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ASSESSMENT OF DRUG UTILIZATION PATTERN DURING PREGNANCY IN ADAMA RIFERRAL HOSPITAL, OROMIA REGION, ETHIOPIA

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ABSTRACT:

Background: Rational drug use in pregnancy requires the benefits and potential risk associated with the use of the drug. The adverse effect of drugs on the fetus varies temporarily with time. The fetus susceptibility to injury depends on its period of development of different organs have different critical periods through the span from gestational day 15 to day 60 is critical for many organs.

Objective: To assess the pattern of drug use among pregnant women in Adama Referral Hospital, Oromia region, Ethiopia.

Methods: All drug prescriptions of pregnant women prescribed from December 1, 2011 to May 30 2011 were reviewed retrospectively using structured data collection format.

Result: A total of 381 pregnant women prescriptions were included in the study. The average maternal age in the study was 26.74 years. A total of 176(24.44%), 336(46.66%) and 208(28.88%) drugs with an average 2.2, 1.13 and 1.83 per pregnant women were used in first, second and third trimesters respectively. Minerals and vitamins 209(29%) were the most frequently prescribed drugs followed by Antibiotics 173(24%) and analgesics 149(20.7%). Majority of the drugs were prescribed from risk category B 449(62.4%) followed by risk category C 131(18.2%) and risk category A 98(13.6%). 37(5.13%) of the drugs were received from risk category D.

Conclusion: Gastrointestinal infection occurred most frequently followed by genitor-urinary tract infections. Vitamins, minerals, paracetamol and amoxicillin were most frequently prescribed drugs. The average number of drugs per prescription was comparable with a standard set by WHO, indicating that poly pharmacy was not practiced. The occurrence of contraindicated medicines was desirably low.

INTRODUCTION: Pregnancy is the period from conception to birth when developing fetus carried in women uterus. Pregnancy is divided into three equal periods which are called trimesters. Each trimester consists of about 13 weeks. Pregnancy is special physiological conditions, where drug treatment presents special concern.

The first few months of pregnancy are the most critical for developing fetus, because during this period fetus brain, legs and internal organs are formed. For this reasons pregnant women should be especially careful about taking any kind of medication except on the advice of clinician who know that she is pregnant [1, 2].

The adverse effect of drugs on the fetus varies temporarily with time. The fetus susceptibility to injury depends on its period of development of different organs have different critical periods, though the span from gestational day 15 to day 60 is critical for many organ. The heart is the most sensitive. The brain skeletons are sensitive from the beginning of the third week to the end of pregnancy and into neonatal period [2].

Pregnancy is a time of profound physiological changes in a woman's body. These unique changes challenge clinicians managing disease states during pregnancy in the selection of medications best suited to treat their patients [3]. Maternal drug use during pregnancy may pose a teratogenic risk to the foetus. However, the recommendation to avoid all drugs during early pregnancy is unrealistic and may be dangerous [4, 5]. Pregnancy should not deter clinicians from providing their patients with appropriate management of their medical conditions, hence, and prescribing in pregnancy is an unusual risk benefit situation [6, 7].

In 1979, the United States Food and Drug Administration (FDA) introduced a system of rating pregnancy-risk associated with pharmacological agents. This system categorised all drugs approved after 1983 into one of five pregnancy risk categories (A, B, C, D, and X). It indicates the effect of the agent on the foetus based on available animal and human data and recommends the degree of precaution that should be undertaken with each drug. However, the risk factors assigned are sometimes difficult to interpret because they may not always reflect the latest findings [8].

Unnecessary and harmful drug treatment should be avoided during pregnancy. Disease requiring drug treatment must be treated adequately if left untreated; exacerbation of mothers' illness not only jeopardizes the mothers' health but also the well being of fetus .Because a medication can present risks in pregnancy and because of not all risks are known, the safest pregnancy related pharmacy is a little pharmacy as possible. However, women with history of psychiatric, seizure related or hematologic illness frequently required medication throughout pregnancy. In such patient care must be taken to select the safest drug from the necessary class of medications [9].

Information on the use of drugs during pregnancy is scarce and rather anecdoctal [10]. Despite the absence of adequate studies on the safety and effectiveness of prescription drugs for pregnant women, evidence available shows that physicians prescribe, and pregnant women take a surprisingly large number of drugs. An international investigation sponsored by WHO showed that pregnant women ingest an average of three prescription medications during pregnancy (range 1-15). Furthermore, 86% of the women had taken at least one prescription medication during their pregnancies [11].

Across-sectional study done in America on the prevalence of medication use during pregnancy in two ambulatory care settings (office based Vs hospital outpatient department) in 2008 indicated that the prevalence of drug use during pregnancy was 44% and 54% in office based and hospital care setting respectively.

Other than vitamins and mineral supplements, top drug classes were mediations for anemia and blood glucose regulation. Prescribed drugs were classified by the FDA pregnancy risk category. Approximately, half of all prescriptions were from class A, followed by category C of all medications prescribed to pregnant women, drugs classified as class D\X accounted for 5% [12, 13].

A study done in Canada in 2008, 19.4% women were found to have used FDA category C, D and X medications at least once during pregnancy, the most common of these being albuterol, bacterium or Cotrimoxazole, Ibuprofen, naproxen and oral contraceptives. Studies from Bratislava's reported that majority of prescribed drugs during pregnancy belongs to category C [13].

A study in Australia showed that, foliate (70%), iron (38%) and multivitamins (27%) were the most frequently taken drugs by pregnant women. Furthermore, a study in northern India indicated that, folic acid, calcium and vitamins were the most frequently used drug by pregnant women with average at 1.72 to 2.89 drugs per pregnant women. Phenobarbital, progesterone, paracetamol, non-steroidal anti-inflammatory drugs (NSAIDS), Antibiotics, Anti-emetics, Antacids and Anti hypertensive drugs were the other commonly used drugs [14].

Another study done in Nigeria in 2000 revealed that the total of 1200 pregnant women attends during the period under review were evaluated. Results indicated that malaria 554(38%) was the most prevalent disease followed by upper respiratory tract infections (URTIs 13%) and GIT disturbance 12%. The average numbers of the drugs prescribed per encounter was found to be 3.0. Mineral or vitamins 2396(42%) were the most frequently prescribed medicine, and antibiotics occurred in 502(88%) of the total medicine all of the medicine prescribed, 984(17%) were included in the fetal risk category C and 286(5%) in category D [9].

A study conducted in Addis Ababa in 2007 showed that a total of 1268 women were included in the study. The number of women for whom drugs were prescribed increased from 379(29.9%) in the first trimester to 893(70.3%) and 892(70.3%) in the second and third trimester, respectively. A total of 1643 drugs were prescribed to pregnant women. Anti-anemic preparations were the most frequently prescribed class of drugs (46.8%) during all the trimesters followed by systemic antibacterial (15%), analgesics (6.3%) and antacids (4.3%). As this study indicated 662(52.2%) of the pregnant women received a drug from category A, 345(27.2%) from category B, 186(14.7%) from category C, 46(3.6%) from category D and 2(0.2%) women received a drug from category X of US FDA risk classification system [15].

METHOD: A retrospective prescription survey was conducted among 381 patient pregnant women attending Adama Referral hospital, Adama city, Ethiopia. The investigation was performed within December to May 2011.

From the study populations systematic random sampling was used to draw a sample (i.e. the first last Six Month patient cards was taken, then from which patient cards were drawn at regular interval). Thirty five patient cards were drawn at regular interval for eleven days. Prescribed medicines in the hospitals are dispensed in the hospital pharmacies when available; otherwise patients are referred to the communities for refills.

Permission was sought from the authorities of the hospitals before commencement of the study. Medical case files of the pregnant women were retrieved and reviewed, and relevant information documented in a specific data collection format designed for the study. Data were gathered on age, gravidity, and medicines prescribed.

The average number of medicines per encounter was calculated by dividing the total number of drugs by the number of encounters. Percentage encounter with generic name, percentage encounter with antibiotics, and percentage of encounter with injections were determined by dividing the number of occurrence by the total number of event, respectively, and multiplying by 100. Data on the United States Food and Drug Administration classification of medicines according to risk to the fetus were obtained based on information provided in the physician's drug handbook [16].

RESULTS: A total of 381 patient cards (for pregnant women) were collected and assessed during the study period. Demographics obtained showed that the average age was 26.74 years. 160 (42%) of the study women were found in their second trimester. Most of the pregnant women 195(51.18%) were found to have age of (24-32) years. From a total pregnant women included in the study were primigravidae 75 (19.69%), secundigravidae 100 (26.25), multigravidae 198 (52%), while in 8 cases (2.1%) the gravidity was not indicated. **Table 1** shows age range, gestational period and gravidity of pregnant women in Adama hospital

TABLE 1: SOME SOCIO-DEMOGRAPHICS AND OBSTETRIC CHARACTERISTICS AMONG PREGNANT WOMEN

Age range (in years)	Number (%)	Gestational age (in Trimesters)	Number (%)	Gravidity	Number (%)
15-23	82 (21.52)	First	100(26.25)	primigravidae	75(19.69)
24-32	195(51.18)	Second	160(42.0)	secundigravidae	100(26.25)
33-40	98(25.72)	Third	121(31.76)	multigravidae	198(52)
41-49	6(1.57)			gravidity not indicated	8 (2.1%)

Table 2 shows the pattern of medical conditions occurring among the women in Adama hospital. Gastrointestinal infections 70 (18.4%) occurred most frequently followed by Genitourinary infection 60 (15.74%) and Anemia 35 (8.8%).

TABLE 2: PROFILE OF MEDICAL CONDITIONS AMONG PREGNANT WOMEN IN ADAMA HOSPITAL,OROMIA REGION, ETHIOPIA JUNE 2011.

Medical condition	Frequency (%)
Gastro intestinal infections	70 (17.6)
Genito Urinary infections	60 (15.07)
Anemia	35 (8.8)
Malaria	30 (7.53)
Respiratory infections	29 (7.3)
Hypertension	28 (7.03)
Pain	21(5.3)
Asthma	20 (5.02)
Topical problems	19 (4.8)
Nausea/vomiting	19 (4.77)
HIV/AIDS	14 (3.5)
Helmentics	17 (4.27)
Others	36 (9.44)
Total	398 (104.5)

A total of 720 prescriptions were obtained from the 381 medical case files. The average number of drugs per encounter was found to be 1.72 (range 1 – 6). Thirty seven different medicines were encountered. Table 3 shows the WHO prescribing indicators that were evaluated. The usage of inject able medications was below that of WHO standard.

TABLE 3: PRESCRIBING INDICATORS FOR PREGNANT WOMEN IN ADAMA HOSPITAL, OROMIA REGION ETHIOPIA JUNE 2011.

Prescription indicators	Value obtained	WHO standard
Average number of drugs per women	1.72 (range 1 – 6)	1.6-1.8
% drugs prescribed by generic name	98.61	100
% encountered with antibiotics	24.0	20-26.8
% encountered with injections	11.25	13.4-24.1

Minerals and vitamins 209(29.02%) were the most frequently prescribed drugs followed by Antibiotics 173(24.02%) and analgesics 149(20.7%). Among minerals and vitamins, Iron sulphate 85(40.7%) was mostly used followed by folic acid 50(23.9%) and vitamin B-Complex 36(17.2%). From Antibiotic groups, Amoxicillin 58(33.5%) was highly prescribed followed by Ampicillin 28(16.2%). Paracetamol 131(87.9%) was the most frequently prescribed analgesic.

The distribution of medicines prescribed to these pregnant women is shown in **Table 4.**

TABLE 4: FREQUENCY DISTRIBUTION OF THE MEDICINES PRESCRIBED FOR PREGNANT WOMEN BY TRIMESTER

Therapeutic classes of the drugs	Name of each drug	Frequency of drugs in each trimester (%)			Total
		1st trimester (100)	2nd trimester (160)	3rd trimester (121)	
Minerals and Vitamins	Iron sulphate	13(7.4)	52(15.5)	20(9.6)	85
	Folic acid	23(13.1)	22(6.54)	5(2.4)	50
	Vitamin B-complex	16(9.1)	13(3.9)	7(3.4)	36
	Multi vitamin	9(5.1)	9(2.7)	5(2.4)	23
	Iron with folic acid	-	9(2.7)	6(2.9)	15
	Total	61(34.7)	105(31.25)	43(20.7)	209(29.01)
Antibiotics	Amoxicillin	16(9.1)	18(5.4)	24(11.5)	58
	Ampicillin	6(3.4)	14(4.2)	8(3.8)	28
	Erythromycin	3(1.7)	12(3.6)	6(2.9)	21
	Bacterium	2(1.1)	13(3.9)	10(4.8)	25
	Chloramphenicol	3(1.7)	17(5.1)	4(2.0)	24
	Ceftriaxone	6(3.4)	7(2.1)	4(2.0)	17
	Total	36(20.5)	81(24.1)	56(27.0)	173(24.00)
Analgesics	Paracetamol	38(21.6)	58(17.3)	35(16.8)	131
	Diclo-denk	2(1.1)	9(2.7)	-	11
	Aspirin	2(1.1)	5(1.5)	-	7
	Total	42(23.9)	72(21.4)	35(16.8)	149(20.7)

TABLE 4 CONTINUED

Respiratory drugs	Dextrometrophan	3(1.7)	4(1.2)	6(2.9)	13
	Sulbutamol	3(1.7)	2(0.6)	2(0.1)	7
	Total	6(3.4)	6(1.8)	8(3.8)	20(2.8)
Antispasmodic	Hyoscine	2(1.1)	1(0.3)	-	3 (0.4)
Immunological agent	Tetanus toxoid	-	2(0.6)	1(0.5)	3(0.4)
Anti diabetic	Insulin	-	2(0.6)	3(1.4)	5(0.7)
Anti-malaria	Chloroquine	6(3.4)	14(4.2)	7(3.4)	27
	Quinine	1(0.6)	2(0.6)	-	3
	Total	7(3.1)	16(4.8)	7(3.4)	30(4.2)
Anti-hypertensive	Aldomet	1(0.6)	9(2.7)	13(6.25)	24
	Hydralizine	-	-	4(1.1)	4
	Total	1(0.6)	9(2.7)	17(8.2)	28(3.9)
Antacids	Magnesium trisilicate	1(0.6)	2(0.6)	5(2.4)	8
	$Mg(OH)_2$ and $AL(OH)_3$	2(1.1)	3(0.9)	12(5.8)	17
	Total	3(1.7)	5(1.5)	17(8.2)	25(3.5)
Anti-emetics	Promethazine	6(3.4)	-	1(0.5)	7
	Chlorpromazine	4(2.3)	3(0.9)	-	7
	Plasil	3(1.7)	2(0.6)	-	5
	Total	13(7.4)	5(1.5)	1(0.5)	19(2.6)
Anti-Retro-Viral drugs	AZT	-	10(2.1)	-	10
	Zidolam	-	2(0.6)	1(0.5)	3
	Zidolam-N	-	-	1(0.5)	1
	Total	-	12(3.6)	2(0.1)	14(2.0)
Anti- helmentics	Niclosamide	2(1.1)	3(0.9)	3(1.44)	8
	Piperazine	1(0.6)	6(1.8)	2(0.1)	9
	Total	3(1.7)	9(2.7)	5(2.4)	17(2.4)
Sedative/hypnotics	Phenobarbitone	-	2(0.6)	1(0.5)	3
	Diazepam	-	2(0.6)	1(0.5)	3
	Total	-	4(1.2)	2(0.1)	6(0.8)

The maximum number of drugs were prescribed in the second trimester 336(46.67%) followed by third trimester 208(28.9%) and first trimester 176(24.44%). In all three trimesters, paracetamol was the most frequently used drug which was 38(21.6%), 58(17.3%) and 35(16.8%) in the first, second and third trimesters respectively. Folic acid 23(13.1%), Iron sulphate 52(15.5%) and Amoxicillin 24(11.5%) were the second most prescribed drugs in the first, second and third trimesters of pregnancy respectively.

Anti-Retro-viral drugs and sedative/Hypnotics were not prescribed in the first trimester. But, higher values of Anti-hypertensive drugs 17(8.2%) were used in the last trimester. Whereas sedative/hypnotics 4(1.2%) and ARV drugs 12(3.6%) constituted a greater value in the second trimester. Anti-emetics 13(7.4%) were mostly prescribed in the first trimester. Whereas, antacids 17(8.2%) were highly used in the third trimester.

According to a classification of drugs based on their risk to fetus indicated that from a total of drugs prescribed 449(62.4%) were belong to US-FDA pregnancy risk category B, 122(1.7%) were category C, 109(15.13%) were from category A and 40(5.6%) were in category D. There were no drugs prescribed from category X. **Table 5** shows drugs and their frequency of occurrence in this study.

TABLE 5: RISK CLASSIFICATION OF MEDICINES AND THEIR FREQUENCY OF OCCURRENCE (N=381)

A	Adequate clinical studies have shown no risk to fetus in any trimester: Folic acid (50), Vitamin B-Complex (36), Multi-vitamin (23)
B	Animal studies have not shown adverse effect on the fetus and there are inadequate clinical studies: Paracetamol (131), Iron sulphate (85), Amoxicillin (58), Ampicillin (28), Methyldopa (24), Erythromycin (21), $Mg(OH)_2$ and $Al(OH)_3$ suspension (17), Iron with folic acid (15), Ceftriaxone (17), Piperazine (9), Magnesium trisilicate (8), Niclosamide (8), plasil (5), Hyoscine (3), Insulin (5), Tetanus toxoid (3), Chlorpromazine (7), Nitrofuconazole (4), Miconazole (1), Chloroquine (27), Bacterium (25), Dextrometrophan hydrogen bromide (13), Dextrometrophan hydrogen bromide (13), Clotrimazole (14), Promethazine (7),Diclo –denk (11)
C	Animal studies have shown adverse effects, no adequate clinical studies. May be useful in pregnancy despite potential risks: AZT (10), Sulbutamol (7), Zidolam (3), Zidolam-N (1), Hydralizine (4),

D	There is evidence of risk to human fetus, but potential benefits may be acceptable despite potential risks: Chloramphenicol (24), Phenobarbitone (3), Diazepam (3), Aspirin (7), Quinine (3)
X	Animal/human studies show foetal abnormalities. Risks involved clearly outweigh benefits: (None)

From category A, folic acid 50(45.9%) was the most frequently consumed drug followed by vitamin B.Complex 36(33.02%). Paracetamol 131(29.2%) was leading from category B; followed by Iron sulphate 85(19.0%) and Amoxicillin 58(13%) respectively. From drugs which were under risk category C, Chloroquine 27(22.1%) was most frequently prescribed. Chloramphenicol 24(60.0%) had a highest value from category D. In category A, the maximum number of drugs was prescribed in the first trimester 48(44.03%). From a category B, higher value of drugs were prescribed in the second trimester 208(46.3) followed by third trimester 145(32.3%) and first trimester 101(22.5%). Majority of the drugs from risk category D were also prescribed in second trimester 28(70.0%).

DISCUSSION: The average maternal age obtained in this study was greater than obtained in study in Nepal [9] and less than that obtained in Netherlands.[17] Multi-gravid women formed the majority of the women attending the Hospital. The pattern of medical conditions obtained in this study was similar to that reported in the Nepal study where drugs use were mainly due to Gastro intestinal problems (dyspepsia, Nausea, vomiting, parasite infections, typhoid).[1] Genito Urinary infections were the second prevalent problem occurred among these pregnant women which is similar to a Brazil study.[17]

The average number of drugs per prescription in this study (1.72) was within the range of the standard set by WHO (1.6-1.8)[18] and comparable with that of the study in Netherlands. [12, 17] The maximum number of drugs prescribed was 12. The implication could be the patient might have more medicines than she can cope in terms of cost and adherence. The higher number of drugs may also increase the risk of adverse drug interactions. Majority of the drugs were prescribed by their generic name. Generic prescription of the drugs in this study was much more than the figure of Nepal study.[9] The higher value obtained on generic prescription probably indicate that rational prescribing was practiced in the hospital. This might be due to continuing education on the principles of rational prescribing and familiarity with generic name of drugs among prescribers.

The occurrence of injectables in this study was lower than the standard set by WHO [18]. This is encouraging because the high frequency usage of injectables may introduce high concentration of drug in the plasma, which could lead to toxicity in the pregnant women exposed and cause an infection. The prescribing indicators also showed that the percentage encountered with antibiotic was in the range of the standard set by WHO [18]. This is also encouraging, since antibiotics are routine drugs used for most bacterial infections and this could help to minimize drug resistance problems that could be promoted with over usage of antibiotics. From antibiotic group Amoxicillin was a highly utilized drug. This could be due to safety and broad in spectrum of the drug which is preferable for empirical treatment.

The usages of Iron and vitamins in this study have similar trends with study done in Addis Abeba [15] and USA.[19] Minerals and vitamins like foliate, iron sulphate and vitamin B-complex were mostly prescribed drugs which compensates nutritional requirements. From analgesics paracetamol were the most frequently prescribed drug that could be the safety reason of paracetamol in relation to other analgesic drugs. The anti-emetic drugs were most frequently prescribed in first trimester than in third trimester. This is due to the elevation of B-hcG (Human chorionic Ganado tropic) in the early stage of pregnancy which is responsible for Nausea and vomiting [17].

The occurrence of contraindicated drugs was low. Proper prescribing demands that such contraindications do not occur but the use of such drugs may be considered in cases where benefits outweigh the risk.[20] Majority of drugs prescribed were in category B of the FDA's classification of medicines according to risk to the fetus, which is higher than the Addis Ababa study, followed by those in category C. However drugs in A and D were also obtained.

Cotrimoxazole was the second mostly used drug from risk category C, which is considered to be teratogenic, especially at early stage of pregnancy. This is due to antagonism actions of Cotrimoxazole to a foliate which lead to a deficiency of foliate at the

site of requirement for fetus that result in Neural tube defect [13]. Chloramphenicol was the most frequently prescribed drug from category D; the drug may cause a cardio vascular collapse (Gray syndrome) in pregnancy.[13] Drugs from risk category D such as sedative /Hypnotics (phenobarbitone, Diazepam), Aspirin and Anti malaria (Quinine) may cause oral cleft, prolongation of bleeding time and abortion respectively [13]. This may have been in cases where benefits outweigh the risk.

CONCLUSION: Gastrointestinal infection occurred most frequently followed by genitor-urinary tract infections. Women with second trimester were received medication mostly for the treatment of urinary tract infections. Most of the drugs were prescribed by their generic name. Occurrence of injectables was desirably low. Vitamins, minerals, paracetamol and amoxicillin were most frequently prescribed drugs. The average number of drugs per prescription was comparable with a standard set by WHO, indicating that poly pharmacy was not practiced. The occurrence of contraindicated medicines was desirably low.

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