An evaluation of medication appropriateness in pregnant women with coexisting illness in a tertiary care hospital

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Abstract

Aim: Prescribing drugs during pregnancy needs careful consideration of benefit to the mother and risk to the fetus. Therefore, this study was conducted to evaluate the appropriateness of medications among pregnant women with coexisting illness in a tertiary care hospital, Western India.

Materials and Methods: It was a hospital-based cross-sectional study conducted in the obstetrics and gynecology department of a tertiary care hospital. The study was conducted over a period of 12 months wherein data from 800 pregnant women suffering from any co-existing illness and being prescribed any medication apart from routine supplementation were analyzed. The Medication Appropriateness Index (MAI) was used to assess the appropriateness of medications. Higher MAI scores indicate more inappropriate prescribing.

Results: Drugs which were most inappropriately prescribed with the highest average MAI scores were albendazole, itraconazole, injection amikacin, oxcarbazepine, warfarin, domperidone, propylthiouracil, and combiflam (ibuprofen + paracetamol). Diseases with the highest average MAI scores were anemia, Grave's disease, umbilical hernia, urinary tract infection, urticaria, allergic rhinitis, and preeclampsia. The MAI criteria which had the highest percentage of inappropriately prescribed medications were "cost of drugs," "duration of therapy," and "indication."

Conclusion: Potentially inappropriate prescribing was seen in the study with some of the common coexisting illness being treated with drugs which fared poorly on the MAI. The study has also highlighted areas in drug prescribing where scope for improvement exists. Further, it can act as a benchmark for comparison of future studies to evaluate medication appropriateness in pregnant women.

Keywords: Drug utilization review, drugs in pregnancy, Medication Appropriateness Index, pharmacoepidemiology

INTRODUCTION

Appropriate use of drugs and pharmaceutical products is the most important and basic requirement in a health-care setting. This is of special significance in vulnerable populations such as the elderly and pregnant women. There is recognition of increasing importance of studying drug use patterns, especially in vulnerable populations such as the elderly and pregnant women.[1,2]

If a pregnant woman requires drug therapy due to any concurrent/coexisting illness, it should be minimal and should strive to achieve the highest standards

of appropriateness. However, inappropriate use of medications in pregnant women has been widely reported. Many of these medications may be ineffective, unnecessary, costly, and impractical. The unwanted effects of such inappropriate medication use are predominant causes of not only direct and indirect costs but also more importantly increased morbidity and even mortality.[2]

Without the knowledge of how drugs are prescribed and used, it is difficult to initiate a discussion on appropriate drug use and to suggest measures to improve drug therapy. To this end, it is important to conduct drug utilization studies (DUS) to study the extent and profiles of drug use and to provide insight into the prevailing trends in drug use over time in pregnant women. These studies also play a key role in helping the health-care system to understand, interpret, and improve the prescribing, administration, and use of medications. While prescribing a drug, the clinician needs to consider many elements of appropriate medication use. On this account, the appropriate use of medications is an active area of research and primary target for quality assurance activities by health-care institutions.[3]

There are various methods of DUS which use data from health facilities to evaluate specific aspects of health provision and drug use. The Medication Appropriateness Index (MAI) is one of the most common implicit approaches used to measure potentially inappropriate prescribing.[4]

The present study was conducted in the obstetrics and gynecology department of a tertiary care hospital on pregnant women who were being treated for any coexisting illness. It was a cross-sectional, descriptive, observational study to analyze the appropriateness of medications prescribed in these pregnant women.

MATERIALS AND METHODS

The study was conducted over a period of 18 months (January 2017–June 2018) in the outpatient and inpatient department of the obstetrics and gynecology department of a tertiary care hospital in Western India. The study was approved by the Institutional Ethics Committee.

Pregnant women at any gestational age who were suffering from any coexisting illness and prescribed medications for the same were included in the study. Pregnant women who were prescribed only routine vitamin, mineral supplements and immunization were excluded. The sample size was calculated to estimate 95% confidence interval for proportion of appropriate prescription with 5% absolute error of margin. The sample size worked out to be 384,

assuming that about 50% of prescriptions were appropriate. Samples of 400 prescriptions each from the outpatient department (OPD) and inpatient department (IPD) (total of 800 encounters) were analyzed during the study period.

Data collection and analysis of medication appropriateness

Data collection was done from January to December 2017. Pregnant women fulfilling the criteria were included in the study, and data were collected from antenatal record cards and case sheets after obtaining informed consent. For data analysis, each patient was included only once, and cases were collected at different time of the days and different days of the week to account for confounding factors such as physician preferences and variable patient load. The data were anonymous for details of the prescriber to avoid any bias in analysis.

Appropriateness of medications was analyzed using MAI.[5,6] The index is based on ten important criteria: indication, effectiveness, dosage, correct directions, practical directions, drug–drug interactions, drug–disease interactions, duplication, duration, and expense. The judgments were based on the best available evidence from standard reference books, namely Williams Obstetrics (24th Edition), Obstetrics: Normal and Problem Pregnancies (7th Edition), High-Risk Pregnancy by James (5th Edition), Drug Monographs, standard treatment guidelines from Federation of Obstetric and Gynecological Societies of India, American Gynecological and Obstetrical Society, the United States Food and Drug Administration website, and current editions of "Drugs Today" and "Current Index of Medical Specialties." For each medication, the weighted sum across the ten criteria is calculated to arrive at the MAI score for that medication. MAI score ranges from 0 (fully appropriate) to 18 (maximally inappropriate) for each medication [Table 1]. Higher score indicates less appropriate prescribing.[5]

Analysis of data

The data were analyzed using IBM SPSS Statistics for Windows, Version 24.0. New York: IBM Corp and Microsoft Excel for Windows, Version 2010. Washington: Microsoft Corp.

OBSERVATION AND RESULTS

A total of 800 participants were included in this study. The most common coexisting illnesses in OPD and IPD are given in Tables 2 and 3.

The drugs with the highest MAI scores in OPD and IPD are shown in Tables 4 and 5. Albendazole, oxcarbazepine, and warfarin were the least appropriately prescribed drugs

Table 1: Medication Appropriateness Index (MAI)

MAI criteria	Score		
1. Is there an indication for the drug?	Indicated (A) 0	Marginally indicated (B) 1	Not indicated (C) 3
Comments -		2	
2. Is the medication effective for the condition?	Effective (A) 0	Marginally effective (B) 1	Ineffective (C) 3
Comments -		2	
3. Is the dosage correct?	Correct (A) 0	Marginally correct (B) 1	Incorrect (C) 2
Comments -			
4. Are the directions correct?	Correct (A) 0	Marginally correct (B) 1	Incorrect (C) 2
Comments -			
5. Are the directions practical?	Practical (A) 0	Marginally practical (B) 0.5	Impractical (C) 1
Comments -			
6. Are there any clinically significant drug-drug interaction?	Insignificant (A) 0	Marginally insignificant (B) 1	Significant (C) 2
Comments -			
7. Are there any clinically significant drug-disease/condition interaction?	Insignificant (A) 0	Marginally insignificant (B) 1	Significant (C) 2
Comments -			
8. Is there unnecessary duplication with other drugs?	Necessary (A) 0	Marginally necessary (B) 0.5	Unnecessary (C) 1
Comments -			
9. Is the duration of therapy acceptable?	Acceptable (A) 0	Marginally acceptable (B) 0.5	Unacceptable (C) 1
Comments -			
10. Is the drug least expensive alternative compared to others of equal utility?	Less expensive (A) 0	Equally expensive (B) 0.5	More expensive (C) 1
Comments -			

Total summated MAI score of drug:_____
Remarks: MAI Score ranges from 0 (Fully appropriate) to 18 (Maximally Inappropriate)

Table 2: Most common coexisting illnesses in pregnant women in outpatient department

Coexisting illness	Number of patients, *n* (%)
GDM	54 (13.50)
Anemia	38 (9.50)
Hypothyroidism	36 (9.00)
Emesis gravidarum	33 (8.25)
ANC with post-LSCS status	14 (3.50)

Total number of patients (*n*=400). GDM=Gestational diabetes mellitus, ANC=Antenatal case, LSCS=Lower segment Caesarean section

Table 3: Most common coexisting illnesses in pregnant women in inpatient department (*n*=400)

Coexisting illness	Number of patients, *n* (%)
GDM	116 (29.00)
Hypothyroidism	41 (10.25)
Threatened abortion	34 (8.50)
Gestational hypertension	26 (6.50)
Hyperemesis gravidarum	22 (5.50)

Total number of patients (*n*=400). GDM=Gestational diabetes mellitus

and had the highest MAI scores in the OPD setting. Albendazole, itraconazole, and injection amikacin were the least appropriately prescribed drugs and had the highest MAI scores in IPD setting.

The MAI scores of all medications given for a particular coexisting illness were summated, and the average MAI score for that particular condition was calculated. The coexisting illnesses with the highest MAI scores in OPD and IPD are mentioned in Tables 6 and 7.

In OPD setting, anemia, Grave's disease, and umbilical hernia had the highest average MAI scores, indicating that the medications were least appropriately prescribed in these conditions. In IPD setting, umbilical hernia, urinary tract infection (UTI), and urticaria had the highest average MAI scores with medications being least appropriately prescribed in these conditions.

Further, analysis was done for the percentage of drugs falling in different degrees of appropriateness, namely appropriate, marginally appropriate, and inappropriate, as shown in Figure 1. As seen, the criterion of "duplication of drugs" had the highest percentage of medications (93.1%) which were found to be appropriately prescribed. "Dosage" and "drug–drug interactions also had a high percentage of medications (76.8%) and (76.3%) being appropriately prescribed on this criterion. In contrast, the criterion of "cost of drugs" had the highest percentage of medications (2 4.60%) which were in the inappropriately prescribed level, followed by the criteria of "duration

Table 4: Drugs with the highest MAI scores (least appropriately prescribed) in outpatient department

Name of medication	Average MAI score
Albendazole	9.58
Oxcarbazepine	9.50
Warfarin	9.00
Ibuprofen + paracetamol (combiflam)	8.50
Propylthiouracil	8.50
Fluconazole	7.50
Injection betamethasone	7.38
Nitrofurantoin	7.05
Cetirizine	6.75
Prednisolone	6.50

Total number of patients (*n*=400). MAI=Medication Appropriateness Index

Table 5: Drugs with the highest average MAI scores (least appropriately prescribed) in inpatient department

Name of medication	Average MAI score
Albendazole	9.59
Itraconazole	9.58
Injection amikacin	9.58
Domperidone	9.00
Ibuprofen + paracetamol (combiflam)	8.50
Injection methotrexate	8.50
Hydroxychloroquine	8.00
Injection tramadol	7.50
Nitrofurantoin	7.10
Injection diclofenac	7.00

Total number of patients (*n*=400). MAI=Medication Appropriateness Index

Table 6: Coexisting illnesses with the highest Medication Appropriateness Index score in outpatient department

Coexisting illness	Average MAI score
Anemia	8.86
Grave's disease	8.50
Umbilical hernia	8.50
UTI	8.00
Allergic rhinitis	7.60

Total number of patients (*n*=400). UTI=Urinary tract infection, MAI=Medication Appropriateness Index

Table 7: Coexisting illnesses with the highest Medication Appropriateness Index scores in inpatient department

Coexisting illness	Average MAI score
Umbilical hernia	8.50
UTI	8.00
Urticaria	7.75
Anemia	7.41
Preeclampsia	7.41

Total number of patients (*n*=400). UTI=Urinary tract infection, MAI=Medication Appropriateness Index

of therapy" and "indication" which had 8.8% and 7% of medications in the inappropriate level, respectively.

DISCUSSION

The appropriateness of medications was analyzed by MAI, and drugs with the highest average MAI scores are shown in Tables 4 and 5.
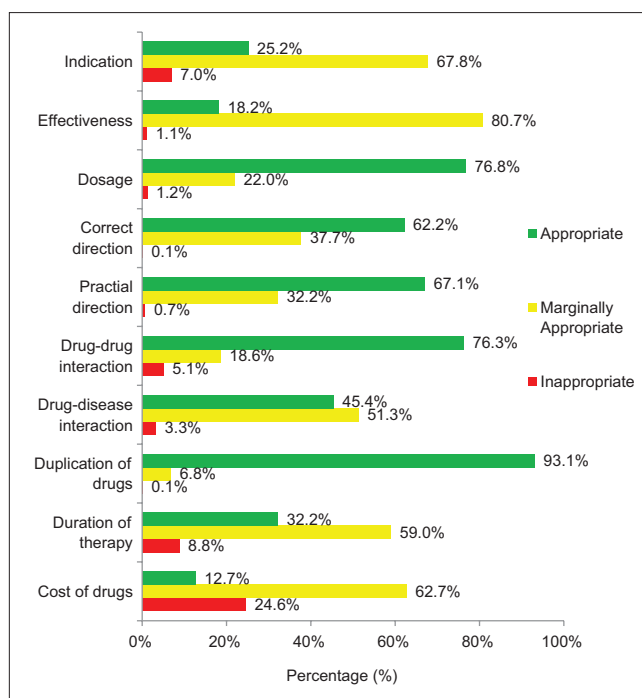
Figure 1: Distribution of Medication Appropriateness Index criteria as per degree of appropriateness (total number of patients [*n* = 400])

As can be seen, albendazole was found to be least appropriately prescribed and had high MAI score. The drug was given as an empirical therapy for anemia due to the evidence of association between anemia and helminthic infection.[7] However, studies have shown equivocal results on the maternal benefits of empiric albendazole when used without documented helminthic infection and may even cause increased risk for allergies in infancy.[8] Safer anthelmintics, namely niclosamide and praziquantel, should be preferred over albendazole.[9]

Further, in our study, itraconazole also had high MAI score. Itraconazole was prescribed in many suspected cases of UTI presumably to cover any fungal component. Although patients suffering from fungal UTI will no doubt benefit from itraconazole, the empiric use of this drug without confirmed positive fungal infection is inappropriate. This is because itraconazole is a Category C drug with dose-related maternal toxicity, embryotoxicity, and teratogenicity in pregnancy.[10]

Amikacin, an aminoglycoside, was another drug which had high MAI score in our study and was given in premature rupture of membrane and post *in vitro* fertilization cases. The antibiotic was given to prevent or treat infections in these conditions. However, the use of amikacin is known to cause ototoxicity and nephrotoxicity, and the drug also concentrates in fetal kidneys. Therefore, amikacin should only be used in pregnancy to treat life-threatening infections when safer first-line antibiotics such as intravenous ampicillin and azithromycin fail.[11]

In our study, oxcarbazepine prescribed for seizures also had high MAI score. Oxcarbazepine is a known teratogenic agent and can cause major malformations in prenatally exposed children. However, untreated seizures can cause bradycardia and fetal death, and it is important to ensure good control of seizures during pregnancy.[11] To mitigate the risk, it is advisable to keep the dose of oxcarbazepine as low as possible, and co-administration of folic acid should be advised.[12]

Warfarin, an oral anticoagulant agent, also had high MAI score. Despite being a well-known teratogenic drug, warfarin was prescribed for patients with rheumatic heart disease and mitral valve regurgitation in our study. This could be because women with prosthetic valves are at high risk of thrombotic complications and Low Molecular Weight Heparin (LMWH) may not provide adequate thromboprophylaxis.[11,13,14] Nevertheless, heparin is considered more appropriate in pregnant women as it does not cross the placenta.[15]

Domperidone was another drug with high MAI score. In our study, it was given to many patients with nausea and vomiting. Domperidone use is associated with adverse outcomes including significant risk of ventricular arrhythmia and sudden cardiac death.[16] The safety of Domperidone is uncertain and it should be used only in moderate to severe vomiting where the benefits outweigh the risks.[9] It should not be given routinely, especially in minor cases, and therefore, domperidone had a high MAI score in our study.

Propylthiouracil also had high MAI score. It is a known hepatotoxic agent and can also cause transient leukopenia in almost 10% of women with rare cases of agranulocytosis in 0.3%–0.4%.[17] However, it has an advantage of not crossing the placenta readily. It is recommended to use propylthiouracil only in the first trimester and to switch to methimazole for the rest of pregnancy.[18] However, in our study, propylthiouracil was used in all trimesters of pregnancy, and the dosage of propylthiouracil was also higher than the recommended dose.

The fixed drug combination of paracetamol and ibuprofen fared poorly on the MAI index, and it was prescribed for pharyngitis and URTI. Paracetamol is considered to be safe in pregnancy.[19] However, ibuprofen exposure during pregnancy is linked to incidences of asthma and allergen sensitization in early and mid-childhood.[20] The cardiac malformations, oligohydramnios, and premature closure of ductus arteriosus due to ibuprofen are also well documented.[21]

Other drugs which also had high MAI scores were injection methotrexate (8.5), hydroxychloroquine,[8] fluconazole, injection tramadol (7.5), injection betamethasone (7.38), nitrofurantoin (7.1), injection diclofenac,[7] cetirizine (6.75), and prednisolone (6.5).

Among the coexisting illnesses, anemia had one of the highest MAI scores in our study [Tables 6 and 7]. This was owing to albendazole being prescribed as an empirical therapy, due to the evidence of association between anemia and helminthiasis which is not desirable as mentioned earlier.[9]

Grave's disease being treated with propylthiouracil was another condition with high MAI scores in our study. Guidelines recommend the use of propylthiouracil only in the first trimester and to switch to methimazole for the rest of pregnancy.[18] In our study, it was found that propylthiouracil was used in all trimesters of pregnancy and its dosage was also higher than the recommended dose. Hence, Grave's disease was one of coexisting illnesses with high MAI scores in our setting.

Umbilical hernia also had high MAI scores for which drugs such as cetirizine and cough syrup were prescribed for symptomatic relief of common cold and cough, possibly to prevent the worsening of umbilical hernia. However, the safety of cetirizine use in pregnancy is uncertain.[21] If antihistaminics need to be used in such cases, first-generation antihistaminics, namely diphenhydramine and chlorpheniramine, should be used.[22]

Another coexisting illness having high MAI scores was UTI. This is because nitrofurantoin was prescribed in all trimesters of pregnancy and can lead to hemolytic jaundice and neonatal jaundice, especially in the third trimester. Studies also report that craniosynostosis, ophthalmic malformations, oral clefts, and cardiovascular defects are associated with nitrofurantoin use.[23,24] Further, as mentioned earlier, itraconazole was also empirically prescribed in many cases of UTI to cover for fungal component. Due to these reasons, UTI had high MAI scores indicating less appropriate prescribing.

Urticaria was also found to have high MAI scores for which drugs such as cetirizine and albendazole were prescribed. However, the safety of cetirizine use in pregnancy is uncertain, and safer first-generation antihistaminics should be used.[22] Furthermore, albendazole was empirically prescribed in urticaria due to the presumed association with helminthiasis which is inappropriate. Owing to the use of cetirizine and albendazole in an inappropriate manner, urticaria had high MAI scores in our study.

On analysis of individual criteria, "cost of drugs" had the highest percentage of drugs (24.60%) in the inappropriate category. This is probably because of comparatively higher percentage of prescribing by brand names in our study which increases the cost of drug therapy. Prescribing by generic names should be encouraged to promote the best utilization of drugs at cheaper cost.

The criterion of "duration of therapy" also had a high percentage of medications given inappropriately. The reason may be due to the "anchoring bias" of the prescribers to prescribe the routine regimen of medications during pregnancy. However, pharmacotherapy during pregnancy should be carefully adjusted according to the need of the individual patients. The duration of therapy should be as per the latest guidelines recommended by the official bodies and authentic textbooks. As pregnancy is a vulnerable condition, the drugs should be given for as minimum duration as possible to avoid the unwanted effects of medications.

CONCLUSION

This study has provided insight into the prevailing trends in drug use in pregnant women and also highlighted the areas in drug prescribing where scope for improvement exists. These data can be used to develop prescribing guidelines and provide training for health-care professionals. The same can also be used as a benchmark for comparison during subsequent studies in the future to better understand and interpret the appropriateness of medications in pregnant women.

Conflicts of interest
There are no conflicts of interest.

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