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DRUG UTILIZATION PATTERN AND POTENTIAL TERATOGENESITY RISK AMONG PREGNANT WOMEN; NEKEMTE REFERRAL HOSPITAL, EAST WOLLEGA ZONE, OROMIA REGIONAL STATE, ETHIOPIA

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ABSTRACT

Back ground: Pregnancy is a special physiological condition where the treatment needs a special concern. It is important to treat the mother whenever needed while protecting the unborn from any side effects to the greatest possible extent. Pharmacotherapy during pregnancy is very challenging. Because, only a few medicines have been specifically tested for safety and efficacy **Objective:** To evaluate the pattern of prescribed only drugs and their risk categories during pregnancy in Nekemte Referral Hospital, Oromia Region, Ethiopia **Method:** A retrospective study was conducted by reviewing medical case files of 338 pregnant women, encountered with at least one drug, from 1876 pregnant women attending antenatal clinics of Nekemte Referral hospital, Oromia region, Ethiopia from January 09/ 2014 to June 02/ 2015. .The prescription pattern was assessed as perspectives of WHO core drug use indicators, and the United States Food and Drug Administration fetal harm classification, in lines with respective trimester. All drugs used during the first, second and third trimesters of pregnancy were further classified into category-A, category-B, category-C, category-D and category-X, according to the classification for drug use during pregnancy, introduced by FDA. **Results:** From 77.22% of pregnant women in this study are between age 20 to 35 years, 18.93% are greater than 35 years of age and 3.85% are under 20 years. 43% are second gravidae 32%multi gravidae 23.08% primigravidae and 2.07% gravidae is not indicated. 80.47% are visited ANC in their first trimester. GIT disorder accounts for 31.73% 38.49% and 47.66% in first, second and third respectively and totally account for 36.62% from all medical conditions.UTI is the second most (13.64%). Category A drugs accounts for 20.83% category, category B (26.34%), category C (24.34%) category C/D (9.65%), category D (9.43%) category X (1.09%) average drug per prescription is 1.41. Percentage of encounter with antibiotics is 31.8% percentage of encounter with injection is 19.30%. Percentage of drug prescribed with generic name is 94.08%. **Conclusion and recommendation:** Approximately half of the pregnant women utilized drugs from FDA category C, D and X which are thought to cause fetal harm, hence the use should be minimized.

KEYWORDS: Teratogens, Pregnancy, Maternal exposure, trimester, FDA category.

1. INTRODUCTION

1.1. Background

The majority of medicinal products or chemical substances administered to a pregnant woman could have effects on the fetus either before the placenta is fully developed or subsequently, if they can cross the placenta to at least some extent. Substances used for therapeutic purposes in the mother have the potential to reach the fetus with the consequential potential for harmful effects, depending on whether the rate and extent of drug transfer results in sufficient concentrations within the fetus.[1]

Medicinal products may have a different impact at different stages of pregnancy. The spectrum of effects varies according to the period of exposure. For example, the exposure to a teratogenic agent during the period of organogenesis may induce major malformation, growth retardation or death, while exposure during the second or third trimester may induce growth retardation, renal

insufficiency, neurological disorders, stillbirth, etc. On the other hand, exposure to a teratogenic agent during the first two weeks of pregnancy (3rd and 4th gestational week) may lead either to the death or to a normal pre-embryo according to the "all or nothing rule"; at this period zygotes and blastocysts contain omnipotent stem cells without any differentiation, therefore, teratogenic agents may lead to seriously damaged pre-embryo, which will not survive, or to less seriously damaged pre-embryo, which will survive with complete regeneration.[1,2]

To minimize the fetal risk of exposure, drug therapy of the mother should be restricted as much as possible. This is, however, not be applied in all cases. The mother may have a serious illness which requires treatment, or a condition that untreated may pose significant risk to the fetus.

In order to optimize the knowledge about any potential teratogenic or embryo toxic/fetotoxic effects of a medicinal product and the doses and concentrations at which such effects will develop, it is desirable to gather information about all medicinal products taken by pregnant women.[1,3]

1.2. Statements of the Problem

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.[2,3] It has been estimated that up to 10% of congenital anomalies may be caused by environmental exposure i.e., exposures to medications, alcohol, or other exogenous factors that have adverse effects on the developing embryo or fetus[4] Medicines are known to account for 1% of the possible external etiological factors of congenital defects.[5,6]

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 increase burden of risk assessment for providers, when treating pregnant women and can have significant on impact therapeutic decision making.[3,4] Therefore 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 strategies.[7]

The potential teratogenesis of some medicines and the physiologic changes which affect medicine disposition in pregnancy are of great concern to clinicians and other health professionals involved in the treatment of pregnant women.[8,9] Correct and cautious use of medicines in pregnancy is therefore important for safe pharmacotherapy to both the mother and her unborn baby. Medicine prescribing in pregnancy would therefore require good knowledge of teratogenicity, fetal and neonatal effects that are associated with the medicines under consideration.[10]

Pharmacological treatment should be avoided in pregnancy, unless absolutely necessary, because most drugs are potentially harmful to the fetus. However, treatment becomes inevitable when a woman with a chronic medical condition becomes pregnant.[11] The chronic medical conditions such as hypertension, diabetes mellitus, epilepsy, bronchial asthma and sickle cell anemia will require ongoing or episodic treatments.[12] In addition, there are multiple medical conditions, some of which directly result from the pregnancy or are worsened by it, that may require pharmacological therapy.[13]

Acute medical problems such as malaria, urinary tract infection, gastrointestinal disorders, migraine and upper respiratory tract infection can also develop during pregnancy and require pharmacotherapy.[11] Therefore failure to manage these acute and chronic medical conditions may adversely affect the health of both the mother and her fetus.[14] Pregnant women are generally excluded, for ethical reasons, from randomized clinical trials in drug development.[15] This has left questions about the safety of new medications on the developing fetus un answered, upon drug approval and marketing. Despite the unanswered safety questions, women may intentionally or inadvertently be exposed to various prescription and non-prescription medicines before and during pregnancy. Post marketing surveillance studies have revealed association between many commonly used medicines and various birth defects.[16]

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.[5,6] 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.[5,17,18]

The category-A includes drugs that have shown no risk to the fetus after adequate, well-controlled studies in pregnant women. For drugs in the category B, animal studies have revealed no evidence of harm to the fetus or any adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus. The category C includes the drugs, which have shown an adverse effect in animal studies and there are no adequate and well-controlled studies in pregnant women. For drugs in the category D, there is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk. However, drugs with classification X are "contraindicated in pregnancy.[18,19]

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).[19]

1.3. Significance of the Study

As there are numerous gaps in knowledge about untoward effects of drugs, prescription drug used by pregnant women should be viewed as a public health issue. The health care delivered to one community should timely reorient and organized based on the available up-to-date information from well-organized research of existing data. In Nekemte hospital there is no such study done before that show the drug use pattern during pregnancy. Therefore, this research can would serve as base line to do further research in that area and give information to prescriber pregnant women and responsible bodies about the patterns of pregnancy drug use.

2. OBJECTIVES

2.1. General objective

To assess the drug use pattern and potential teratogenicity risk among pregnant women taking prescribed drugs in Nekemte Referral Hospital, Eastern Wollega, Oromia Region, Ethiopia from January 09/2014 to June 02/2015.

2.2. Specific objectives

To evaluate drug use pattern using WHO core prescribing indicators in each trimesters.

To evaluate different FDA category drugs prescribed in each trimester.

To determine the percentages of pregnant women prone to possible teratogens, namely category C, D and X.

3. METHODS AND MATERIALS

3.1. Study Area and Period

The study was conducted in Nekemte Referral Hospital (NRH), Nekemte town, Eastern Wollega zone, Oromia region, Ethiopia which is found 312 km from Addis Ababa. NRH has different departments and wards like Outpatient department (OPD), medical ward, gynecology and obstetrics ward, pediatrics ward and surgical ward. It delivers diversified health services and clinics including the emergency services, eye clinic, dental clinic, mother and child health (MCH),orthopedics, psychiatry clinic, laboratory,X-ray, Physiotherapy and follow up of chronic disease like TB ,DM and HIV AIDS. The Hospital possesses outpatient, inpatient, emergency and ART pharmacies. It has also one nursing school.

3.1.1. Study Design

Record based retrospective cross-section study design was used in this study to extract data.

3.1.2. Study Period

This study was conducted from January 09/2014 to June 02/ 2015.

3.2. Population

3.2.1. Source Population

All pregnant women who are on antenatal care follow up at Nekemte Referral hospital East Wollega, Oromia region, Ethiopia, 2015

3.2.2. Study population

Pregnant women who are on ANC follow up of one year from January 09/ 2014 to June 02/2015 in Nekemte referral hospital, east Wollega, Oromia region, Ethiopia.

3.3. Eligibility criteria

3.3.1. Inclusion Criteria

All pregnant women who visited greater than or equal to two times in their gestational period.

The prescribed drugs are clearly corresponds with the trimesters.

3.3.2. Exclusion Criteria

Clients with less than 2 times visit in 270 days of pregnancy.

The drugs that are prescribed without clear date is indication.

Redundant medical case cards of the same person.

Self-medication drugs by pregnant women, i.e. drugs taken without documented order Sheet on patient card.
Topically applied drugs except ophthalmic and vaginally applied topical formulations.

3.4. Study variables

3.4.1. Independent variables

- Age
- Disease
- Address
- Body weight
- Pregnancy trimester.

3.4.2 Dependent Variables

- Dosage regimen (route, dose, frequency, dosage form, duration)
- FDA drug category.
- Average number of drugs per women.
- Percentage encounter with drug
- Percentage encounter with injection
- Percentage drugs prescribed by generic name.

3.5. Sampling Technique and Sample Size Determination

3.5.1. Sampling Technique

A retrospective study design was conducted based on systematically selected medical profiles of ANC follow up pregnant women in the hospital, who have on ANC follow up in the last one years (January 09/2014 to June 02/2015).

3.6. Sample Size Determination

In Nekemte Referral Hospital each year around 2000 pregnant women attend ANC follow up. From the last one year follow up pregnant women are selected as study population. From January 09/2014 to June 02/2015, there are 2162 pregnant women registered on ANC registration book. 1876 pregnant cards fulfill the criteria for follow up and actually present in the card room. From 1876 pregnant women 323 pregnant women had encountered with at least one drug. These the sample size is 323.

3.6.1. Data Collection and Management

Pregnant women who are on ANC follow up with at least more than one visit at NRH from Registration book of antenatal care follow used so that the Patient medical record (PMR) of January 09/2014 to June 02/2015 was accessed. Required information like Patient age, address, gravidae, and drugs prescribed, dosage form, and route of administration, main diagnosis, the trimester during drug administration, and other related issues was collected from the patient profile using a structured data collection sheet.

3.6.2. Data analysis and Consideration

After data collection, data edition and clearing was done and the collected data was checked manually for completeness and then, the data was coded and analyzed using FDA pregnancy drug category and WHO core prescribing indicators and the data was presented using tables, figures and frequencies.

3.7. Ethical Consideration

A formal letter was written from department of pharmacy, Wollega University to NRH in order to get permission to conduct the study. Staff members of gynecology and obstetrics ward of NRH including the physician, HOs, Nurses and other health care providers, permission for any cooperation was politely asked. The confidentiality of patients is secured throughout the study periods without writing full patient names by using codes.

3.8. Limitation and challenges

Lack of time, budget and unwillingness of the respondents.

The harm caused to the fetus from drug is dependent on many factors. The bioavailability of the drug that reaches to the fetus through the placenta is dose and duration dependent. This study does not include the dose and duration of the exposure.

This research focused only on prescribed drugs by the health professionals, despite vast drugs exist as OTCs that may need as great cautions as prescription only medication(POM) to use during pregnancy.

3.9. Operational Definitions

ANC follow up: ANC visit of greater than one time in full pregnancy period.

FDA category A/C: manufacturer's difference in assigning the category.

FDA category C/D: Categorized as D above 30weeks of pregnancy and category C otherwise.

Gestational age or length: the duration of gestation is measured from the first day of the last normal menstrual period to dates of delivery irrespective of term delivery

Non FDA category medications: drugs that are either in fixed dose of different category or single drugs that are not in clear category.

Prescribed drug: drugs that are written on order sheets of patient card

Prevalence: number of instances of an occurrence in a study population

Risk: any actual or possible unintended effect of the drug on the fetus Trimester: pregnancy duration every 90 days

Teratogens: drugs administered during pregnancy, which can cause an intended effect on the fetus either before or after the delivery.

4. RESULTS

A total of 323 women received 456 prescriptions excluding HAART and anti-TB drugs. The age of patients was within the range of 16-49 years with average age of 26.02 years. Majority of the patients in the study were in the age group of 20-35 years(77.22%), which represents the normal reproductive age group, followed by>35 years (19.20%) and<20 years (3.85%). Of the pregnant women 43.00% were second gravidae, 32.00% primigravida, and 23.07% are multi gravidae, but in 2.07% gravidae is not indicated. Most of the pregnant women visited ANC in their first trimester (61%), followed by second and third trimester which accounts for 25%, 13.61% respectively. Majority (80.47%) of them visited three to five times in their full pregnancy period.

Table 1: Characteristics of pregnant women attending ANC at Nekemte Referral Hospital, East Wollega Oromia region, Ethiopia from January 09/ 2014 to June 02/2015.

Parameter	Number of subjects	Parameter	Number of subject
Age (in years)		**Time of first ANC Visit**	
<20	12(3.85%)	In first trimester	197(61%)
20-35	249(77.22%)	In second trimester	91(27.86%)
>35	62(19.2%)	In third trimester	35(10.84%)
Gravidae		**Total numbers of ANC Visit**	
Prime gravidae	75(23.21%)	2 times	58 (17.12%)
Second gravidae	139(43%)	3-5	272 (80.47%)
Multi gravidae	104(32%)	>5	272 (80.47%)
Gravidae not Indicated	7(2.07%)		

Majority of pregnant women encountered with drugs were those women in the first trimester of gestation (43.96%) followed by second trimester (32.84%) and third trimester (23.20%).

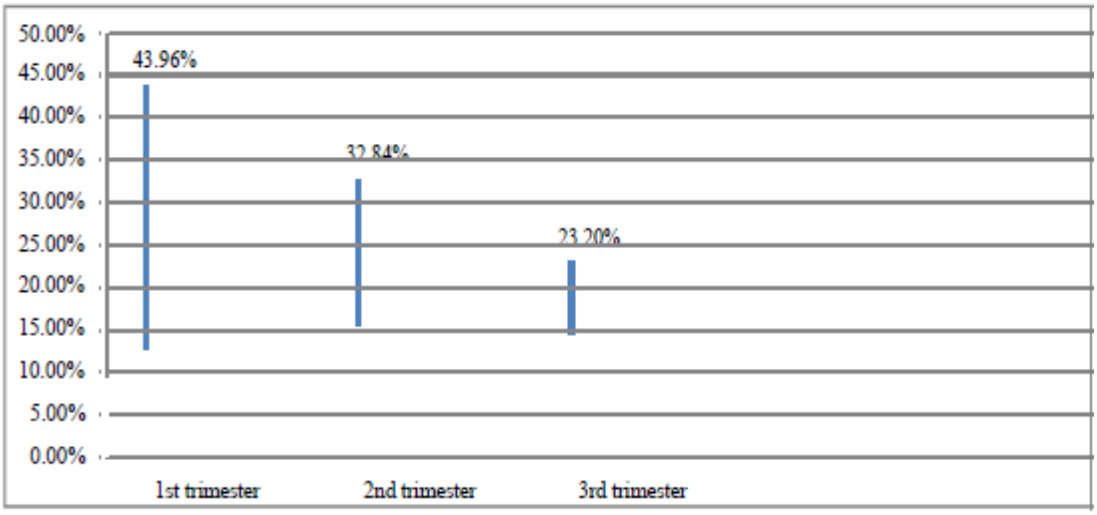

Fig 1: Frequency distribution of trimesters in pregnant women encountered with at least one drug, at Nekemte Referral Hospital, East Wollega, Oromia region, Ethiopia, from January 09/ 2014to June 02 / 2015.

Among medical condition that necessitates drug treatment in different trimesters, gastro intestinal disorder was the major ailment(36.62%) which comprises 31.73%, 38.49% and 47.66% in first, second and third trimester respectively. Dyspepsia was the highest in first trimester, and second trimester gestation.

Table 2: Distribution of medical conditions among pregnant women at Nekemte Referral Hospital, East Wollega, Oromia region, Ethiopia, from January 09/ 2014 to June 02 / 2015.

Main diagnosis	Frequency (%)		
	1st trimester	2nd trimester	3rd trimester
Dyspepsia	11.27	17.12	0
UTI	8.45	17.97	17.97
Abdominal discomfort	7.80	4.70	12.00
AFI	7.75	6.66	4.00
PUD	6.34	3.81	10.66
HEG	0	2.83	21.00
CAP	9.15	7.50	4.10

Among the dosage forms prescribed to pregnant women tablet (57.02%) is the highest across all trimesters. Solution is relatively high (32.93%) in third trimester and low (13.38%) in second trimester. Vaginal cream is the least across all trimesters compared with other dosage forms.

Table 3: dosage form of drugs prescribed to pregnant women who attend ANC follow up at Nekemte Referral Hospital, East Wollega, Oromia Region, Ethiopia from January 09/ 2014 to June 02/2015.

Dosage form	Frequency (%)			
	1st trimester	2nd trimester	3rd Trimester	Total
Tablet	60.46	60.01	44.61	57.02
Capsule	6.52	11.89	14.63	9.65
Syrup	8.69	10.49	6.10	8.77
Gels	2.17	2.09	1.22	1.97
Vaginal cream	0.43	1.44	0	0.66
Solution	16.08	13..38	32.93	18.86
Ointment	5.65	0.7	0	3.07
Total	**100**	**100**	**100**	**100**

In all trimesters oral route of administration was the most prescribed followed by intravenous route. Intramuscular route of administration was the least in all trimester except in third trimester in which topical medication was not used.

Table 4: route of administration of prescribed drugs for pregnant women attending ANC at Nekemte Referral Hospital, East Wollega, Oromia Region, Ethiopia from January 09/ 2014 to June 02/2015.

Route of administration	Frequency (%)			
	1st trimester	2nd trimester	3rd trimester	total
PO	72.17	50.35	59.75	61.62
IV	16.08	13.38	32.93	18.86
IM	2.17	2.09	1.22	1.97
Vaginal	2.06	4.89	2.44	3.24
Topical	5.65	0.7	0	3.07

Topical formulation in this study refers to ophthalmic formulation that is thought to be absorbed significantly systemically.
IM = intramuscular, IV= intravenous, PO= oral route.

From the total drugs prescribed for pregnant women FDA category B was the highest (26.75%) prescribed drugs followed by category C, A, C/D, D which account for 24.34%, 20.83%, 9.65%, and 9.43%, respectively. Category A/C (2.20%) and category X (1.09%) were the least prescribed drugs. Category A drugs were highly utilized in second trimester (10.53%) and the least (2.20%) in third trimester. Category B, C, D drugs were the most frequently prescribed drugs in first trimester which account for 11.62%, 13.38% and 7.01%, respectively. Category B and C drugs were the least prescribed drugs in third trimester with values of 2.20% and 4.17%, respectively, but category D is the least prescribed drugs in second trimester (0.88%). Category X was prescribed only in first trimester. None FDA category drugs account for 5.70% from the total drugs prescribed in different trimester. Category C and D together comprises 52.17%, 33.57% and 36.58% in first, second, and third trimester, respectively. Category D and X together comprises 16.08%, 2.79% and 8.53% in first, second and third trimesters, respectively. From the total drugs prescribed category C, D together is 44.52% while category C, D and X together is 44.61%.

Table 5: frequency distribution FDA drug category of the drug prescribed during ANC follow up at Nekemte Referral Hospital, East Wollega, Oromia Region, Ethiopia from January 09/2014 to June 02 /2015.

FDA drug category	1st Trimester	2nd Trimester	3rd trimester	Total
A	37 (8.11%)	48 (10.53%)	10 (2.2%)	95 (20.83%)
A/C	6 (1.32%)	4 (0.88%)	0	10 (2.2%)
B	53 (11.62%)	36 (7.9%)	33 (7.24%)	122 (26.75%)
C	61 (13.38%)	35 (7.67%)	19 (4.17%)	111 (24.34%)
C/D	27 (5.92%)	9 (1.97%)	4 (0.88%)	44 (9.65%)
D	32 (7.01%)	4 (0.88%)	7 (1.53%)	43 (9.43%)
X	5 (1.09%)	0	0	5 (1.09%)
Non-FDA Categorized	9 (1.97%)	7 (1.53%)	9 (1.)09%	26 (5.7%)

A/C = Refers to manufacturer's difference in categorizing.
C/D = Categorized as D above 30weeks of pregnancy.

Table 6: frequency distribution and individual drug prescribed to pregnant women at Nekemte Referral Hospital, East Wollega, Oromia Region, Ethiopia from January 09/2014 to June 02 /2015.

FDA drug category	Frequency (%)	Representative drugs
A	95(20.83%)	Ferrous sulphate,folicacid, multivitamine, vitamine B complex, pyridoxine,
A/C	10(2.2%)	Magnesium trisilicate, Magnesium sulphate
B	122(26.75%)	Ampicillin, metochlorpromide, Ceftriazone, Amoxicillin Amoxacillin/ Clavulinic acid Erythromycin, cephalexin, cloxacillin, meclizine, metronidazole, methyldopa,CAF eye oin., calcium gluconate,
C	111(24.34%)	Norflxacillin, CAF, APAP, antacid, syrup, cimetidine, omeprazole, Dexamethasone eye oin., mebendazole, Hyosine, Ketoconazole cream, nifedipine, promethazine,tramadol, amytryptline furosemide, cotrimoxazole,hydralizine, hydrocortisone, vit.K, bisacodyl, indomethacin, albuterol
C/D	44(9.65%)	Ibuprofen, enalapril, diclofenac,
D	43(9.43%)	Doxycycline,gentamcin,Cpz,TTC eye oin., diazepam, phenytoin, Phenobarbital
X	5(1.09%)	Mesoprustole
Non-FDA Categorized	26(5.7%)	Calciumgluconate,H2O2,maintenance fluids, combined cough syrup

Average numbers of drugs per prescription is relatively high in first trimester (1.62), and it is relatively low in third trimester (1.09). Percentage of encounters with antibiotics is the highest in second trimester (41.46%) and the lowest in third trimesters (25.87%). Percentage encountered with injection is the highest in third trimester (35.36%), followed by the second (16.08%) and first trimester (15.65%). Percentage of drugs prescribed by generic name is almost the same across all trimester. On average 94.08% drugs were prescribed by their generic name.

Table 7: prescribing pattern indicators with respective WHO references at Nekemte Referral Hospital, East Wollega, Oromia region, Ethiopia from January 09/2014 to June 02 /2015.

Indicators	1st trimester	Value n (%) 2nd trimester	3rd trimester	Total	Reference (30)
Average number of drugs per prescription	230/142 (1.61)	230/142 (1.61)	82/75 (1.09)	456/323 (1.41)	1.6 – 1.8
Percentage of encounters with antibiotic	74/230 (32.17%)	74/230 (32.17%)	34/82 (41.46%)	145/456 (31.8%)	20 -26.8
Percentage of encounters with an injection	36/230 (15.65%	36/230 (15.65%	29/82 (35.36%)	88/456 (19.30%)	13.4-24.1
Percentage of drugs prescribed by generic name	215/230 (93.48%)	215/230 (93.48%)	77/82 (93.90%)	429/456 (94.08%)	100

5. DISCUSSIONS

Out of 323 pregnant women on ANC follow up, about 77.22%%, were between 20 to 35 years which is represents the normal reproductive age groups. Similar result is found in prospective study done in India 94% the pregnant women aged between 20- 35.[25] Average age of the pregnant women is 26.02, this result is similar to study done in Adama Referral Hospital.[33] Greater than half of the patients first visited antenatal OPD in first trimester. Scandium gravidae women formed relatively high percent of the women attending the ANC. This result is similar to research done in is Adama Referral Hospital (45.3%).[28]

From pregnant women encountered with at least one drug, first trimester (43.96%) comprises relatively high numbers of pregnant women followed by second trimester (32.84%) and third trimesters (23.20%). This result is incomparable with the research done in Tigray region Hyder Referral Hospital in which first, second and third trimester is 8.30%, 9.20% and 82.5% respectively .this difference is probably due to inclusion of gynecology and obstructs department in the study in the latter cases.[31]

In study conducted in India majority of patients in the study were in second trimester of gestation followed by third trimester and first trimester. And still the difference in distribution frequency of pregnant in different trimester exists.

The pattern of medical conditions (i.e. dyspepsia (28.39%), UTI (44.2%9), abdominal discomfort (16.4%), HEG (23.83%), PUD (20.81%). comparing this result with study conducted in Adam Referral Hospital is somewhat similar. Drugs used were mainly due to Gastro intestinal problems (dyspepsia, Nausea, vomiting, parasite infections, and typhoid) (18.4%), Genito-urinary infection (15.74%) were the second prevalent problem occurred among these pregnant women followed by community acquired pneumonia. The most medical

problem in third trimester is hyperemesis gravidae in this study. It is expected due to bulging of the uterine that pushes the gastric content upward.

From the dosage forms prescribed for pregnant women tablets are highly used across all trimester, followed by solution, capsules, syrup, and ointment. This result is somewhat similar to the finding of the study conducted in Hyder Hospital except for capsule which is the second most prescribed dosage form.

Oral dosage form comprises the highest percentage across all trimester (61.62%), and it is relatively high in first trimester (72.17%), followed third (59.75%) and second trimester (50.35%). Intra venous dosage form are 32.93%, 16.08% and 13.38 in third, first and second trimesters, respectively. Intra muscular dosage form is the least from total dosage form prescribed. This result is almost comparable with the study done in Hyder Hospital except for vaginal cream which is the least prescribed dosage form across all trimester.

FDA category A drugs include Ferrous sulphate, folic acid, multivitamine, vitamine B complex, pyridoxine, comprises 21.20% from total drugs prescribed. Relatively, it is high in second trimester (10.53%), followed by first (8.11%) and third trimester (2.20%). Compared to the study conducted in USA category A which comprises 2.4% from total drugs prescribed minerals and vitamins are prescribed more in this study.[20] And in another research done in united Kingdome 4.00% of category A drugs were prescribed in the first trimester (Though slightly increased in second and third trimester) still the result in this study is lower than the result in this study.[23] A result from original articles of "Indian Medical Gazette showed higher rates of category A prescribing pattern which are 85.76%, 55.96% and 53.30% in second, first and third trimester, respectively; which is much higher than the result of the this study.[24]

A result from study conducted in Nigeria indicated that category A (10.9%) drugs prescribed is less frequent than this study. When it is compared with the result from research done in Jimma University,[30] and Adama Referral Hospital,[28] category A comprises 35.4%, and 34.1% respectively which is relatively higher than the result observed in this study. The difference between this study results and the finding of literatures mentioned above is probably due to the inclusion and exclusion criteria for one thing and geographical medical condition difference for the other. The practice of using category A is greater than some literature from developed country. But it is still low when compared with some literature from India. In the study conducted in Adama Referral Hospital, mineral and vitamins prescribed made up 29% from the total which is relatively higher than this study.[28]

FDA category B drugs include Ampicillin, metochlorpromide, Ceftriazone, amoxicillin/ amoxaciliin clavulunate. Erythromycin, cephalexin, cloxacillin meclizine, metronidazole, methyldopa, CAF eye ointment. Calcium gluconate. It comprises 26.75%from total drugs prescribed. This result is about half when Compared to results from USA (50.00%). Compared to the study result from united king dome (34.00%) [20], Nigeria (34.8%),[27] Adama referral hospital, Ethiopia (62.4%),[28] the present study finding is low. However, it is higher than the study done in India,[25] which is 12.64%.

Prescribing pattern is slightly higher in first trimester (11.62%) followed by the second (7.24%) and third (7.09%) trimester. From all category B drug beta-lactam antibiotics comprises three fourth of the prescribed drugs.

Category C drugs were used in all trimesters which account for 24.34%. Compared to research done in USA,[21] (i.e. 37.8%) and research done in Nigeria,[27] (i.e 39.1%) it is utilized less in this study. But compared to another study conducted in Nigeria,[26] (i.e. 17.0%) it is relatively higher.

Compared to the study conducted in United King dome,[23] which is 49% the prescribing of potentially harmful drugs for pregnant women in this study is less. In the study conducted in Jimma University specialized hospital,[30] category C comprises 56.3%, which is high compared to this study. This discrepancy is probably due to the inclusion of OTC drug in this literature. The prescribing pattern of potentially harmful drugs to pregnant women is low in India compared to this study,[24,25] The Prescribing pattern of category C is highest in first trimester (13.38%) followed by 7.67% and 4.17% in second and third trimester, respectively. Acetaminophen (30) is the most drugs prescribed from FDA category C drugs. Antacid syrup (27) is the second most while promethazine (2) is the least prescribed drug.

Category D is the most prescribed in first trimester (7.01%) followed by third (1.55%) and second (0.88%) and comprises 9.43% from the total drugs prescribed. Compared to research in USA (i.e. 4.8%),[21] India[24] (i.e. 5.5%), Nigeria,[26] (i.e. 0.72%), the result in this study is relatively high. However, compared to another studies conducted in India (i.e. 13.00%),[25] and Jimma university specialized hospital (i.e. 16%),[30] the value in this study is relatively low. From category D drugs Doxycycline (11) is the most prescribed drug, followed by TTC eye ointment (7), diazepam (6), gentamycin (5), and phenytoin (2).

Category X is prescribed only in first trimester which account 5% from the total drug prescribed. This is comparable to the study in USA (1.1%) but slightly higher than the study conducted in India. Compared to the study in Jimma University Specialized Hospital (i.e

7.1%), it is relatively lower. Category C, and D comprises about half from total drugs prescribed (44.52%); which is almost comparable to the study conducted in United king dome which account for 49%,[23] this result shows that about half fetus are prone to possible teratogens. In study done in India It was found that 20.4% of women purchased at least one drug classified as potentially harmful (category C) during pregnancy, and 3.4% (category D and X) purchased at least one drug classified as clearly harmful, but, in this study it is 24.34%, 10.49% respectively. This shows that pregnant women at Nekemte Referral Hospital are using irrational treatment. Category A/C includes Magnesium trisilicate, magnesium sulphate. These comprise 2.20% from total prescribed drugs.

Average numbers of drugs per prescription is 1.62, 1.34, and 1.09 in first, second and third trimester respectively with the average value of 1.41. This result is lower than the WHO core drug prescribing indicators. This difference might be for one thing from exclusion of HAART and Anti- TB drugs prescribed and exclusion of some pregnant women that only visit once in their pregnancy period.

Percentage of encounter with antibiotics prescribed is 32.17%, 25.87% and 41.46% in first, second and third trimester. Except in the second trimester the result in this study is greater than WHO core drug prescribing indicators. And highest in the third trimester this might be due to high gastrointestinal complain in third trimester for which antibiotics are prescribed.

Percentage of encounter with injection prescribed is highest in third trimester (35.36%) followed by 16.08% and 15.65% in second and first trimester. In this study during third trimester the prescribed injection is higher than WHO standard. This might be due to increased hyper emesis gravidum that need fluid maintenance. Percentage of drugs prescribed by generic name is almost the same across all trimester which is 94.08% on average. Even though the gap is small this result shows 5% of pregnant women might be disadvantaged from extra cost.

6. CONCLUSION AND RECOMMENDATION

6.1. Conclusion

Percentage of encounter with drugs is high in first trimester than other trimesters. FDA category B are the most prescribed drugs and category C is the second most prescribed category. Approximately half of the pregnant women encountered with drugs from category C, D and X which is thought to cause possible fetal harm.

Gastrointestinal complain is the most frequent medical condition for those drugs prescribed for pregnant women. Prevalence of urinary tract infection was increased as trimester goes from first to third.

The practice of poly pharmacy is low. Antibiotics use indicators are within the range of standard except in third trimester. Percentage encounter with injection is high in third trimester. Only few drugs are prescribed by brand name.

6.2. Recommendation

Based on the above result and conclusion the following recommendations are given.

The prescriber should aware presence of pregnancy to prescribe drugs to patient as most ANC follow up start in second trimester; first trimester women are forgotten to be considered in drug selection.

Use of drugs from category C, D and X should be limited as much as possible. Medication selection should consider the trimester in which drug prescribed because some drugs are in different category in different trimesters.

The hospital administration should encourage prescribing by generic name.

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Abbreviations and Acronyms

ANC	**:**	Antenatal Care
Anti TB	**:**	Anti Tuberculosis
APAP	**:**	Acetaminophen (paracetamol)
CAF	**:**	Chloramphenicol
CPZ	**:**	Carbamazepine
HAAT	**:**	Highly Active Ant retro viral Therapy
HEG	**:**	Hyper emesis Gravidum
IM	**:**	Intramuscular,
IV	**:**	Intravenous,
MCH	**:**	Mother and child health
NRH	**:**	Nekemte Referral Hospital
Oin.	**:**	Ointment
OPD	**:**	Outs Patient Department
OTC	**:**	Over the counter drugs
PMR	**:**	Patient Medication Record
PO	**:**	Oral route
SC	**:**	Subcutaneous
TTC	**:**	Tetracycline.

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