Maio V, Berghella V, Louis DZ, Gonnella JS. Prescription drug use during pregnancy: a population-based study in Regione Emilia-Romagna, Italy. Eur Jpornal of Clinical Pharmacology 2008; 64:1125–32.
8. Anonymous. Reviewer Guidance Evaluating the Risks of Drug Exposure in Human Pregnancies. US Department of Health and Human Services, FDA Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). 2005.
9. Ferenc BR, Brian L, Andrew E. Risk and Benefit of Drug Use during Pregnancy. International Journal of Medical Scinces 2005;2:100-6.
10. WHO. Iron deficient anameia assessment, prevention, and control. A guide for program managers. WHO information sheet. 2001;WHO/NHD/01.3:1-132.
11. Parul Christian, Christine P. Stewart, Steven C. LeClerq, Lee Wu, Joanne Katz, Keith P. West Jr and Subarna K. Khatry. Antenatal and postnatal iron supplementation and childhood mortality in rural nepal: A Prospective Follow-up in a Randomized, Controlled Community Trial. American Journal of epidemiology 2009; 170 (9): 1127-1136.
12. Kalaivani K.Prevalence and consquences of anemia in pregnancy. Inian Journal of Med ical Research 2009;130 :627-633.
13. Leppée M, Culig J, Eric M, Sijanovic S. The effects of benzodiazepines in pregnancy. Acta Neurol Belg. 2010;110(2):163-7.
14. McElhatton P. The effects of benzodiazepine use during pregnancy and lactation. Reprod uctive Toxicology 1994; 8(6):461-5.
15. Whitelaw AGL, Cummings AJ, Mcfadyen IR. Effect of maternal lorazepam on the neonate. British Medical Journal 1981;282:1106-8.
16. Hecker A, Hasan S, Neumann F. Effect of spironolactone on sexual differentiation of rat fetuses. Acta Endocrinology 1978;87(32).
17. Conover E. Over-the-counter products: nonpresciption medications, neutraceuticals, and herbal agents. Clin Obstet Gynecol 2002; 45(1):89-98.
18. Siu K, Lee W. Maternal diclofenac sodium ingestion and severe neonatal pulmonary hypertension. Journal of Paediatrics and Child Health. 2004;40(3):152-3.
19. Charles F L, Lora L A, Morton P G, Leonard L L. Drug Information Handbook: A Comprehensive Resource for All Clinicians and Healthcare Professionals. Lexi-Comp's drug reference handbooks. Hudson, Ohio: Lexi-Comp, Edition 15th:2007: 20-1600.

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