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Study of drug utilization pattern and adverse drug reactions among pregnant women attending antenatal outpatient department at tertiary care hospital

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Abstract

Background: Antenatal care is the care provided by skilled health-care professionals to pregnant women and adolescent girls to ensure the best health conditions for both mother and baby during pregnancy. Pregnant women are usually excluded from clinical trials and results from animal studies need not apply to the human population. Prescribing drugs that are contraindicated in pregnancy is of great concern among health professionals. Hence, the current study was planned to evaluate the drug utilization pattern in pregnant women.
Materials and methods: A cross sectional, observational study was carried out in pregnant women who attended the antenatal outpatient department of at a tertiary care hospital. Patient details and medications were recorded in the Case Record Form. Prescribing indicators were evaluated as per WHO criteria.
Results: study was done in 600 participants and majority of the participants were in their third trimester. A total of 2040 medications were prescribed & the total number of drugs per prescription was 4±2 (mean ± SD). The most common co-morbidity found was anaemia (82.16%) & commonly prescribed drug was ferrous sulphate plus folic acid FDC (94.5%).92% drugs were prescribed by their generic names. C and id CL (Clindamycin+Clotrimazole pessary) was the most commonly prescribed drug (16.33%) by its brand name. 50% drugs were prescribed from the NLEM. The highest prevalence of prescribed drugs belonged to category A (46.66%). It has been observed that Tenofovir, Lamivudine and Efavirenz FDC was the most commonly associated drug with ADR.
Conclusion: This study provides an insight regarding utilization pattern of a wide variety of drug classes in pregnant women who attended the antenatal outpatient department of Obstetrics and Gynecology in a tertiary care hospital.
Keywords: Drug utilization, pregnant women, WHO criteria, Comorbidities.

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1. Introduction

The World Health Organization (WHO) emphasizes that every pregnant woman must receive quality health care throughout the pregnancy. [1] The United Nations launched Sustainable Development Goals (SDGs) in 2015. Total of 17 SDGs are set over a period of 15-years. Out of these, SDG3 focuses on ensuring healthy lives and promote well-being for all ages. WHO in consensus with the SDGs have planned strategies for ending preventable causes of maternal mortality. The target is to reduce global maternal mortality ratio (MMR) to less than 70 per 100000 live births by 2030. Around 94 % of maternal deaths occurred in low and lower-middle-income countries. India had one of the highest estimated numbers of maternal mortality cases, accounting for nearly 35,000 maternal deaths (12% of global maternal

deaths) in 2017.[2] Most of these can be prevented through optimal antenatal care. WHO has defined antenatal care as, 'the care provided by skilled health-care professionals to pregnant women and adolescent girls in order to ensure the best health conditions for both mother and baby during pregnancy. Thus, antenatal care is the routine health control of presumed healthy pregnant women without symptoms in order to diagnose diseases or complicating obstetric conditions without symptoms and to provide information about lifestyle, pregnancy and delivery. There is a special concern for drug treatment in pregnancy due to the risk of the teratogenic potential of the drug.[3] The concern regarding medication use during pregnancy has been influenced by historical events, including the thalidomide crisis in the 1960s which led to a range of severe and debilitating malformations.[4] All marketed drugs are not studied to a complete extent to be proved safer in pregnancy and hence, for this obvious ethical reason, most of the drugs are not recommended to be used during the gestational period. However, total avoidance of pharmacological therapy in pregnancy is not possible. Women can enter pregnancy with pre-existing medical conditions which may require ongoing treatment. Discontinuing treatment of a serious condition can have profound, long-term implications on the health of both the mother and her baby.[5,6] Also, new medical condition scan develop during pregnancy and old ones can be exacerbated requiring pharmacological therapy.[7] pregnant women are usually excluded from clinical trials and results from animal studies need not apply to the human population. Fear of causing fetal harm, the threat of legal liability; concern about the complicated physiology of pregnant women has resulted in many challenges to clinical research in pregnancy. Therefore, medication safety information in pregnancy is obtained through animal studies , epidemiological studies and case reports; all of which have limitations making the risk assessment difficult for determining risks of drug use in pregnancy. [8,9] All medications should, therefore, be prescribed after thorough risk-benefit analysis. Prescribing guidelines have been developed for specific conditions or medication types for the use of certain drugs during pregnancy.[10,11] However, there is considerable variation in prescribing pattern which continues to change over time. Prescribing drugs that are contraindicated in pregnancy is of great concern among health professionals.[12] studies based on the use and appropriateness of drug consumption during pregnancy can provide additional information and update the current knowledge. These studies are of pivotal importance for healthcare providers to help them follow the evidence- based practice. Hence, the current study was planned to evaluate the drug utilization pattern in pregnant women visiting the antenatal outpatient department of a tertiary care hospital.

1.1 Aims and objectives:

1) To study the drug utilization pattern in pregnant women with or without co- morbidities.
2) To analyze the respective prescriptions on the basis of WHO prescription indicators.
3) To study the adverse drug reactions in prescribed drugs among pregnant women attending the antenatal outpatient department.
4) To study the management of adverse drug reactions.

2. Materials and methods

2.1 study design

A cross sectional, observational study carried out in pregnant women who attended the antenatal outpatient department of Obstetrics and Gynecology of the tertiary care hospital with or without any co-morbidity.

2.2 Study duration

Two years (November2017-2019).

2.3 Sample size:

Prescription audit was done according to the World Health Organization (WHO) guidelines for investigating drug use in health facilities. It recommendsatleast600 encounters in a cross-sectional survey. [13] Thus, we have recruited 600 participants.

2.4 Selection Criteria

2.4.1 Inclusion criteria

1) All cases of pregnant women attending the antenatal outpatient department.
2) Participantswithageabove18years, with or without co-morbidities.

2.4.2 Exclusion criteria

1) Pregnant women diagnosed with acute and chronic medical conditions requiring hospitalization.
2) Pregnant women who were not willing to give consent
3) Pregnant women with medico legal issues.

This study was commenced after getting approval from the Institutional Ethics Committee. Permission of Head of Obstetrics and Gynaecology department was taken to conduct the study in their OPD. It was made clear to the participants that at no point of the study their identity will be revealed. Strict confidentiality was maintained. The participants were assessed for their eligibility to enter the study as per the inclusion / exclusion criteria. Demographic details were recorded in the Case Record Form & prescriptions were reviewed for the profile of drugs and its details with the provisional or final diagnosis. Any adverse drug reaction related to the ongoing therapy was documented in suspected adverse drug reaction reporting

form with its management. The causality assessment was done using the Naranjo Scale. [14]

WHO Prescribing indicators include average number of drugs per encounter, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic prescribed, percentage of encounters with an injection prescribed, percentage of drugs prescribed from essential drugs list.

Formulae for prescribing indicators:

(a) Average number of drugs per encounter (C)

C = B/A

Where

B is total number of different drug products prescribed

A is the number of encounters surveyed

Purpose: To measure the degree of Polypharmacy

(b) Percentage of drugs prescribed by generic name (E)

E = D/B x 100 where

D is the number of drugs prescribed by generic name

B is the total number of drugs prescribed

Purpose: To measure tendency to prescribe by generic name

(c) Percentage of encounters with antibiotic/s prescribed (G)

G = F/A x 100

Where

F is the number of patient encounters with one or more antibiotic/s prescribed

A is the total number of encounters surveyed

Purpose: To assess the prescribing frequency of these often inappropriately used agents

(d) Percentage of encounters with an injection prescribed (K)

K = J/A x 100

Where

J is the total number of patients who received 1 or more injections

A is total number of encounters

Purpose: To measure overall level of use of this commonly overused and expensive form of drug therapy

(e) Percentage of drugs prescribed from essential drugs list (M)

M = L/ B x 100

Where

L is the number of products prescribed from National List of Essential Medicines

B is the total number of drugs prescribed

Purpose: To measure the degree to which practices conform to the National Drug Policy

2.5 Statistical analysis:

Demographic data that is continuous [age] were expressed as mean± standard deviation. Continuous variables were presented as mean± standard deviation (SD). Drug details were analyzed using descriptive statistics in SPSS software version 21.

3. Results

A total of 600 pregnant women with or without co-morbidities participated in the study. Demographic details and medication details as listed in the OPD case notes were recorded and analysed. Participants were enquired regarding any present co-morbid conditions and relevant past history. The mean age of participants was 24.79 ±4.07 years (mean±SD). The mean weight of the participants was 58.12 ±10.43kg (mean±SD). The mean height of the participants was 154.41±6.79cm (mean±SD).

It has been observed in figure 1 that, out of 600 participants, 5% participants were in their first trimester, 43% participants were in their second trimester while 52 % participants were in their third trimester.

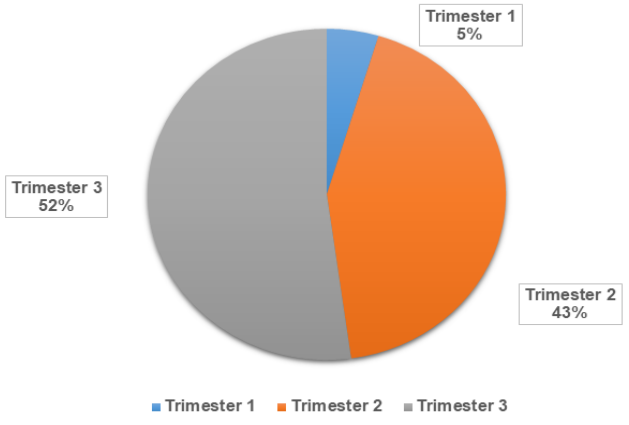

Figure 1: Trimester of pregnancy

The details of associated co-morbidities in pregnant participants are shown in Figure 2. Most common co-morbidity found was anaemia in 493 cases (82.16%) followed by vaginal candidiasis and acidity in 94 and 44 participants respectively.

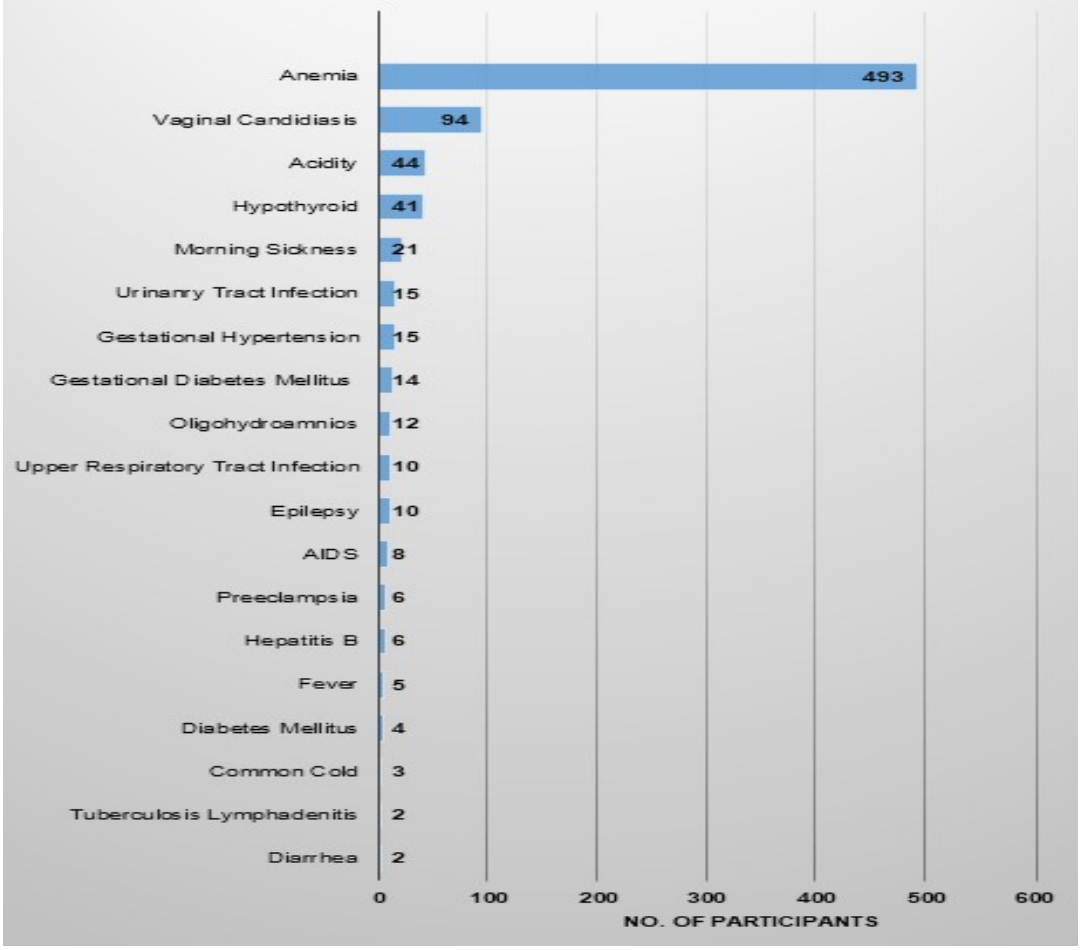

Figure 2: Co-morbidities associated with pregnancy

Table 1: Results of prescribing indicator

Sr. No.	Prescribing indicator	Results
1.	Average number of drugs per encounter	4±2 (mean±SD)
2.	Percentage of drug prescribed by generic name	92 %
3.	Percentage of encounters with an antibiotic prescribed	120/600 (20%)
4.	Percentage of encounters with an injection prescribed	208/600 (34.66 %)
5.	Percentage of drug prescribed from hospital formulary	1849/2040 (90.53 %)

Table 1 shows the results of prescribing indicators as per WHO.

Figure 3 shows the details of drugs prescribed. Most commonly prescribed drug was ferrous sulphate plus folic acid FDC in 567 participants (94.5%), followed by Calcium lactate in 513 (85.5%) participants, multi-vitamin B-complex tablets in 312 (52%) participants, tetanus toxoid injection in 208 (34.6%) participants, Clindamycin plus Clotrimazole pessary in 98 (16.33%) participants.

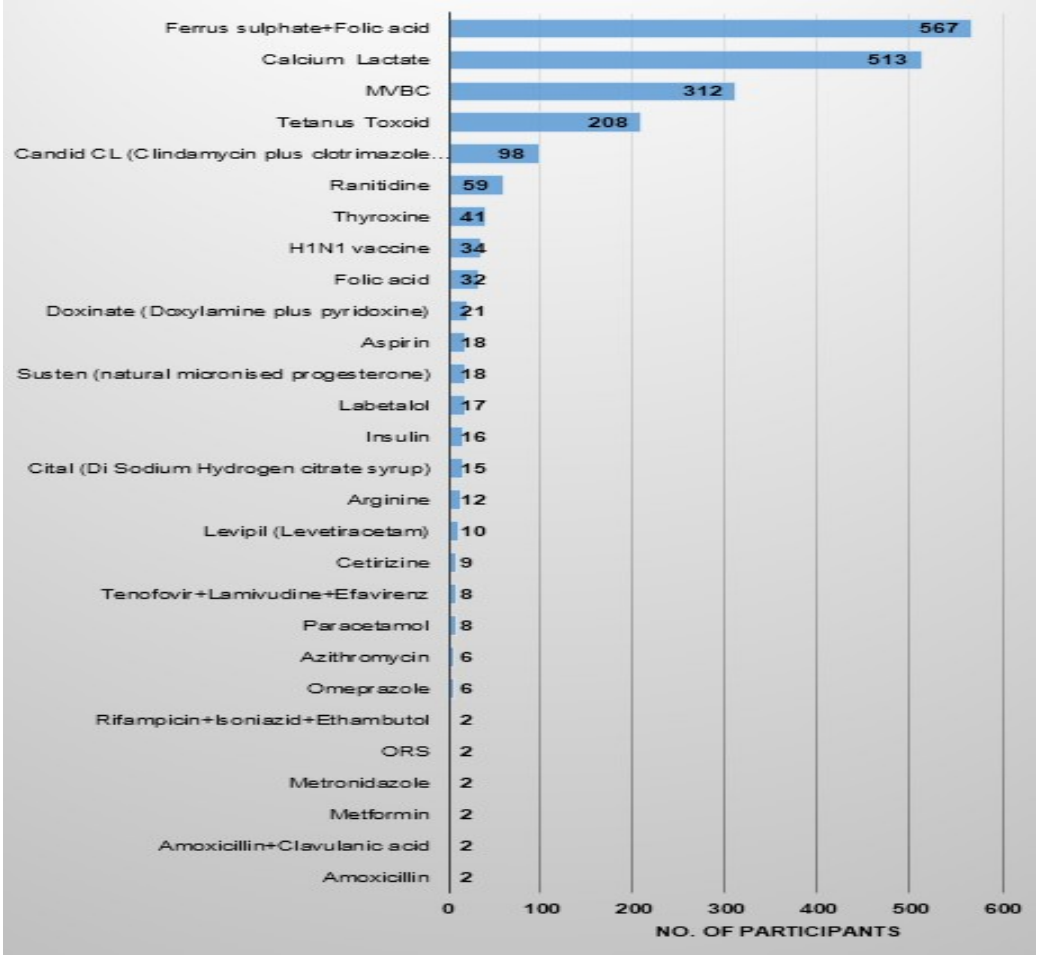

Figure 3: Drugs prescribed to the participants

It was observed in figure 4. C and id CL (Clindamycin plus Clotrimazole pessary) was the most commonly prescribed drug by its brand name. It was prescribed to 98 (16.33%) participants. Doxinate (Doxylamine plus pyridoxine), Susten (Natural micronized progesterone tablet), Cital syrup (Di Sodium Hydrogen Citrate syrup), and Levipil (Levetiracetam) were the other drugs prescribed by their brand names.

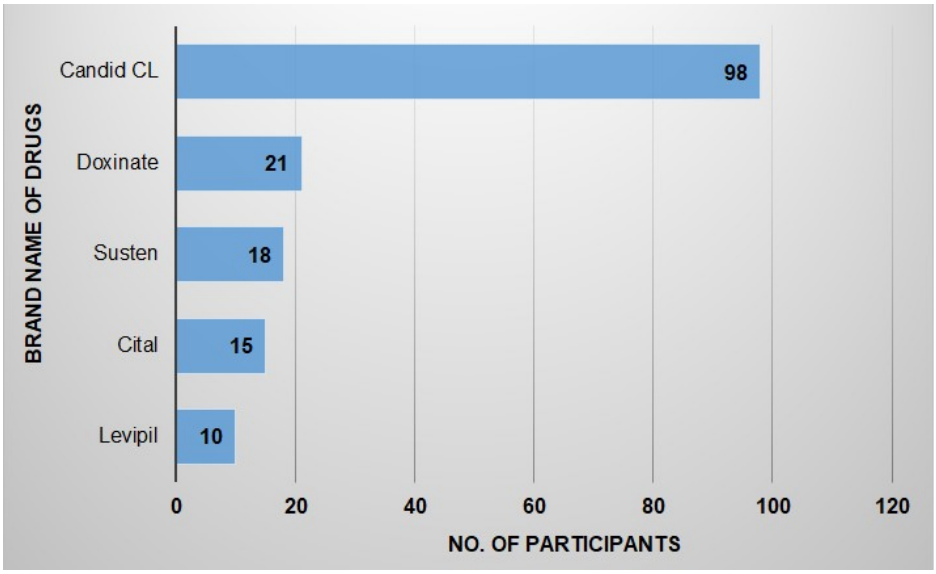

Figure 4: Drugs prescribed by their brand names

Figure 5 summarize the details of the drugs not available in the hospital formulary. Clindamycin plus Clotrimazole pessary was prescribed to 98 (16.33%) participants (as it was not available in hospital formulary). Other drugs not available in the formulary were Doxylamine, Micronized Progesterone, Labetalol etc.

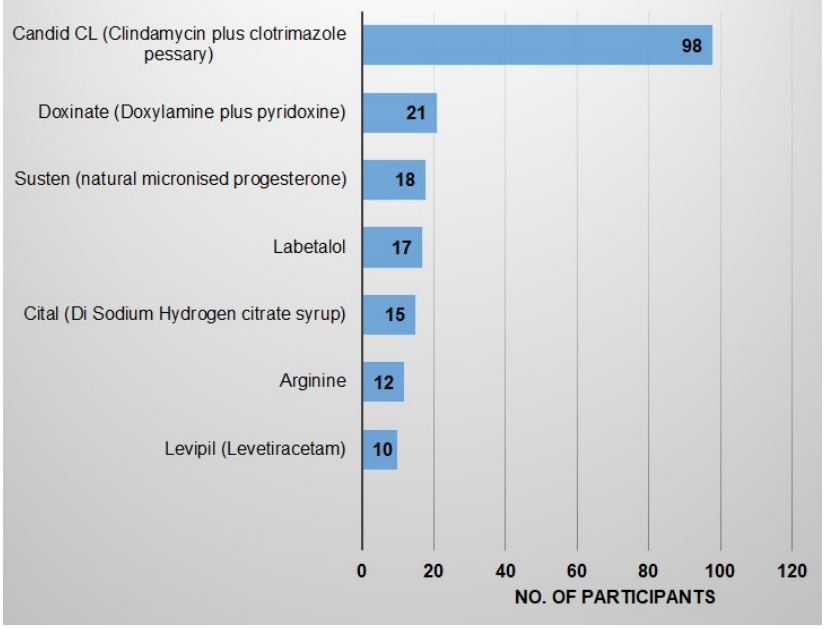

Figure 5: Non Availability of drugs in hospital formulary

Figure 6 shows, out of 2040 medication, 1017 drugs (50%) were prescribed from the national list of essential medicines (NLEM) while 1023 drugs were not from the essential list.

Figure 6: Drugs prescribed from NLEM

It was observed in figure no.8 that out of 600 participants, 120 were prescribed antimicrobials. Clindamycin plus Clotrimazole pessary was the most commonly prescribed antimicrobial agent in 98 participants

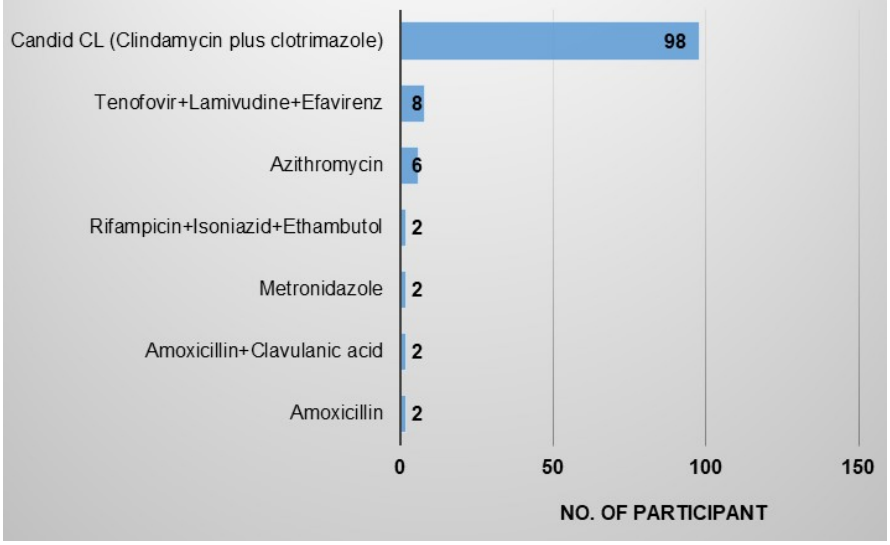

Figure 7: Antimicrobials prescribed to participants (n=120/600)

Table 2: Shows the general distribution of the drugs consumed by pregnant women attending ANC OPD

US FDA pregnancy risk category	Drug Name	Percentage of the total prescribed drugs
A	Ferrous sulphate, Thuroxine, Folic acid, Pyridoxine, MVBC	46.66 %
B	Clindamycin, Clotrimaxzole, Ranitidine, Progesterone, Azithromycin, Amoxicillin	9.65 %
C	Calcium lactate, Tetanus toxoid, H1N1 vaccine, Labetalon, Levetiracetam, Lamivudine, Rifampicin, Isoniazide, Ethambutol	38.82 %
D	Efavirenz	0.39 %
Not assigned	Doxylamine, Aspirin, Cetrizine, Tenofovir, Paracetamol, Omeprazole, Metformine, Metronidazole	3.23 %
Other drugs	ORS, Arginine, Cital (Di-sodium hydrogen citrate syrup), Insulin	1.61 %

Table 2 shows the general distribution of the drugs consumed by pregnant women attending ANC OPD, according to the risk category for pregnant women proposed by the US FDA.

The type of ADR associated with the prescribed drug along with the management is summarized in Table 3.

Table 3: ADR associated with the drug and its management.

Drugs Prescribed	Type of ADR	Suspected Drug Stop/ Continue	Causality assessment	Management of ADR
Aspirin (n=2)	Epistaxis	Drug stop	Probable	Symptomatic Treatment
	Gastritis	Drug stop	Possible	Proton pump inhibitors
Calcium Lactate (n-4)	Constipation (n=4)	Continue	Possible	Duphalac
Ferrous sulphate + Folic acid (n=3)	Constipation	Continue	Possible	High fibre Diet & Symptomatic Treatment
	Constipation	Reduce dose Frequency	Possible	High fibre Diet & Symptomatic Treatment
	Diarrhoea	Reduce dose Frequency	Possible	Symptomatic Treatment
Rifampicin + Isoniazd + Ethambutol (n=1)	Skin rash +Pruritus	Continue	Probable	Symptomatic Treatment
Tenofovir + Lamivudine + Eavirenz (n=7)	Dizziness, Vomiting	Continue	Probable	Antiemetic
	Gastritis	Continue	Probable	Proton Pump Inhibitors
	Skin rash	Continue	Possible	Symptomatic Treatment
	Vomiting (n=4)	Continue	Possible	Antiemetics drugs

4. Discussion

This was a cross-sectional, observational study carried out to analyze the prescription pattern of drugs, using WHO drugs indicators and to study the adverse drug reactions in the treatment. Study was conducted in 600 participants and majority of the participants were in their third trimester. The mean age of participants was 24.79 ± 4.07 years (mean ± standard deviation). This was similar to the finding of Adhikari *et al*. [15] wherein 63.9% of the pregnant women attending antenatal clinic were between 20–24 years. Similar demographic pattern has been observed in other studies conducted in India. [16,17] The total number of drugs per prescription was found to be 4±2 (mean ± SD). This is higher than the other studies conducted in India.[15,18] Similar finding has been observed in the study conducted by Sasidharan *et al*. [19]

In this study, majority of the drugs (92%) were prescribed by their generic names. The finding of the studies conducted in Mumbai and South India are also coherent to this study. [19,20] This reveals a greater tendency of prescribing drugs by generic name rather than by brand name in our hospital. This reduces the economic burden on the patients.

It has been observed in our study that Clindamycin plus Clotrimazole pessary was the most commonly prescribed drug by its brand name. In the Indian scenario, many of the drugs are not available in generic forms as against the western World, so our patient ends up being prescribed brand -name drugs. Indian medical council encourages the treating physician to prescribe drugs with generic names legibly and preferably in capital letters. It is the responsibility of the physician to ensure the rationality of the prescription and use of drugs. [21]

91% of the prescribed medications were available in hospital formulary. This shows that maximum drugs were available in the tertiary care hospital where the study was conducted. 50% of the prescribed drugs were from the national list of essential medicines (NLEM).This is significantly lower when compared with other studies conducted in the southern part of India where it was 95.53%. [19]Calcium lactate was the most commonly prescribed drug which is not mentioned in NLEM. None of the formulations of calcium is part of NLEM of India. [22]

Clindamycin plus clotrimazole pessary was the most commonly prescribed antimicrobial combination for vulvovaginal candidiasis. This finding was found in concordant with previous studies conducted in Andhra Pradesh. [23] The FDA five-letter system (A, B, C, D and X) of pregnancy risk category has been used since 1979. This system highlights toxicological consideration of drug use during pregnancy based on some evidence collected from preclinical and clinical trials. A majority of drugs used in our study were from category A. This finding is similar to study conducted by Inamdar *et al*. [17] In the present study; no drug was utilized by pregnant women from FDA pregnancy risk category X. This finding is similar to studies conducted in other parts of India. [17,24] In our study, 17 participants experienced some side effects with the prescribed medications. Tenofovir, Lamivudine, and Efavirenz FDC were the most commonly used combination found to be associated with ADR.

5. Conclusion:

Study was done in 600 participants and majority of the participants were in their third trimester. A total of 2040 medications were prescribed & the total number of drugs per prescription was 4±2 (mean ± SD). The most common co-morbidity found was anaemia (82.16%). & commonly prescribed drug was Ferrous sulphate plus folic acid FDC (94.5%). 92% drugs were prescribed by their generic names, this is a good sign as it reduces the economic burden on the patients. C and id CL (Clindamycin+Clotrimazole pessary) was the most commonly prescribed drug(16.33%) by its brand name. 91% of the prescribed medication were available in hospital formulary. 50% drugs were prescribed from the national list of essential medicines (NLEM). According to the risk classification, the highest prevalence of prescribed drugs belonged to category A (46.66%), followed by category C (38.82%), category B (9.65%) and category D (0.39%). It has been observed that Tenofovir, Lamivudine, and Efavirenz FDC were the most commonly associated drug with ADR.

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Conflict of interest: Nil

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