Evaluation of the pregnant women's approaches regarding drug utilization

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ABSTRACT

OBJECTIVE: Drug utilization habits of the pregnant are a critical aspect of rational use of the medicine (RUM). This study aimed to analyze the RUM related attitudes and the behaviors of women during their pregnancies.

METHODS: The data were collected between May 2016–October 2016 by conducting surveys to 71 pregnant women admitted to the private and governmental hospitals in five districts of Northern Cyprus. The sociodemographic characteristics of the pregnant as well as their attitudes and behaviors concerning drug use were evaluated.

RESULTS: The mean age and the gestational week of the patients was 29.7±4.3 years and 25.7±11.2 weeks, respectively. Planned pregnancies constituted 71.8% of all. The percentage of patients with an unplanned pregnancies who were using drugs at the time of the survey (25.0%) was lower than that in those with planned pregnancies (49.0%, p<0.05). Almost two-thirds (66.2%) of the women were exposed to a drug during pregnancy, mostly for "vitamin/mineral prophylaxis" (38.3%) and agents controlling nausea/vomiting (19.1%). Two out of eleven women (18.2%) were using folic acid when they learned about their pregnancy. One of the drugs used for the chronic disorder in the third trimester was acetylsalicylic acid (11.1%), a category D drug in this setting. Most of the patients stated that they frequently read the instructions (60.9%), "often" paying attention to side effects (56.5%). Considering some of the habits related to drug use, 8.7% and 10.9% of pregnant women declared that they sometimes "did not follow the instructions" and "dosage/duration of the drug usage", respectively. Seven patients (15.2%) declared that they did not consider side effects on the medication guide while more than half (56.5%) did it "often". Near one in five (19.6%) of the pregnant women stated that they hesitated about the drug usage due to teratogenicity risks.

CONCLUSION: Our study highlights the drug utilization attitudes and behaviors of pregnant women during pregnancy in Northern Cyprus, indicating several shortcomings, including insufficient prenatal folic acid use, occasional use of risky drugs, and unsatisfactory medication guide handling. Available findings underline the necessity of education not only for patients but also for healthcare providers to disseminate RUM in pregnancy.

Keywords: Drug use; first visit; planned; pregnancy; teratogenicity.

Drug use in pregnancy is a critical issue that may deeply impact the health of both the mother and the fetus. Teratogenic effects of many drugs currently used have not yet been fully elucidated while those with known profiles may be subject to alterations with revised guidelines, resulting in a very limited number of drugs without risk of

teratogenicity. These prompt all addresses of drug use in pregnancy to handle the situation more carefully [1].

Worldwide studies on drug use in pregnancy show that up to 95.5% of pregnant women are exposed to various drugs [2–4]. Exposure to teratogens within two weeks of conception may cause "all or nothing" effects. In addition, the first 18–60 days after conception that coincides with organogenesis is the most critical period where structural anomalies may develop [5]. Therefore, prenatal care regarding the rational use of medicine (RUM) is widely recommended for every pregnant woman to prevent potential teratogenicity. RUM is defined as "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate time, and at the lowest cost to them and their community" [6]. Pregnancy is obviously one of the most special practices of the RUM that should be applied rigorously and carefully to maximize the benefits as well as reducing the potential risks for the mother and the fetus.

Several factors, including the income and the education of the mother, planned nature of pregnancy, or timing of first pregnancy examination, may interfere with RUM and adequate prenatal care. Women who had planned their pregnancy were reported to receive early and adequate prenatal care than those with an unplanned pregnancy [7–10]. In fact, unplanned pregnancies result in poorer outcomes, such as abortion, postnatal depression, lower birth weight, and poorer mental and physical health during childhood [7–10].

This study aimed to evaluate the attitudes of pregnants regarding drug use and its patterns in Northern Cyprus (NC).

MATERIALS AND METHODS

In this pharmacoepidemiological study, the data were obtained by conducting surveys to the 71 pregnant women (response rate: 71%) applied to the private and governmental hospitals in five districts of NC between May 2016–October 2016. Women constituted 52.6% of the around 300,000 permanent inhabitants of Northern Cyprus and were provided gynecology and obstetrics health care service by 78 specialists [11, 12]. The survey was performed in Nicosia, Lefke, Famagusta, Kyrenia, and Omorpho.

The survey was performed using a face-to-face interview fashion with a total of 27 questions. Data on the sociodemographic characteristics of the pregnant as well

Highlight key points
- Women with planned pregnancies were more likely to use drugs during pregnancy.
- Pregnant women used prenatal folate insufficiently.
- Women exhibited unsatisfactory medication guide handling during pregnancy.

as their attitudes and behaviors regarding drug use were collected as follows:

- First six questions were about the sociodemographic characteristics of the pregnant, such as age, education, occupation, location of residence and insurance.
- Questions 7 to 10 were about their parity, abortion/miscarriage experiences in the previous pregnancies, and whether they were told or aware that these events were related to drug use.
- In questions 11 to 19, the drug use habits of the pregnant was evaluated by asking the drugs that they had used in certain periods of the pregnancy, the presence of chronic disorders, and regular follow-up times.
- In questions 20 to 27, the attitude and the behaviors of the pregnant regarding drug usage were asked.

The drugs that were declared to be used by the questioned women were classified in accordance with the Food and Drug Administration's (FDA) pregnancy letter categories from A to X, which is still used in the official summary of product characteristics of the drugs to help in clinical decision making by physicians.

For this study, a protocol was established with the Health Ministry of the NC and the ethical approval was obtained from the Ethics Committee of Marmara University Health Sciences Institute (approval no: 241, 28.03.2016-8).

Statistical Analysis

The collected data were analyzed using statistical software SPSS (version 15.0). Analyzed data were expressed as means±standard deviation values and numbers and/or percentages, where appropriate. Categorical variables between the study groups were compared via Chi-square or Fisher's exact test. An overall 5% of type-I error level was used to infer statistical significance.

RESULTS

The majority (47.9%, n=34) of the participants were from Nicosia, 32.4% (n=23) from Lefke, and the rest

TABLE 1. The impact of education, occupation, location and insurance on planning of pregnancy and timing of first pregnancy examination

	Planning of pregnancy			Elapsed time to first examination of pregnancy[#]		
	Planned %	Unplanned %	Total %	≤4 weeks %	>4 weeks %	Total %
Education						
University degree	64.7	60.0	63.4	70.6	57.6	64.2
High school and lowest degree	35.3	40.0	36.6	29.4	42.4	35.8
Occupation						
House-wife	29.4	25.0	28.2	23.6	36.4	29.9
Working	70.6	75.5	71.8	76.5	63.6	70.1
Location						
City center	54.9	50.0	53.5	44.1	48.5	46.3
Village-town	45.1	50.0	46.5	55.9	51.5	53.7
Insurance[#]						
Yes	64.7	63.2	64.3	45.5*	21.9	33.8
No	35.3	36.8	35.7	54.5	78.1	66.2
Planning of pregnancy						
Planned	n/a	n/a	n/a	82.4	63.6	73.1
Unplanned	n/a	n/a	n/a	17.6	36.4	6.9
Total	100.0	100.0	100	100.0	100.0	100

#: Insurance status and timing of pregnancy examination was not known in two and four patients, respectively. *: $p<0.05$; n/a: not applicable.

(19.7%, n=14) from Famagusta, Kyrenia, and Omorpho. The mean age of the patients was 29.7±4.3 (21–41 years) and the mean gestational week was 25.7±11.2. The majority of the pregnant (71.8% n=51) stated that their current pregnancies were planned. Among those who had unplanned pregnancies, the mean time to learn that they were pregnant was 6.7±3.6 gestational weeks (range: 1–16 weeks), with four of them using the contraceptive method but none orally administered. About half (49.2%, n=33) of the pregnant women had their initial pregnancy examination after >4 weeks of gestation. The mean time to first pregnancy examination was 4.0±2.5 weeks.

It was recognized that 63.4% of the participants graduated from a university, 71.8% of them has an occupation, 53.5% of them were living in the city center and 62.0% of them has insurance. None of these patients' characteristics differed concerning the planning of pregnancy or timing of pregnancy examination, except that the percentage of patients with no insurance was higher among late (>4 weeks) attendees of initial examination (78.1%) compared to that in early (≤4 weeks) attendees (54.5%, $p<0.05$; Table 1).

The majority of the pregnant women (59.2%) reported having their second or subsequent pregnancies. Sixteen (38.1%) pregnant women declared that they had miscarriage/abortion (75% experienced miscarriage, 56.3% experienced abortion) in their previous pregnancies; all of these patients stated that their miscarriage/abortion problem was not due to drug usage. The percentage of the patients who stated that they received medical treatment to become pregnant constituted 13.7% of those with planned pregnancies.

Almost all patients (98.6%) declared to attend their follow-ups regularly (median: 9 visits). Around one in nine women (11.3%) stated to have chronic disorder requiring drug therapy. While 15.5% were using any medication when they had learned that they were pregnant, six patients (8.5%) did not remember their medication use. At the time-point of the survey, 42.3% and 5.6% of pregnant women were using drugs or herbal products/food supplements, respectively (all were upon physician's recommendations). A significantly less percentage of patients with unplanned pregnancies (25.0%) were using drugs at the time of the survey compared to that in those with planned pregnancies (49.0%, $p<0.05$). Other

TABLE 2. The impact of patients' clinical and drug use characteristics and attitudes on planning of pregnancy and timing of first pregnancy examination

	Planning of pregnancy			Elapsed time to first examination of pregnancy[#]		
	Planned %	Unplanned %	Total %	≤4 weeks %	>4 weeks %	Total %
Regular follow-up						
Yes	100.0	95.0	98.6	97.1	100.0	98.5
No	0	5.0	1.4	2.9	0	1.5
Presence of chronic disorders						
Yes	9.85	15.0	11.3	8.8	15.2	11.9
No	90.2	85.0	74.6	91.2	84.8	88.1
Drug use while pregnancy was learned						
Yes	19.6	5.0	15.5	14.7	18.2	16.4
No	80.4	95.0	84.5	85.3	81.8	83.6
Drug use during the survey						
Yes	49.0*	25.0	42.3	44.1	48.5	46.3
No	51.0	75.0	57.7	55.9	51.5	53.6
Herbal product/food supplement use during the survey						
Yes	3.9	10.0	5.6	5.9	6.1	6.0
No	96.1	90.0	94.4	94.1	93.9	94.0
Total	100.0	100.0	100	100.0	100.0	100

#: Timing of pregnancy examination was not known in four patients; *: p<0.05.

clinical or drug use characteristics did not differ by the planning of pregnancy or timing of initial pregnancy examination (Table 2).

For the eleven women who declared to be using drugs when they heard of their pregnancy, only clomiphene belonged to the X category (9.1%). Three of them could not be remembered, and two drugs were of category A, namely levothyroxine (n=2) and folic acid (n=2). There were nine drugs required to be used in chronic disorders of the women. Only one of these drugs (11.1%) belonged to the category D, which was acetylsalicylic acid used in the third trimester. Two drugs, namely gliclazide and salbutamol, used by pregnant women, were of category C (22.2%).

Almost two-thirds (66.2%) of the pregnant women stated that they had to use at least one drug during their pregnancy. Metoclopramide (10.6%) and progesterone (10.6%) were the most commonly used drugs other than vitamins/minerals (Table 3). Most of these drugs were for "vitamin/mineral prophylaxis" (38.3%), and this was followed by the drugs using for nausea/vomiting (19.1%),

urinary tract infection (10.6%), bleeding (8.5%) and miscarriage risk (6.4%). While 95.7% of patients decided to use their drugs upon their physicians' recommendations, two patients remembering the names of drugs declared to practice self-medication, consisting of amoxicillin+-clavulanate and paracetamol.

Given some of the habits related to drug use, 8.7% and 10.9% of pregnant women declared that they sometimes "did not follow the instructions" and "dosage/duration of the drug usage", respectively. Four patients (8.7%) stated that they "sometimes" bought the drug from the pharmacy "without prescription". Twenty-eight women (60.9%) expressed that they frequently read the instructions. Seven patients (15.2%) declared that they did not consider side effects on the medication guide while more than half (56.5%) did it "often".

Near one in five (19.6%) of the pregnant women stated that they hesitated about the drug usage due to teratogenicity risks. Overall, none of these drug use habits significantly varied concerning the categories of planning of pregnancy (planned vs. unplanned;

TABLE 3. Distribution of health problems of the pregnant women that require drug usage during pregnancy

Health problems	%	Used drug(s)	#%	%	FDA risk classification
Vitamin/mineral prophylaxis	38.3	Vitamin/mineral	100.0	38.3	U
Nausea/vomiting	19.1	Metoclopramide	55.6	10.6	B
		Trimethobenzamide	11.1	2.1	C
		Unknown	33.3	6.4	U
Miscarriage risk	14.9	Progesterone	71.4	10.6	B
		Unknown	28.6	4.3	U
Urinary tract infection	10.6	Cefuroxime	20.0	2.1	B
		Fosfomycin	20.0	2.1	B
		Unknown	60.0	6.4	U
Upper respiratory tract infection	4.3	Amoxicillin+clavulanate	100.0	2.1	B
Pain	4.3	Paracetamol	50.0	2.1	B
		Unknown	50.0	2.1	U
Anemia	4.3	Iron+folic acid	50.0	2.1	U
		Unknown	50.0	2.1	U
Constipation	2.1	Lactulose	100.0	2.1	B
Diabetes	2.1	Gliclazide	100.0	2.1	C
Total	100.0			100.0	

#: Distribution within its indicated/intended problem.

p>0.05) or timing of the initial visit for pregnancy (≤4 weeks vs. >4 weeks; p>0.05).

DISCUSSION

Patients could be regarded as the main addressees of RUM. Critical issues like potential teratogenicity concerns, pharmacokinetic or pharmacodynamic variations may affect the functions and became much more important concerning drug use during pregnancy [13]. In this study, the attitudes and behaviors of the pregnant women on RUM were evaluated with survey. The results of this study could provide a base for the ways of dissemination of RUM practices in pregnancy not only in NC but also in Turkey and other countries.

Patients were found to attend their first pregnancy visit at a mean of 4.9th gestational week. Although scarce in the literature, existing data showed the timing to vary from a median of six weeks to 16 weeks [14]. An Indian study reported that near two-thirds of pregnant women applied physicians for initial examination after 25 weeks of gestation [15]. In fact, this variation was reported to be influenced by several factors, including level of education, awareness, perceived health needs and economic situation [16, 17]. A study conducted in Turkey reported a positive association of late pregnancy recognition to the lower level of education and the absence of health insurance [17]. Consistently, our study showed pregnant women with no insurance to be more likely to attend initial pregnancy visit lately compared to those who had insurance. One of the reasons for the comparably earlier first visit of pregnants in NC might be the high rate of the planned pregnancies (71.8%) in our study. It was also reported to exhibit variations from 54.8% to 77.5% [7–9, 18]. While unplanned pregnancy was associated with a lower level of education and being a housewife in the literature [8–10], we did not observe such an association in the current study.

The high rate of planned pregnancy may reduce the likelihood of teratogen drug usage before and/or after conception and provide adequate prenatal care. In fact, inadequate prenatal care with more physical and mental problems was mostly encountered in unplanned pregnancies [9, 10]. In our study, compared to those with unplanned pregnancies, the women who had planned their pregnancy had a higher rate of drug use during pregnancy, mostly including several vitamins/minerals, such as folic acid, iron preparations and omega-3. This

finding may be considered important concerning contribution to RUM in pregnancy. Folic acid is used for the prevention of neural tube defects and other congenital anomalies before pregnancy and in the first months of pregnancy, based on an important body of evidence [19–21]. This prophylaxis should start at least four weeks before conception, considering that the neural tube closes within 28 days after conception [22]. On the other hand, there are also contradictory views about the usage of folic acid in this critical period. For instance, a German study reported that only 1% and 10% of the women were using folic acid before and within the first trimester, respectively [23]. Contrarily, the fact that near one-fifth of women declared to be using the drug when they had heard of their pregnancy seemed to be a better attitude, if not deemed unsatisfactory.

More than one-third (38.3%) of the women stated that they used vitamin/iron preparations for supplemental purposes. Compared to the prescribed medicines, herbal products and food supplements are used based on very limited pieces of information and may cause many unwanted effects and/or interaction problems, which becomes more critical during pregnancy in terms of risks [24]. The use of such products has generally increased in recent years, albeit with a wide variation from 17.8% in Saudi Arabia to 54.0% in the United States and up to 57.8% in Europe for herbal products [25–29]. The conflicting reports of the studies regarding the possible adverse effects and risks of herbal products restrict their usage in pregnancy [26–28]. The observed lower frequency of herbal product/food supplement use in NC overall could be regarded as indicative of a rational approach in this respect.

Around one in every seven women declared that they were using prescription drugs when they learned about their pregnancy, where 27.3% of these included antibacterial agents and 9.1% clomiphene. The latter was an "X" category ovulation stimulator, which was most probably used for conceiving with medical treatment. On the other hand, 8.4% of the participant stated that they "sometimes" used drugs during their pregnancy without prescription, namely paracetamol and antacid. While a recent study also reported similar utilization of drugs without prescription, 23% to 63% of pregnant women in different countries reported such use [30–33]. A study from Nepal reported the prevalence of self-medication as 64.2% among women, where three-fourth changed this habit during their pregnancy [34]. Available findings in the literature suggest positive findings regarding RUM in

NC, considering lower percentages of declared self-medication or non-prescribed drug use habits of the pregnant than that in the other countries. However, "lack of adequate regulation on over-the-counter drugs" in NC may compel the evaluation of the drug use decisions by the patients. Therefore, it is thought that this confusion may have an effect on the lack of declarations.

Almost two-thirds of pregnant women stated to use at least one drug during pregnancy. The use of medications during pregnancy in many countries across Europe was similar to or higher than (64.1–96.4%) that observed in our study, except in Denmark (46.8%) [4, 23, 35–37]. This might be attributed to the declared frequency of chronic disorders (11.2%), which was lower than reported in the literature varying between 22–46%.[15, 36–38]. Among every drug user during pregnancy, more than one-third (38.3%) stated that they used vitamins/minerals, the rest consisting of metoclopramide, progesterone, amoxicillin+clavulanate, trimethobenzamide, cefuroxime, fosfomycin, paracetamol, lactulose, and gliclazide. While a Saudi study reported vitamins, paracetamol, antibiotics, antiemetics as the most commonly used drugs, an Italian study reported these as folate/iron preparations, antibiotics, and progesterone [25, 39], indicating an overall similarity to our findings. On the other hand, it is interesting that acetylsalicylic acid was declared by a pregnant woman to be used for a chronic condition at the third trimester, in which setting is a category D drug, whereas it was not listed by the patient among ever drug use in pregnancy. This may suggest that the use of risky drugs needs to be better clarified by health care professionals to pregnant women, especially if they are also available over-the-counter.

In this study, it was observed that pregnant women exhibited lower performance concerning their attitude to pay attention to side effects of drugs in the label and to read the medication guide/label in comparison with studies in Saudi Arabia and Turkey [2, 25]. This points to another disadvantage in terms of RUM and needs to be corrected by a focus on the education of women of childbearing age. On the other hand, although the majority of pregnant women stated that they did not go against the recommended instructions or the recommended dose/duration of use, around 10% of pregnant women declared to "sometimes" exhibit negative attitudes in this respect, suggesting that there is still a room for improvement in RUM. Drug use attitudes and behaviors during pregnancy can improve with education. For instance, a

study reported that the knowledge, attitudes and behaviors of pregnant women showed a positive increase after education [34]. It has been advocated that rational drug use habits can be improved by making interventions, such as providing more information about drugs and enhancing communication and consulting services for women [40]. We believe that the areas in which pregnant women in NC are troublesome regarding drug use in this study can be corrected with proven improvement activities, and thus contributing to the dissemination of rational drug use during pregnancy.

Our study is not without limitations. No subsequent action was taken to test the accuracy of the information and attitudes declared by the participants in the patient surveys. The conclusion drawn from this study should be interpreted based on this assumption. Identifying teratogenicity problems that may arise from the drugs in the risk group requires follow-up during the pregnancy and in the postpartum period. The failure of follow-up of the patients who received D or X category drugs may also be regarded as another limitation of this study. In this respect, further studies are warranted to investigate the impacts of the use of these risky drugs on fetuses and/or babies in NC. Finally, although the use of the risk categories in approval documents of the drugs was abolished by FDA, no strong assumptions could be made upon the use of such drugs declared in this study as we did not have patient's other clinical data to justify appropriateness or inappropriateness of the pharmacotherapy or personalized harm from not administering or discontinuing any drug during pregnancy.

Conclusion

In conclusion, our survey study highlights the drug utilization attitudes and the behaviors of pregnant women in NC. This study indicates several shortcomings in the attitudes and behaviors of patients for RUM, especially for insufficient prenatal folic acid use, occasional use of risky groups of drugs, and unsatisfactory medication guide handling. Available findings underline the necessity of education not only for patients but also for healthcare providers to disseminate RUM in pregnancy.

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