

SAFETY OF DRUGS PRESCRIBED DURING PREGNANCY IN DUHOK CITY

Rabie Gabriel Abdullah*, Rozheen Shukri Karam, Hiba Shawkat Ibrahim, Aveen Abed Mohammed Saleh, Vaheen Ali Taher, Awaz Issa Sadeq

Department of Pharmacology, College of Pharmacy, University of Duhok
Duhok, Iraq

ABSTRACT

Objectives: The aim of this study was to identify the errors in prescribing drugs in pregnancy through retrieving the written prescription in both private and health care institutions in Duhok city, Kurdistan Region, Iraq. Methods: A total of 502 prescriptions were collected from private pharmacies and inpatient/outpatient pharmacies of Azadi Teaching Hospital/Duhok. Results: approximately one-half medication were dispensed during the first trimester and lowest dispensed in third trimester and most prescribed drugs belong to category A and B. The most popular prescribed classes of drugs were systemic antibiotics (17.7%), Vitamins/Supplements (14.9%), folic acid (13.4%), gynecological (12.5%), and analgesics (9.8%). Conclusions: Our results indicate that pregnant in Duhok city are more drug consumer than average worldwide number of items per prescription, therefore, active participation of pharmacists in detection and prevention of drug-related injuries, could considerably prevent the consequence of dispensed drugs in pregnancy.

Keywords: pregnancy; community; pharmacist; hospital; category.

1. INTRODUCTION

In pregnancy drug treatment presents a special concern due to the threat of potential teratogenic effects of the drug and physiologic adjustments in the mother in response to the pregnancy [1]. The physiology of pregnancy affects the pharmacokinetics of medications used and certain medications can reach the fetus and cause harm[2]. The concern about medication use during pregnancy and lactation has been influenced by historical events, including thalidomide crisis in the 1960's and the teratogenic effects discovered related to the use of diethylstilbestrol in 1971 [3]. These events led the US Food and Drug Administration to establish strict regulations regarding drug labeling, the use of medications in pregnancy, requiring demonstrations of safety and efficacy of any drug before it becomes commercially available[4]. When it comes to concerns regarding medication risk/safety in pregnancy, we need to consider not only the effects on the pregnant woman who is the intended recipient of a given pharmaceutical product, but also effects on the "innocent bystander" that results from the

pregnancy. ADRs caused by exposures in pregnancy may manifest in the embryo, fetus, newborn, or in the offspring as late as adolescence or adulthood. At the extremes, some drugs may lead to embryonic loss, while others may lead to effects only apparent in late adolescence (e.g., diethylstilbestrol-induced adenocarcinoma of the vagina)[5].

Exposure before conception, or during the first trimester of pregnancy, has been of particular concern regarding malformations. However, drugs may exert their effects upon the fetus at other times during pregnancy; for example, the use of ACE inhibitors during the second or third trimesters may be fetotoxic, causing prolonged fetal hypotension, renal tubular dysplasia, growth retardation and fetal death[6].

Another important point regarding prescriptions in pregnancy and put large number of women and their physicians in difficult situation is the fact that many women exposes their fetuses to drugs before they even know they are pregnant. This can be attributed mainly to unplanned pregnancy[1].

Drug use during pregnancy may be necessary to ensure maternal and fetal health. While the safety or the value of some medications has been established, others have been identified as potentially or certainly toxic for pregnancy. Several studies had been carried out around the world concerning medications prescription during pregnancy [2][6][7][8][2]. However, very few studies made about this subject in our region, and to our knowledge, there is no such study in Kurdistan Region, Iraq especially in Duhok city.

METHODS

A descriptive cross-sectional study was conducted on prescriptions of different community pharmacies and inpatient and outpatient pharmacies of Azadi teaching hospital.

Prescriptions for pregnant women were selected, and data were extracted on predesigned forms including patient characteristics. A consent approval has been taken from all

women to use prescription reports related to their maternity drug use. Data were written down directly from the original prescriptions.

For evaluation of possible risks imposed by drugs on pregnant women and their fetuses, we used the US Food and Drug Administration (FDA) risk classification: category listed in table 1 (Briggs et al., 1994).

Information about whether the prescription written by a specialized physician or a general practitioner, and which trimester of pregnancy while receiving the prescription was recorded. All the drugs prescribed was categorized as analgesics, vitamins and supplements, antibiotics, etc.

This study was conducted between November 2017 and April 2018. It included all pregnancies whose duration was longer than 9 weeks of amenorrhea and excluding voluntary terminations of pregnancy.

Data analyses were done by SPSS version 23.0 (SPSS Inc., Chicago, Ill., USA) for calculations of frequencies, percentages, and making comparisons. The statistical significance was set at $p \leq 0.05$.

Table 1. Drug-pregnancy category.

Category	Risk Rating
A	controlled studies in women do not show risk to the fetus in the first trimester
B	animal reproduction studies do not show risk to the fetus but there are no controlled studies in pregnant women
C	studies in animals show adverse effects on the fetus but there are no controlled studies in women
D	there is positive evidence of human fetal risk, but benefits from use in pregnant women may be acceptable despite the risk
X	studies in animals or human beings show fetal abnormalities and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit

RESULTS

General statistics:

The total number of prescriptions collected during the study was 502, of which 311 prescriptions belong to

community pharmacy and 191 prescriptions to the hospital pharmacy.

Number of prescriptions per each trimester during pregnancy was shown in Table (2):

Table 2. Summation of prescriptions for each trimester

Trimester	Number of Prescriptions N(%)	Drugs prescribed/woman
1 st	238 (47.4 %)	2.69
2 nd	154 (30.7%)	2.93
3 rd	70 (13.7%)	2.88
Unknown	41 (8.2%)	3.2

Number of drugs prescribed

The total number of drugs prescribed in all the collected prescriptions was 1427 medications with an average of 2.84 items for each prescription (i.e. for each pregnant woman). For each trimester, the number of prescribed drugs was shown in figure 1.

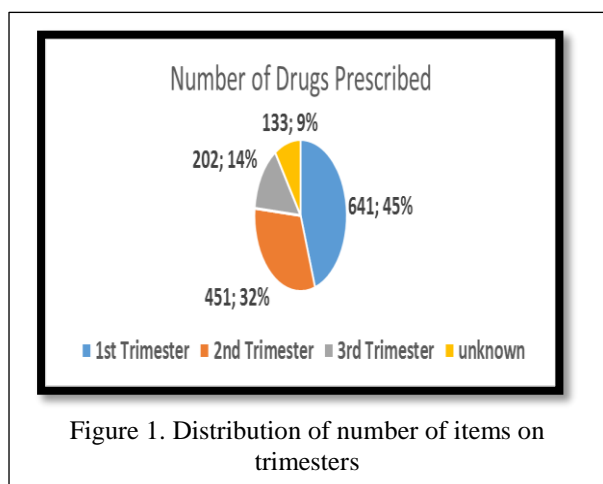


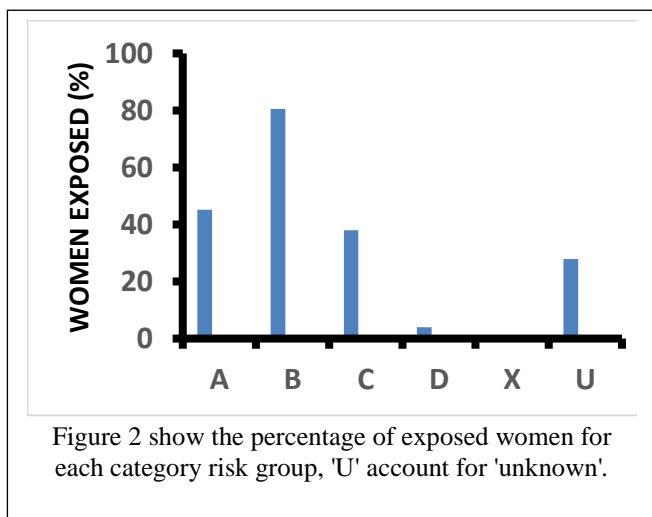
Figure 1. Distribution of number of items on trimesters

FDA pregnancy risk categories

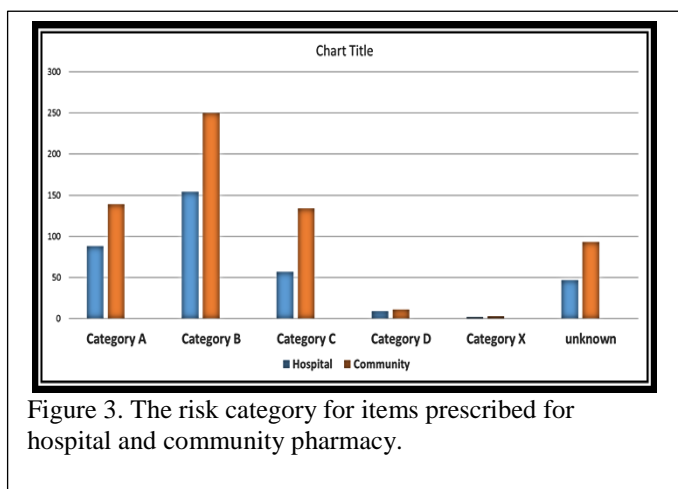
For each risk category, the number of prescriptions with their percentages are shown in table 3 and figure 2 below:

Table 3. Number of prescribed drugs for each pregnancy risk category

FDA Risk Category	Number of prescribed items N (%)
A	265 (18.6)
B	697 (48.8)
C	259 (18.15)
D	21 (1.47)
X	5 (0.35)
Unknown	180 (12.6)



If we plotted the above dispensed drugs per category risk on their correspondent source (community and hospital pharmacies), this will yield a comparative chart like the one in Figure 3.



No significant differences found using Chi-square analysis except for category C drugs where frequency of prescribed medications dispensed in community pharmacy significantly higher than that of hospital pharmacy (p= 0.013).

Types of drugs prescribed

Figure 4. Shows the frequency of prescribed drugs according to their therapeutic class. Systemic antibiotics are the most frequently prescribed medications, to be followed by Vitamins\Supplements, and Folic acid.

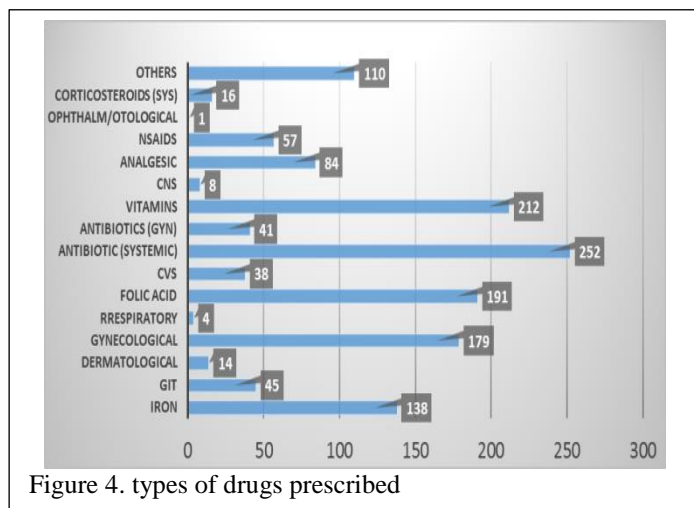


Figure 4. types of drugs prescribed

DISCUSSION

The largest proportion of pregnant women use medication during pregnancy, because these medications may carry a danger of possible teratogenicity and physiologic dose refinement in the maternity in response to the pregnancy make it an important aspect to be studied [6].

The safety is not the similar for all drugs, some are confirmed to be potentially safe, and some have been reported as possibly or certainly toxic for prenatal, whereas the danger of other medications is obscure, but the drug indication during pregnancy in some diseases is essential to ensure maternal and fetal health.

There are many studies around the world that concern prescription of medications during pregnancy [2][6][7][8]. However, very few studies made about this subject in our region, and to our knowledge, there is no such study in Kurdistan Region, Iraq especially in Duhok city.

This descriptive cross sectional study has been carried out to assess the drug prescription pattern during pregnancy in Duhok city, Kurdistan region, Iraq. During this study the data was collected from November 2017 to April 2018.

We were able to collect data from 502 prescriptions, about 62% from community pharmacy and 38% from gynecology hospital[9].

Most of the prescriptions was taken during the first trimester (47.4%). The average rate of written drugs per woman was lower in the early months of pregnancy, this result in agreement with Lacroix et al, 2000[8]. Because the first trimester is the period of organogenesis of the fetus.

Recently reports about risk-perception investigations demonstrated that pregnant mothers tend to overrate the scale of teratogenic danger particularly during the first trimester [10].

Another finding in this study is that the rate average of prescribed drugs per prescription was found to be 2.84 items .this result which is slightly higher than the average observed by Al-Hamimi and Al-Balushi, 2016[11].

As compared to WHO standard for average drugs prescription per pregnancy which is (2.0) [12], the average of this study shows higher average because a third of the included woman have at least one chronic disease. As the prevalence of chronic disease, specially hypertension [13] and diabetes[14][15][16], is high this percent of women will be expected.

Our study also revealed that only 0.8 % of pregnant dispensed one or more prescriptions from the hazardous category (X) examples include methotrexate, human chorionic gonadotropin, and diethylstilbestrol and 4% of women used drugs for category D for example magnesium sulfate, diazepam, potassium iodide...etc. We assigned a U category (U for unclassified) for drugs for which evidence of danger in pregnancy was unclassified available from studies in human research or in laboratory animals (no FDA code), and 27.9 % of women were exposed to drugs in the U category.

No significance difference was found between the drug prescribed at hospital and those in community pharmacy, except for category C where the prescribed drugs in community pharmacy are significantly higher than those in hospital.

This can be explained in the light of restriction of drug prescription for pregnancy to be more in hospital than in clinics due to the protocol of the hospital.

When calculated as a rate of exposed women, the popular prescribed classes of drugs were systemic antibiotics (17.7 %), Vitamins\Supplements (14.9 %), folic acid (13.4 %), gynecological (12.5 %), and analgesics (9.8 %).in contrast to Lacroix et al. (2000), who stated that iron was most prescribed drug many studies refer to analgesic as the most commonly medication used during the pregnancy. However, our study focus only on the prescriptions and the source of most analgesics is usually non-prescription.

CONCLUSION

The study concluded that, the average number of drugs per prescription was slightly higher compared to the WHO standards. systemic antibiotics were the most prescribed drugs followed by vitamins/supplements. Most of the prescribed drugs fell in category B and A. Only 21 drugs fell in category D and 5 drugs classified as category X. drugs prescribed per prescription (woman) in first-trimester lower than the second and third trimester.

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