

DRUG UTILIZATION PATTERN DURING PREGNANCY IN ALEXANDRIA, EGYPT

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ABSTRACT

Background: Drug use (DU) in pregnancy is a global public health concern in both developed and developing countries. **Aim:** To assess the magnitude and pattern of DU during pregnancy in Alexandria, Egypt. **Methods:** A cross-sectional study was carried out among 600 pregnant women from 20 antenatal care (ANC) clinics affiliated to the three institutional health facilities in Alexandria Governorate, Egypt; Ministry of Health, Health Insurance Organization and Alexandria University. **Results:** The findings revealed a high prevalence (96.3%) of DU during pregnancy. The proportion of prescribed-only- medications (POM) was 95.6%, compared to only 4.4% over-the-counter (OTC) medications. Category B medications (41.3%), 30.2% unclassified, 15.0% category C, 12.1% category A, 0.9% category X and 0.5% category D. Most commonly used medications were for GIT disorders (25.3%). The majority of respondents (88.0%) took supplements and a relatively high prevalence (41.8%) of herbal intake was observed with 56.3% of herbs consumed in the first trimester. **Conclusion:** There is an irrational prescribing trend of drugs during pregnancy. The prevalence of teratogenic medications of category D and X is of concern even if it is low. High herbal use especially in first trimester warrants special attention.

KEYWORDS: Drug use, prescribed-only-medications, over-the-counter medications, supplements, herbs, pregnancy.

INTRODUCTION

Drug use (DU) by pregnant women should be viewed as a public health problem, since there are numerous gaps in knowledge of the consequences for both the mother and the fetus.^[1] Pregnant women consume drugs including prescription and non-prescription (OTC) medications as well as herbal products and dietary supplements.^[2] Concern about the safety of drugs prescribed to pregnant women has been increasingly evident since the thalidomide tragedy in the 1960s.^[3] However, despite that drug use (DU) during pregnancy may pose a teratogenic risk for the embryo, the recommendation to avoid all drugs during pregnancy is unrealistic and may be dangerous. About 8% of pregnant women worldwide need permanent drug treatment; for chronic diseases such as: diabetes, for acute illnesses such as influenza, or for treating pregnancy complications such as vomiting.^[4] The prescription of medications during pregnancy presents a great challenge to the physicians who must consider the risk-benefit relation for both the mother and the fetus^[5], that's why DU by pregnant women should be viewed as a public health problem.^[1]

Many studies were conducted later to describe patterns of use of prescription drugs during pregnancy by therapeutic category and potential for fetal harm. Epidemiological studies have determined that about more than 50% of pregnant women take at least one prescription or non-prescription drug during pregnancy.^[6,7] It has been estimated that over 90% of women take three or four medicines at some stage of pregnancy.^[8] Different studies have shown that most pregnant women use either prescribed or OTC drugs during pregnancy to treat acute or chronic conditions, with a prevalence as high as 84–99%.^[9] Limited research about the use of medications by pregnant women presents a twofold challenge for pharmacists and prescribers. First is the difficulty they face in gaining access to comprehensive drug information on medication use by pregnant women. Most clinicians rely solely on the Food and Drug Administration (FDA) categorization of medications based on risk despite of the existing limitations to this system. The second challenge for clinicians lies in managing the available information, both in terms of identifying teratogenicity studies on new medications and their potential impact on pregnant women and on staying up-to-date of new research on existing drugs.^[10]

Herbal use during pregnancy raises particular concerns, because many herbs are traditionally used for symptoms that occur commonly during pregnancy, such as nausea and vomiting. Ignorance of the potential harm of herbs to pregnant woman is complicated by even greater ignorance of the potential effects on fetal safety. Herbs may contain substances that can cause miscarriage, premature birth, uterine contractions, or injury to fetus.^[11] Thus, it is important to understand the extent to which herbs are used in pregnancy, the specific products used and the reasons for which they are used.^[12] Drug utilization research (DUR) studies provide insights into aspects of drug use and drug prescribing.^[13,14] These studies provide important indicators of which drugs are most commonly used by pregnant women, for which conditions, and whether this use might be problematic for mothers and infants. By identifying frequently used medicines with unknown risks, priorities could be established for epidemiological research.^[15]

Drug use in pregnancy is a global public health concern in both developed and developing countries. There appears to be considerable international variations in both overall rates of medicinal use and use for drugs with potential risk in pregnancy. Despite that studies done on medication use in pregnancy were few in the developing world, they widely report inappropriate use of medications.^[16] India^[17,18,19] and Ethiopia^[20,21] are the most prominent developing countries working on DUR in pregnancy. In the Arab world, DUR during pregnancy is still evolving with very few studies done as in Palestine, Saudi Arabia and Oman.^[16,22,23] Nevertheless, in Egypt, DUR among pregnant women is scarce. That's why pharmaco-epidemiological studies like this study can help minimize the inherent risks in drug treatment establishing a profile of drug consumption during pregnancy and identifying intervention measures. The objectives of this study were to assess the magnitude and pattern of DU during pregnancy including: prescription medications, OTC medications, supplements and herbs in Alexandria, Egypt, to categorize the taken medications in terms of their FDA pregnancy risk.

METHODS

A cross-sectional study was carried out among pregnant women from antenatal care (ANC) clinics affiliated to the three institutional health facilities; Ministry of Health, Health Insurance Organization and Alexandria University, in Alexandria Governorate, Egypt. The study participants were pregnant women, in any trimester, attending ANC clinics of the three institutional health facilities.

The WHO recommends that cross sectional studies describing current treatment practices should include 20 health facilities with at least 600 encounters from the sampled health facilities, comprising at least 30 encounters per facility.^[24] The study comprised a representative sample of ANC clinics, which was proportionately allocated according to the type of

institutional health facility (Ministry of Health, Health Insurance Organization and Alexandria University). A total of 600 pregnant women from 20 ANC clinics affiliated to the three institutional health facilities were consecutively included in the study. The number of encounters per ANC clinic amounted to 30 pregnant women.

Data were collected using a pre-designed, pre-coded, pre-tested questionnaire. Record review of medicinal prescriptions was also done. Each pregnant woman was face-to-face interviewed only once. The questionnaire comprised the following: women's socio-demographic data, obstetric history, past medical history, present medical history as regards pregnancy-related medical conditions, acute and chronic conditions, intake of POM and OTC medications, supplements and herbs throughout their pregnancy. The data collection took place from Feb- Sept, 2012, during the daily working hours of ANC clinics. A pilot study was conducted to test the reactions of the respondents to the questions, the clarity of the study tool, the time needed to carry out the interviews and the difficulties that may rise throughout the study.

Data entry, cleaning and analysis were done using Statistical Package for Social Sciences (SPSS) version 16.0 statistical software. Medications were classified into therapeutic classes according to the WHO Anatomical Therapeutic Chemical (ATC) classification system.⁽¹⁹⁵⁾ Medications were evaluated based on the US-FDA pregnancy risk classification system.^(66,77) FDA risk classification (A, B, C, D, or X) was assigned to individual medications. Descriptive statistics including (i) count and percentages used for describing and summarizing qualitative data, and (ii) arithmetic mean and standard deviation used as measures of central tendency and dispersion, respectively for normally distributed quantitative data.

Ethical considerations

The study was approved by the Ethics Committee of the High Institute of Public Health, Alexandria University, Egypt. The researcher complied with the international guidelines for research ethics. A verbal informed consent was obtained from the participants after explanation of the purpose and benefits of research. There was no refusal to participate in the study. All interviews were conducted at a suitable place at the ANC clinics that allows complete privacy and confidentiality. The researcher advised all pregnant women who were taking a risky drug to stop taking it until re-consulting their physician. There was no conflict of interest.

RESULTS

Socio-demographic results

The sociodemographic characteristics of the studied pregnant women are shown in table 1. It appears from the table that the age of pregnant women ranged from 16 to 43 years. Out of the studied 600 pregnant women, 265 (44.2%) of the respondents were in the age group of 30-

40 years with a mean age of 29.1 ± 6.4 years. One hundred sixty one (26.8%) of the respondents had completed preparatory education, 140 (23.3%) had secondary education, 86 (14.3%) were illiterate or just read and write, 60 (10.0%) attended primary school, 80 (13.3%) had diploma, while only 73 (12.2%) were university graduates. Most of the pregnant women 508 (84.7%) were housewives and more than half (54.8%) of them lived in urban areas.

Table 1: Socio-demographic characteristics of pregnant women (n=600) attending ANC clinics, Alexandria, 2012.

Characteristics	No.	%
Age (years)		
16-	46	7.7
20-	261	43.5
30-	265	44.2
40-43	28	4.7
Education		
Illiterate	47	7.8
Read/write	39	6.5
Primary	60	10.0
Preparatory	161	26.8
Secondary	140	23.3
Diploma	80	13.3
University	73	12.2
Occupation		
House wife	508	84.7
Clerical	49	8.2
Manual	26	4.3
Professional	15	2.5
Student	2	0.3
Residence		
Urban	329	54.8
Rural	271	45.2

Gestational, obstetric and medical information

Table 2 shows that 279 (46.5%) of respondents were multigravida and 147 (24.5%) were primigravida. Out of the 426 women who got pregnant, 252 (59.2%) were multipara and 160 (37.6%) were primipara. Less than one fifth (14.3%) of them delivered infants with birth defects. Among those who got pregnant (426), 122 (20.3%) experienced one or more abortions. Only relatively small percentages of women had still births (1.8%), neonatal deaths (4.2%) and preterm deliveries (2.6%).

Out of the 600 interviewed pregnant women, 262 (43.7%) were in the third trimester, 229 (38.2%) were in the second trimester and 109 (18.2%) were in the first trimester of pregnancy. Almost all respondents (98.2%) had an early ANC visit (within the first trimester of pregnancy). More than half (52.5%) of them attended more than the minimum four WHO recommended visits until the time of interview. Maternal and child health (MCH) centers were attended by most of the study

women (85.5%) for ANC visits, followed by private clinics, public hospitals and Health Insurance Clinics (38.3%, 14.8% and 11.0% respectively). The majority (84.7%) of pregnant women experienced pregnancy related conditions during their current pregnancy, 442 (73.7%) experienced acute conditions and 70 (11.7%) had chronic conditions.

Table 2: Gestational, obstetric and medical information of pregnant women (n=600) attending ANC clinics, Alexandria, 2012.

Information	No.	%
Number of previous pregnancies		
Nulligravida	174	29.0
Primigravida	147	24.5
Multigravida	279	46.5
Parity (n=426)		
Nullipara	14	3.3
Primipara	160	37.6
Multipara	252	59.2
Children with birth defects	61	14.3
History of abortion	122	20.3
Still births	8	1.8
Neonatal deaths	18	4.2
Preterm deliveries	11	2.6
Pregnancy trimester at current ANC visit		
First trimester	109	18.2
Second trimester	229	38.2
Third trimester	262	43.7
Pregnancy trimester at first ANC visit		
First trimester	589	98.2
Second trimester	9	1.5
Third trimester	2	0.3
Total number of ANC visits (including current visit)		
< 4	204	34.0
4	81	13.5
> 4	315	52.5
Place of ANC Visits*		
Public Hospital	89	14.8
MCH center	513	85.5
Health Insurance Clinic	66	11.0
Private Clinic	230	38.3
Medical conditions during current pregnancy*		
Pregnancy related conditions	508	84.7
Acute conditions	442	73.7
Chronic conditions	70	11.7

*Multiple responses allowed

Drug use among pregnant women

1. Prevalence of drug intake among pregnant women

Out of 600 interviewed respondents, 578 (96.3%) women ever utilized drugs throughout current pregnancy. The total intake of drugs (including medications, supplements and herbs) was 3046 drugs of which 86.0% were prescribed drugs, and 14.0% were non-prescribed drugs. The mean number of drugs consumed by pregnant women was 5.27 drugs per woman. Fig.1 shows that out

of the total drug intake during pregnancy, medication intake constituted 45.0%, followed by supplements (42.5%) and herbs intake (12.5%).

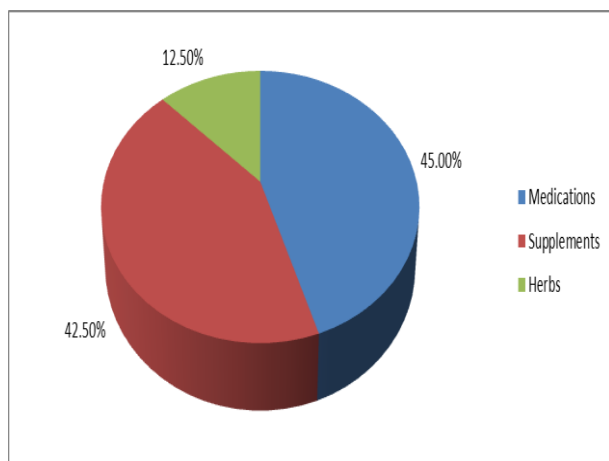


Fig. 1: Medications, supplements and herbs intake among pregnant women in Alexandria, 2012.

Table 3 shows that the proportion of prescribed only medications (POM) taken by pregnant women was 95.6% (mean number POM = 2.36) compared to only 4.4% over-the-counter (OTC) medications (mean number OTC=1.02). Prescribed supplements consumed by study women constituted 98.3% (mean = 2.46). The majority of herbal intake 89.8% (mean= 1.51) was non-prescribed. Further analysis revealed that 40.2% of medication users (POM and OTC) used three or more medications while those who used one or two medications constituted 32.9% and 26.9% respectively. With respect to POM medications, nearly same percentages of respondents used one or two medications (27.9% and 27.7% respectively) while 44.3% used three or more medications. Regarding OTC medications, the majority of OTC users (78.1%) used one medication compared to 18.6% who consumed two OTC medications and 1.7% who consumed three or more OTC medications.

Table 3: Distribution of pregnant women according to type and number of used drugs and type of prescription, Alexandria, 2012.

Prescription	Type of drugs	Number of drugs taken		Mean no of drugs
		No.	%	
Prescribed drugs	POM*	1309	95.6	2.358
	Supplements	1273	98.3	2.457
	Herbs	39	10.2	1.625
Non-prescribed drugs	OTC**	60	4.4	1.017
	Supplements	22	1.7	2.200
	Herbs	343	89.8	1.511

*POM = Prescription only medications, ** OTC = Over-the-counter-medications

2. Medication intake during pregnancy

Out of 600 study pregnant women, 555 (92.5%) ever took medications during current pregnancy. A reduction in the overall medications use across pregnancy trimesters was demonstrated from 54.0% in first trimester to 35.4%, and 10.6% in second and third trimesters respectively. Fig.2 shows medication intake by pregnant women according to type of medical conditions. Out of total 1369 medications used by study women, 782 (57.1%) were used for pregnancy related conditions, followed by 524 (38.3%) medications used for acute conditions and 63 (4.6%) medications used for chronic conditions. Medications for obstetric and gynecological (OB/GYN) disorders 266 (34.0%) were the most frequently used category of medications for pregnancy related conditions; mainly progestogens. Medications for dental disorders 169 (32.3%) were the most frequently consumed category for acute conditions; mainly analgesics. Out of 63 medications used for chronic conditions, about one third (30.2%) were indicated for CVS conditions; mainly penicillins for rheumatic heart disease.

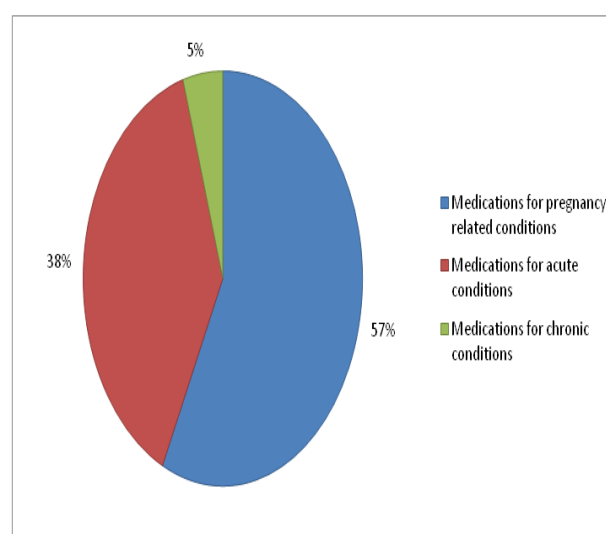


Fig. 2: Medication intake by pregnant women according to type of medical conditions in Alexandria, 2012.

Based on the Anatomical Therapeutical Chemical (ATC) classification for medications, out of total 1369 medications used by pregnant women in this study, medications used for GIT disorders constituted 25.3%, followed by medications for (OB/GYN) disorders (19.4%), medications for CVS disorders (9.6%), medications for respiratory disorders (9.1%), medications for blood disorders (8.5%), medications for diabetes (1.7%) and medications for UTIs (1.5%). Other subgroups accounting for large numbers of medications included analgesics (16.2%), antacids (9.2%), systemic antibiotics (8.2%), anti-emetics (8.0%), progestogens (6.7%), anti-diabetics (1.7%) and antiparasitics including; anthelmintics and antiprotozoals (1.3%). (Fig. 3)

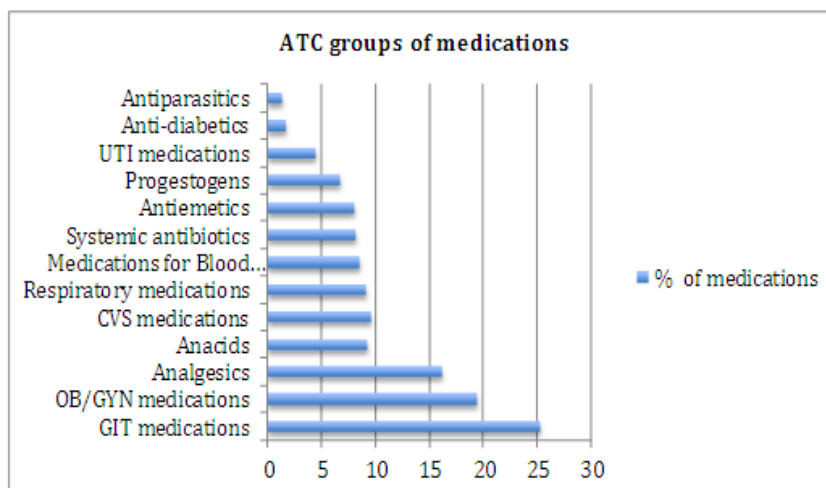


Fig. 3: Medications used by pregnant women according to Anatomical Therapeutic Chemical (ATC) groups in Alexandria, 2012.

3. US-FDA pregnancy risk classification of medications

Table 4 shows that 566 (41.3%) of the medications taken by the study women were from category B, followed by 414 (30.2%) unclassified, 205 (15.0%) from category C, 165 (12.1%) from category A, 12 (0.9%) from category

X and 7 (0.5%) from category D. A relatively high proportion of teratogenic medications from category D and category X amounted to 1.4%. The respondents used about 1% of these medications during the first trimester. These medications included: ovulation-stimulating drugs (0.9%) and NSAIDs (0.5%).

Table 4: Medications used by pregnant women according to US-FDA risk category and pregnancy trimester in Alexandria, 2012.

	Pregnancy trimester			
	First n (%)	Second n (%)	Third n (%)	All Trimesters* n (%)
Unspecified category	215 (29.1)	148 (30.5)	51 (35.2)	414 (30.2)
A	110 (14.9)	41 (8.5)	14 (9.7)	165 (12.1)
B	274 (37.1)	233 (48.0)	59 (40.7)	566 (41.3)
C	126 (17.1)	60 (12.4)	19 (13.1)	205 (15.0)
D	2 (0.3)	3 (0.6)	2 (1.4)	7 (0.5)
X	12 (1.6)	0 (0.0)	0 (0.0)	12 (0.9)

*A pregnant woman could be exposed to more than one drug / classes of drugs

4. Supplements intake during pregnancy.

The majority of the study women 528 (88.0%) took supplements during pregnancy, where the proportion of supplement intake constituted 1295 (42.5%) of the total 3046 drugs taken. As reported by the respondents, the use of iron, folic acid, vitamin B12, calcium, multivitamin and vitamin C among all participants was 75.5%, 51.6%, 40%, 30.5%, 12.2% and 6% respectively. (Fig. 4).

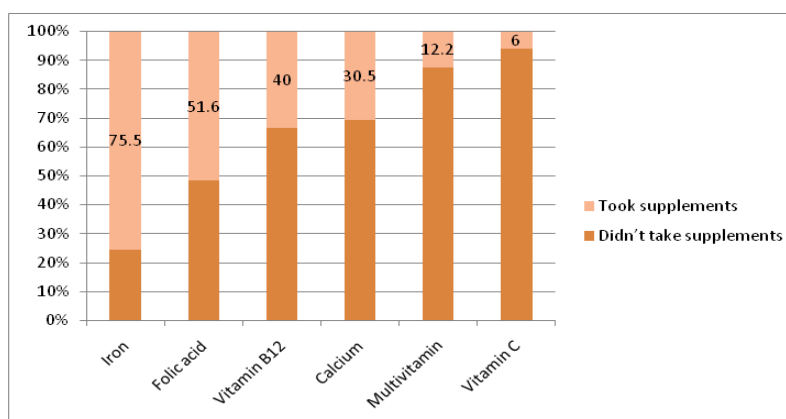


Fig. 4: Pregnant women attending ANC clinics according to supplement intake, Alexandria, 2012.

Among those who have taken these supplements, the percentages for total intake were 35.0%, 23.9%, 18.5%, 14.1%, 5.6% and 2.8% for iron, folic acid, vitamin B12, calcium, multivitamin and vitamin C, respectively. A reduction in the overall supplement intake was observed from 80.0% in the first trimester, to 17.1% and 2.2% in second and third trimesters, respectively. (Table 5)

Table 5: Supplement intake by pregnant women according to timing of intake, Alexandria, 2012.

Supplements intake	Pregnancy trimester							
	Before pregnancy		First		Second		Third	
	No.	%	No.	%	No.	%	No.	%
Iron (n=453)	0	0.0	334	73.7	102	22.5	17	3.8
Folic acid (n=310)	13	4.2	294	94.8	3	1.0	0	0.0
Vitamin B12 (n=240)	0	0.0	226	94.1	11	4.6	3	1.3
Calcium (n=183)	0	0.0	104	56.8	74	40.4	5	2.7
Multivitamin (n=73)	0	0.0	58	79.5	15	20.5	0	0.0
Vitamin C (n=36)	0	0.0	17	47.2	16	44.4	3	8.3
Total (n= 1295)	13	1.0	1033	80.0	221	17.1	28	2.2

5. Herbal intake during pregnancy

Table 6 shows that 251 (41.8%) of respondents took herbs during pregnancy; namely: peppermint (33.5%), hibiscus (23.1%), anise (20.7%), cumin (17.5%), halfa barr (15.5%), fenugreek (12.7%), ginger (6.0%), liquorice (6.8%), telio (4.4%), lupine (4.4%), guava leaves (3.2%), cinnamon (1.6%), marjoram (1.2%) and others (curcum, clove and coriander) constituted 1.6%. More than half (56.3%) of herbal intake was consumed by pregnant women in the first trimester, while 33.0% was in the second trimester and 10.7% in the third trimester. Halfa barr was most commonly used in the first trimester as a GIT antispasmodic, while hibiscus was most commonly used in second trimester as an antihypertensive. Fenugreek was reported as the most commonly used herb in the third trimester.

Table 6: Herbal intake by pregnant women according to pregnancy trimester, Alexandria, 2012

Herbal intake	Pregnancy trimester						Total (n=251)*	
	First		Second		Third			
	No.	%	No.	%	No.	%	No.	%
Peppermint	55	65.5	23	27.4	6	7.1	84	33.5
Hibiscus	22	37.9	27	46.6	9	15.5	58	23.1
Anise	25	48.1	21	40.4	6	11.5	52	20.7
Cumin	28	63.6	15	34.1	1	2.3	44	17.5
Halfa barr	29	74.4	10	25.6	0	0	39	15.5
Fenugreek	16	50	7	21.9	9	28.1	32	12.7
Ginger	7	46.7	6	40	2	13.3	15	6.0
Liquorice	10	58.8	7	41.2	0	0	17	6.8
Telio	7	63.6	1	9.1	3	27.3	11	4.4
Lupin	5	45.5	4	36.4	2	18.2	11	4.4
Guava leaves	5	62.5	1	12.5	2	25	8	3.2
Cinnamon	1	25	3	75	0	0	4	1.6
Marjoram	3	100	0	0	0	0	3	1.2
Other herbs	2	50	1	25	1	25	4	1.6
Total (n=382)*	215	56.3	126	33.0	41	10.7		

Regarding the purposes for use, herbs were most frequently consumed by the respondents for GIT disorders (30.9%), followed by respiratory disorders (23.3%), as a casual drink/tonic (13.8%), hypertension (9.4%), uterine contractions (6.3%), headache (6.0%), hypotension (5.8%), gestational diabetes (2.9%), labor stimulant (1.0%), anemia (0.3%) and analgesic mouth wash (0.3%). (Fig. 5)

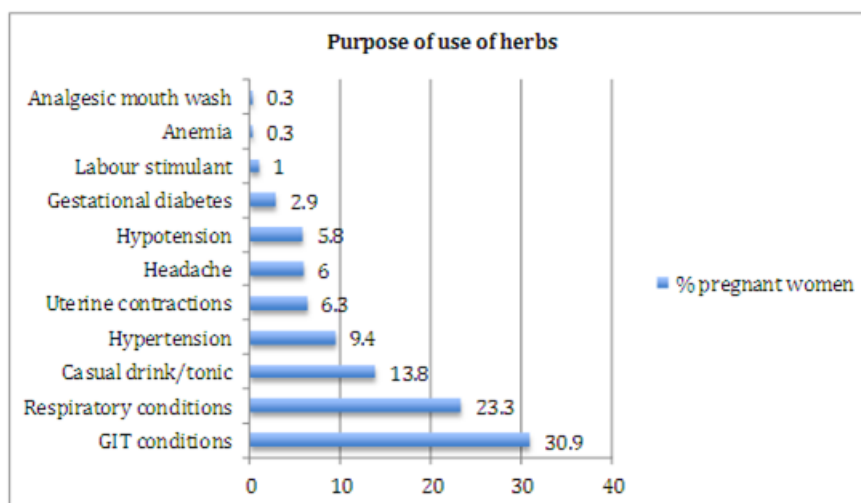


Fig.5: Purpose of use of herbs by pregnant women in Alexandria, 2012.

DISCUSSION

1. Prevalence of overall drug intake during pregnancy:

The use of drugs during pregnancy is increasing worldwide.^[6,7, 25] The current study highlighted a high prevalence of drug use of 96.3%. Similarly, studies published from Germany^[26] and Ethiopia^[27] revealed somewhat same prevalence (96.4% and 96.75%, respectively). On the other hand, studies done in France^[28] and Sudan^[29] reported higher prevalence (99.0% and 98.2%, respectively). On the other hand, other studies conducted in Norway^[30] and USA^[31] reported lower prevalence (86.3% and 56.0%, respectively). Lower prevalence was also reported in Arab countries for example: Palestine^[22], Saudi Arabia^[23] and Oman^[16] 80%, 69% and 49% respectively. In Egypt, Risk *et al.*, 1993 conducted a study in Alexandria and reported a lower prevalence (86%) of drug intake among pregnant women compared to findings of the current study.^[32]

The current study showed that the mean number of drugs consumed per pregnant woman was 5.27 drugs per woman. This finding is comparable with findings reported in a study in Saudi Arabia^[23] where the average number of drugs taken during pregnancy was 4.17. In contrast, studies conducted in developed countries such as Croatia^[33] and USA^[34] reported lower mean number of drugs taken throughout pregnancy (2.1 and 2.6 respectively). Variation in mean number of drugs is probably due to differences in the prescribing behavior and it may also reflect the extent of morbidity.

2. Medication use pattern during pregnancy:

With respect to medication use (excluding vitamins and minerals), the prevalence of POM medication use was 95.6% with the mean number of 2.36 POM per pregnant woman, compared to only 4.4% OTC medication use with the mean number of 1.02 OTC per pregnant woman. These findings were comparable with a systematic literature review done in developed countries from 1989

to 2010, which revealed wide variation in estimates of overall POM use in pregnancy (27–93%) among pregnant women who had at least one POM excluding vitamins and minerals. Among studies of similar design, estimates were lowest in Northern European countries (44–47%) and highest in France (93%).^[15]

Lower prevalence of POM medication use was reported in developing and Arab countries. Bayew *et al.*, 2013, reported lower intake of POM and OTC medications among Ethiopian pregnant women (55.2% and 52.2% respectively) with the mean number of 1.6 POM and 1.5 OTC medications respectively.^[27] Sawalha, 2007, declared a prevalence of 56% for POM medications among Palestinian pregnant women (mean 1.60).^[22] Al-Humayyd and Babay, 2005, also reported lower mean number (1.4) of medications per woman in Saudi Arabia.^[23]

In the present study, 27.9 % of POM medication users used one medication while those who used two and three or more medications constituted 27.7% and 44.3% respectively. These findings are comparable with the findings reported from Palestine^[22] where 44.5% took one medication, 30.8% took two while only 9.3% took more than two medications. Mitchell *et al*, 2011 declared the use of 4 or more medications was more than tripled in the USA over the last 3 decades due to the increased prevalence of chronic diseases with maternal age.^[35] The high prevalence of POM medication use in the current study could probably be attributed to the high prevalence of medical conditions experienced by the respondents who also attended more than one antenatal care clinic and more than one physician prescribed them POM medications.

3. Trend of medication use across pregnancy trimesters.

The trend of medication use across pregnancy trimesters revealed an inverse relation. Despite the fact that 18.2% of respondents in the current study were in their first

trimester, 38.2% and 43.7% were in second and third trimester of pregnancy, respectively, a reduction in the trend of medication use across pregnancy trimesters was demonstrated from 54.0% in first trimester to 35.4%, and 10.6% in second and third trimesters, respectively. This indicates that prescribers were not reluctant to prescribe medications during the first trimester of pregnancy and the pregnant women weren't afraid to take medications during their first trimester.

Findings of the current study are different from those of Mohammed *et al.*, 2013, who declared an increased trend of POM use across pregnancy trimesters from first (19.2%), to second (26.7 %), and third (54.0%) trimesters.^[20] Similarly, an increase in OTC medication use was observed from 17.9% in the first trimester, to 21.6% and 60.5% in the second and third trimesters of pregnancy. Also, the increase in trend of medication use across pregnancy trimesters was also reported by studies done in Ethiopia and Pakistan.^[21,36] Mohammed *et al.*, 2013, suggested that the reason for the increased use of medications across pregnancy trimesters could possibly be because the majority of respondents were in their third and second trimester of pregnancy (57.2% and 26.3%, respectively).^[20] Other reasons suggested by Kebede *et al.*, 2009, were that pregnant women started their ANC visits late in the second and third trimester of pregnancy and that prescribers were reluctant in prescribing drugs during the first trimester of pregnancy.^[21]

4. Classification of medication categories according to therapeutic use:

The current findings showed that the highest proportion (25.3%) of medications used among respondents was for GIT disorders, particularly in the first trimester. The most frequent medications categories included antacids (36.4%) and anti-emetics (31.8%). Similar to the present findings, the study in Oman reported increased use of medications used to relief common GIT disorders of pregnancy such as antacids and anti-emetics.^[16]

As regards systemic antibiotics, the current study revealed that the proportion of systemic antibiotics used by pregnant women amounted to 8.2% of the total medications and they were mostly used in the second trimester. Penicillins (i.e. ampicillin and amoxicillin) and cephalosporins were the most frequently taken antibiotics by pregnant women in this study. They have selective safety (FDA category B), and this finding was similar to what was reported by Lodi 2009.^[37] Systemic antibiotics were most frequently used for dental disorders (44.3%) followed by respiratory disorders (27.0%) among study women. Sawalha 2007 also reported an increase in antibiotics used for dental disorders among Palestinian pregnant women.^[22]

The current study also revealed that most of the pregnant women with chronic CVS disorders (for example rheumatic heart disease and aortic stenosis) continued to use long acting penicillin throughout pregnancy. The

proportion of long acting penicillins amounted to 7.4% of total systemic antibiotics used among the study women. This is in agreement with the CDC guidelines of the Rheumatic Heart Disease Program, stating that long acting penicillin injections should continue throughout pregnancy.^[38] On the other hand, only 4 out of 10 pregnant women discontinued long acting penicillin once pregnant. This was in agreement with Ostensen *et al.*, 2002, who reported that rheumatic disease activity improves in most women during pregnancy.^[39]

As regards analgesics, this study demonstrated that the proportion of analgesics used by the respondents amounted to 16.2% of total medications and they were mostly used in the second trimester. Other studies for example in Ethiopia reported a lower proportion (6.3%) of analgesics used during pregnancy.^[26] These findings support the need for raising awareness as regards the irrational use of analgesics during pregnancy. Analgesics used for headache relief, constituted the highest proportion (47.3%) of total analgesics used by pregnant women, followed by analgesics used for dental disorders (41%) and analgesics used for respiratory disorders (10.8%). The present study also revealed that analgesics for headache were most frequently used in the first trimester (25.4%), then the rate of use decreased in second and third trimesters (23.8% and 4.1%, respectively). Marcus 2002, who mentioned that hormone fluctuations correlate with migraine incidence during pregnancy, explained this phenomenon; where estrogen levels increase steadily throughout the first trimester and stabilize during the second and third trimesters.^[40]

5. US-FDA pregnancy risk classification of medications:

The current study revealed that 41.3% of medications used during pregnancy were from category B, followed by 30.2% unclassified, 15.0% from category C, 12.1% from category A, 0.9% from category X and 0.5% from category D. In Egypt, according to the Egyptian National Drug Formulary, many drugs were regularly consumed during gestation including some that are potential teratogens.^[41] The present findings are comparable to studies reported in Nigeria^[42] which have shown that categories A and B medicines are prescribed more frequently than category C or D medicines, and very rarely were category X medicines prescribed during pregnancy. However, in the Danish study^[43], the majority (40.9%) of all prescriptions during pregnancy were classified as safe category A.

A relatively high proportion (1.4%) of teratogenic medications (category D and category X) were highlighted in the present study, which were considered contraindicated in pregnancy. The respondents used about 1% of these medications during the first trimester. Harmful medications included ovulation stimulating drugs (0.9%) and NSAIDs (0.5%). Similarly, Bakker *et al.*, 2006 found that 2.4% of all drugs prescribed in the

first trimester were harmful drugs; which were mainly ovulation-stimulating drugs.^[44]

The present study also revealed that a meaningful proportion (30.2%) of medications used by the respondents were unclassified because they were either not approved by the FDA or they had not been given a category yet. Mohammed *et al.*, 2013^[20] and Sawalha 2007^[22] mentioned the same problem and believed that absence of pregnancy category labeling could potentially lead to a false sense of security or overestimation of risk leading to poor maternal fetal outcomes.

6. Pattern of supplement intake during pregnancy

The majority of the study women (88.0%) took supplements during pregnancy where the use of iron, folic acid, vitamin B12, calcium, multivitamin and vitamin C among them was 75.5%, 51.6%, 40%, 30.5%, 12.2% and 6% respectively. Among those who have taken these supplements, the percentages for total intake were 35.0%, 23.9%, 18.5%, 14.1%, 5.6% and 2.8% for iron, folic acid, vitamin B12, calcium, multivitamin and vitamin C, respectively.

Comparing these findings to those of the study in Palestine, among those who had taken iron, folic acid, calcium and vitamins, the percentages were 37%, 1%, 24% and 40%, respectively. The total intake of iron, folic acid, calcium and vitamins among all participants was 63.3%, 48.6%, 57.8%, and 56.4%, respectively.^[22] Other studies reported higher prevalence of supplement intake compared to the findings of the current study. Picciano *et al.*, 2008, declared that 97% of women in the USA took supplements during pregnancy.^[45]

A low prevalence (51.6%) of folic acid intake was observed mainly in the first trimester of pregnancy, where only 4.2% of them took pre-conceptional folic acid. These findings indicate irrational intake of folic acid during pregnancy due to physician's under-prescription and/or women's poor compliance as regards the importance of folic acid intake before and during pregnancy. Other studies reported higher prevalence of folic acid intake compared to the findings of current study. The study among Qatari and Omani pregnant women showed that 88.7% took their folate supplements during pregnancy while 13.2% of them took it during the pre-pregnancy period.^[46]

7. Pattern of herbal intake during pregnancy

The current study reported that 41.8% of the study sample took herbs during pregnancy. The types of herbs used included peppermint which was the most commonly used herb (33.5%), followed by hibiscus (23.1%), anise (20.7%), cumin (17.5%), halfa barr (15.5%), fenugreek (12.7%), ginger (6.0%), liquorice (6.8%), telio (4.4%), lupine (4.4%), guava leaves (3.2%), cinnamon (1.6%), others (curcum, clove and coriander) 1.6%, and marjoram as the least commonly used herb (1.2%).

A study in Norway reported the common use of herbs during pregnancy with a somewhat similar prevalence (39.7%) to the current study.^[47] However, Sawalha 2007^[22] reported a higher prevalence of herbal intake (45.8%) in Palestine while Al-Riyami *et al.*, 2011^[16], reported a lower prevalence of 23.8% in Oman; and the most commonly used herbs were: ginger, honey, thyme and green tea. In Egypt, a recent study conducted in Alexandria revealed a lower prevalence (27.3%) of herbal intake compared to the current study. The most common herbs used by pregnant women were anise (40.2%), fenugreek (31.7%), ginger (29.3%), garlic (22%), green tea (19.5%) and peppermint (11%).^[48]

The current study reported that 56.3% of herbal intake was consumed by pregnant women in the first trimester (the most critical stage of pregnancy), while 33.0% was in the second trimester and 10.7% in the third trimester. Halfa barr was found to be most commonly used in the first trimester as a GIT antispasmodic, while hibiscus was most commonly used in second trimester as an antihypertensive. Fenugreek was reported as the most commonly used herb in the third trimester, which is in agreement with the study conducted in Alexandria as women believed that fenugreek produces oxytocic effect so they used it in the third trimester to facilitate labor.^[48] However, it is worth mentioning that a small proportion (7.4%) of fenugreek intake was consumed by the study women in the first trimester, although it is contraindicated in the first trimester as it induces abortion.

CONCLUSION

The high prevalence of POM medications during pregnancy indicates the irrational prescribing trend of drugs. The low prevalence of OTC medications reflects high level of women's awareness regarding the risk they could cause to their fetus by taking any medication during pregnancy without the doctor's advice. The highest prevalence of medication use was observed in the first trimester, which is considered the most critical stage of pregnancy.

The prevalence of teratogenic medications of category D and X is of concern even if it is low. Despite the fact that the majority of women took supplements during pregnancy, yet irrational underuse of some important supplements was observed.

The reduction in the overall supplement intake was observed in all trimesters of pregnancy indicates either physician's under-prescription or women's poor compliance with recommended supplement intake. The low prevalence of folic acid intake emphasizes the need to target women to take folic acid before and during the first trimester of pregnancy. High herbal use especially in first trimester warrants special attention due to the unknown risks that may be associated with their use.

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