

Adherence with prescription drugs in pregnant and breastfeeding women consulting with the Israel Poison Information Center Teratology Service

Yael Lurie , Michal Bar , Iris Avital Lev dov , Dina Tkachenko , Yedidia Bentur & Daniel Kurnik


To cite this article: Yael Lurie , Michal Bar , Iris Avital Lev dov , Dina Tkachenko , Yedidia Bentur & Daniel Kurnik (2020): Adherence with prescription drugs in pregnant and breastfeeding women consulting with the Israel Poison Information Center Teratology Service, Clinical Toxicology, DOI: [10.1080/15563650.2020.1823405](https://doi.org/10.1080/15563650.2020.1823405)

To link to this article: <https://doi.org/10.1080/15563650.2020.1823405>



Published online: 23 Oct 2020.



Submit your article to this journal 



View related articles 



View Crossmark data 

CLINICAL RESEARCH



Adherence with prescription drugs in pregnant and breastfeeding women consulting with the Israel Poison Information Center Teratology Service

Yael Lurie^{a,b}, Michal Bar^b, Iris Avital Levdo^a, Dina Tkachenko^a, Yedidia Bentur^{a,b} and Daniel Kurnik^{b,c}

^aClinical Pharmacology and Toxicology Section, Israel Poison Information Center, Rambam Health Care Campus, Haifa, Israel; ^bRappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel; ^cClinical Pharmacology and Toxicology Section, Clinical Pharmacology Institute, Rambam Health Care Campus, Haifa, Israel

ABSTRACT

Introduction: During pregnancy and breastfeeding, many women require prescription medications. Concerns about drug effects on the fetus or breastfed infant may lead to decreased adherence. Our objective was to evaluate the adherence of pregnant and breastfeeding Israeli women to prescription drugs, the information they received regarding drug safety, and the women's awareness and pattern of the use of Teratogen Information Services (TIS) in Israel.

Methods: We conducted a prospective observational cohort study among pregnant and breastfeeding women who had contacted the Israel Poison Information Center (IPIC) to consult about prescription medications. In a follow-up telephone call, we assessed adherence (defined as medication initiation by the time of the follow-up call) and the patients' recollection of the safety information given by the prescribing physician. In an additional cohort of post-partum women, we assessed their awareness about TIS in Israel.

Results: We included 59 pregnant women (62 prescriptions), 75 breastfeeding women (80 prescriptions), and 49 postpartum women. About two-thirds of all prescriptions were for antimicrobial drugs. By the time of the follow-up call, most participants (89% of pregnant and 89% of breastfeeding women) had initiated medications. Eight (11%) breastfeeding women stopped breastfeeding their babies while using the medication. Patients reported receiving explicit and unequivocal information concerning medication safety by the prescriber for 50% and 55% of prescriptions to pregnant and breastfeeding women, respectively. 70% of postpartum women interviewed in the maternity ward were not aware of TIS in Israel.

Discussion and conclusions: We observed high adherence rate to prescription medication therapy among pregnant and breastfeeding women in our cohort. Only about half of the women reported receiving comprehensive drug safety information by the prescriber. Raising awareness of the importance of medication safety counseling among both physicians and patients may contribute to the quality of medical care of pregnant and breastfeeding women in Israel.

ARTICLE HISTORY

Received 17 May 2020
Revised 25 August 2020
Accepted 8 September 2020

KEYWORDS

Pregnancy; breastfeeding; adherence; medication safety; information

Introduction

During pregnancy and breastfeeding, many women require prescription medication therapy for chronic diseases, medical conditions associated with pregnancy, or unrelated acute diseases. In the US, up to 70% of women use at least one prescription medicine any time during pregnancy [1,2], while little is known about the prevalence of prescription medication use during pregnancy in Israel. When a pregnant or breastfeeding woman receives a prescription by her physician, concerns about drug effects on the fetus or breastfed infant may arise and lead to decreased adherence to drug therapy, even after comprehensive drug consultation [3–5]. Untreated acute illness (e.g., urinary tract infection) or chronic illness (e.g., diabetes, HIV infection) can adversely affect maternal health and result in obstetric complications and fetal morbidity [6–8]. In fact, an exaggerated perception

of teratogenic risk increases anxiety and may even lead a pregnant woman to consider the unnecessary termination of pregnancy [9]. In breastfeeding women, concerns about drug safety can lead to temporary or permanent cessation of breastfeeding, although this is rarely medically indicated. Thus, when prescribing to pregnant or breastfeeding women, it is important that physicians provide the patient with updated, comprehensive, and clear information about the medication's safety during pregnancy and/or breastfeeding.

To date, little is known about the adherence of pregnant and breastfeeding Israeli women to prescription drugs. We therefore conducted a prospective cohort study based on telephone interviews with pregnant or breastfeeding women who called the Israeli Poison Information Center (IPIC), in order to evaluate their adherence to prescription drugs, the information they received regarding drug safety during

pregnancy or breastfeeding, and the women's awareness and pattern of use of Teratogen Information Services in Israel.

Methods

Study design and participants

After approval by Rambam Health Care Campus Institutional Review Board, we performed a prospective observational cohort study between January 2015 and December 2015. Study participants were pregnant and breastfeeding women who received a medication prescription and then contacted the teratology information phone service of the IPIC, at the Rambam Health Care Campus. The IPIC is a national service, serving the Israeli population of 9 million inhabitants. It provides clinical toxicology consultation and drug information to both the general public and health care systems and is active 24 h a day. The IPIC also operates a teratology information service (TIS), one of three services in Israel providing on-line telephone counseling concerning drugs, chemicals, radiation, and occupational exposures during pregnancy and breastfeeding. During 2015, the IPIC recorded 35,616 calls, 3578 (10%) concerning drug safety during pregnancy or breastfeeding. The consultation is based on computerized databases like TERIS Teratogen Information System, REPROTOX[®], LactMed Drugs and Lactation Database (as a primary reference for medication safety during breastfeeding), and also textbooks and PubMed search. Women were eligible for inclusion if they were pregnant or breastfeeding and had received from a physician a new prescription for an oral, parenteral, or inhaled medication, or for a local anti-hemorrhoid preparation. Women who only received prescriptions for topical dermal and ear, nose, and throat preparations were excluded, since the low systemic absorption of these preparations makes them generally safe during pregnancy and breastfeeding. At the end of the telephone IPIC consultation, we asked eligible women to participate in the study, and scheduled a follow-up phone call if they gave oral consent.

Data collection

The follow-up study call was performed by one of the researchers between 5 and 30 days after the consultation call, in order to interview the women after they already started therapy and to minimize recall bias. The study interview included collection of demographic and obstetric data, data about the medication(s) prescribed and their indication, type of prescriber (primary care physician, obstetrician/gynecologist or other medical specialist), whether any teratologic information had been provided by the prescribing physician, and whether other pharmacological information resources were used (drug leaflet, pharmacist, websites, or other teratology information services). The teratologic information from the prescribing physician was classified as "No consult", "Unequivocal recommendation", or "Equivocal recommendation" (e.g., "I think it is safe to use, but also ask your

gynecologist or Teratogen Information Service (TIS)"; "You should use it, but there may be some (unspecified) concerns"; or that the prescriber sounded hesitant and unconvincing). In breastfeeding women, we also recorded the physician's recommendation "Use the medication but discontinue breast-feeding for the treatment period". We recorded the lag time between prescription date and medication initiation, and also the lag time between the prescription date and the original (patient-initiated) IPIC telephone consultation date. In our study, not initiating the prescribed medication until the follow-up study call was defined as non-adherence, unless the IPIC consult recommended not to start the medication. We also asked the women about the reasons for non-adherence. Patients who had initiated the medication before consulting with the IPIC were considered as adherent. Breastfeeding women were also asked about whether breastfeeding was interrupted due to the drug therapy. In order to assess the women's recollections of the IPIC consultation, we asked the participants during the study interview what the IPIC consultant had recommended during the initial IPIC consultation, and compared their recollections with the consultations as documented in the IPIC database.

Questionnaire-based survey in hospitalized postpartum women

We also performed a survey among postpartum women in order to evaluate the accessibility of teratologic medication information to pregnant women in Israel. On 14 survey days, consecutive consenting post-partum women hospitalized in the maternity ward of the Rambam Health Care Campus were recruited on day 2 or later after an uncomplicated birth by one of the study researchers for a face-to-face questionnaire-based interview, and then asked questions on demographic parameters, obstetric history, prescription and actual use of medications during pregnancy and their medical indications. We also asked if any teratologic consultation had been provided, and if they were aware of Teratology Information Services in Israel.

Data analysis

For the descriptive analyses, we presented continuous variables as means with standard deviations (SDs) or medians with interquartile ranges (IQRs), and categorical variables as absolute numbers and percentages. Our main outcome was non-adherence versus adherence to the prescribed drug, as previously defined. To identify variables associated with non-adherence, we then used the *t*-test or Mann-Whitney *U*-test (for continuous variables), the χ^2 test or Fisher's Exact test, as appropriate, for categorical variables to compare independent variables between adherent and non-adherent women. In this explorative study, our sample size did not allow multivariate analysis of the effect of independent variables on participant's adherence. A *p*-value of <0.05 was considered significant. All analyses were performed using the statistical software IBM SPSS v.25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Results

Telephone interview study

We recruited 59 pregnant women who contacted the IPIC to consult regarding 62 prescriptions, and 75 breastfeeding women who were consulted regarding 80 prescriptions. The follow-up study call was performed a median of 11 days (IQR,

5–21.5 days) after the original IPIC phone consultation. Table 1 presents the demographic and obstetric characteristics of the study participants. The most frequent prescriptions were for antimicrobial drugs (Figure 1). Most prescriptions were prescribed by a primary care physician.

Non-adherence to prescription drug

Most women (75% of pregnant women and 67% of breastfeeding women) called the IPIC within one day after receiving the prescription (Figure 2). Figure 3 shows the time from prescription to medication initiation for pregnant and breastfeeding women. By the time of the study follow-up call, most women had initiated the prescription medications (55/62 prescriptions [89%] for pregnant women and 71/80 prescriptions [89%] for breastfeeding women), the majority of them within one day of receiving the prescription (Figure 3). Pregnant women initiated 11 (18%) prescription medications before IPIC consultation, while breastfeeding women started 14 (18%) prescriptions before IPIC consultation. 52 prescriptions (84%) to pregnant women were assessed as “no increased risk in pregnancy” by the IPIC staff, and 10 prescriptions (16%) were assessed as “may be used with some precautions”. Examples included medications that would require adjustment/caution later in pregnancy (e.g., codeine), requires special follow up for prolonged treatment (e.g., prednisone), medications for which changes might be considered later in pregnancy (e.g., propylthiouracil), or medications considered probably safe based on limited data only (e.g., duloxetine). None of prescriptions were categorized as contraindicated in pregnancy by the IPIC staff.

For pregnant women, there were no statistically significant differences in demographic or clinical parameters between adherent and non-adherent women (Table 2). Among breastfeeding women (Table 3), the distribution of medication classes was different between adherent and non-adherent women (p -value for overall differences in the medication class distribution = 0.036). Comparing the various medication subclasses individually, prescriptions for antimicrobials and GI/anti-hemorrhoids agents were more common among adherent patients (56% and 17% of all prescription)

Table 1. Demographic, obstetric, and breastfeeding data in pregnant and breastfeeding women.

Variable	Pregnant women (<i>n</i> = 59)	Breastfeeding women (<i>n</i> = 75)
Age (years)	32 (26–36)	32 (28–35)
Median (Interquartile range)		
Highest Education level ^a		
<i>n</i> (%)		
Primary/Secondary ^a	19 (32%)	12 (16%)
Tertiary	40 (68%)	63 (84%)
Religion		
<i>n</i> (%)		
Jewish	58 (98%)	74 (99%)
Muslim	1 (2%)	1 (1%)
Christian	0	0
Age of pregnancy (weeks) ^b	20 (14–29)	na
Median (Interquartile range)		
Trimester of pregnancy, <i>n</i> (%) ^b		
1st	11 (19%)	na
2nd	30 (52%)	
3rd	17 (29%)	
Number of pregnancies (including current), <i>n</i> (%)		
1	15 (25%)	na
2	12 (20%)	
3	10 (17%)	
4	12 (20%)	
≥5	10 (17%)	
Previous abortion ^c , <i>n</i> (%)	19 (32%)	na
Age of the breastfed baby (months)	na	3 (2–7)
Median (Interquartile range)		
Exclusive breastfeeding, <i>n</i> (%)	na	37 (49%)
Prescriber's medical specialty ^d		
Primary care physician ^e	35 (59%)	48 (64%)
Obstetrics-Gynecology	3 (5%)	4 (5%)
Other medical specialist ^f	18 (35%)	23 (31%)

Na: not applicable/not assessed.

^aOne woman had primary education (elementary school) only. Secondary education = high school diploma; tertiary education = college/university degree;

^bData missing for 1 pregnant patient; ^cIncluding spontaneous and elective abortions; ^dData missing for 3 pregnant patients; ^eFamily medicine or Internal medicine; ^fDental, Dermatology, Ear nose and throat, General surgery,

Ophthalmology, Orthopedic surgery, Psychiatry, Pulmonology.

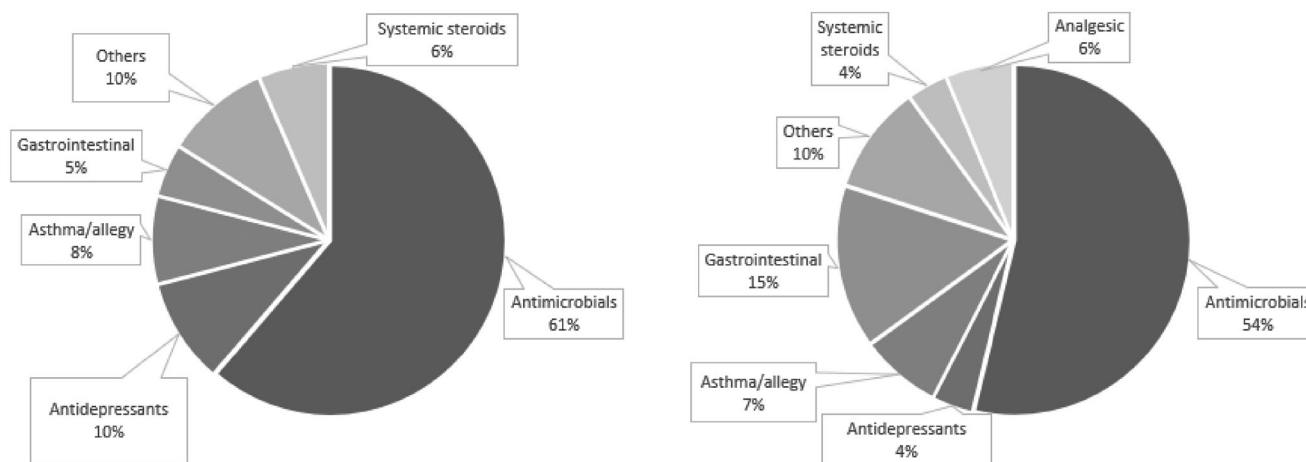


Figure 1. Distribution of medication classes among prescriptions to pregnant (left panel) and breastfeeding women (right panel).

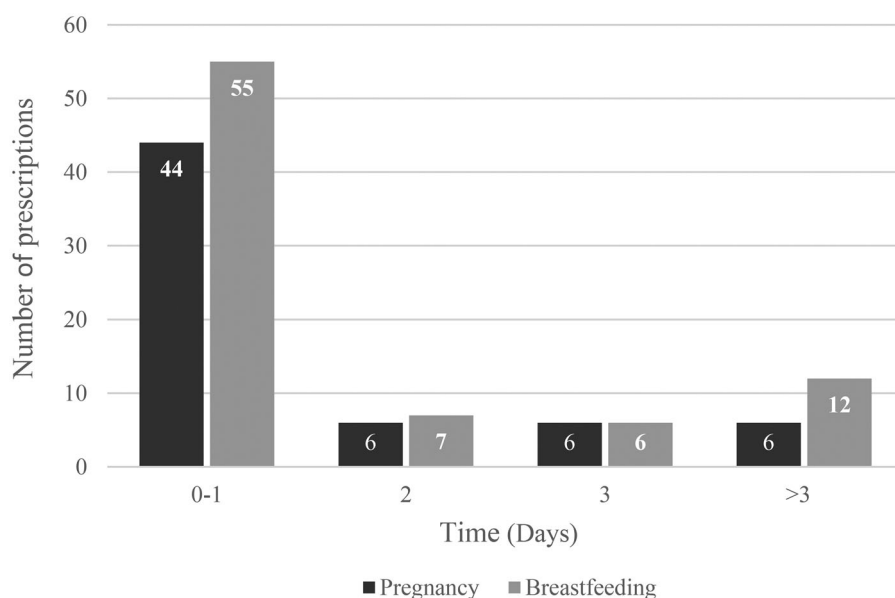


Figure 2. Time from prescription to IPIIC consultation by pregnant women (62 prescriptions) and breastfeeding women (80 prescriptions).

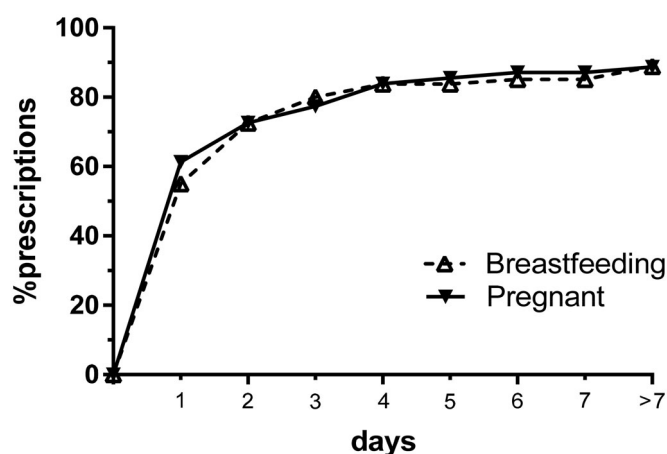


Figure 3. Time from prescription to drug use by pregnant women (62 prescriptions) and breastfeeding women (80 prescriptions).

compared to non-adherent patients (33% and 0%, respectively), and antidepressants/anxiolytics were more common among non-adherents (22%) than in non-adherent women (1%), but in *post-hoc* analyses these differences for individual medication subclasses were not statistically significant.

Asked about the reasons why they did not initiate the prescription medication, most non-adherent women cited safety concerns, even after the IPIIC consult advised that taking the medication was safe (at times with some qualifications, e.g., for the given stage of pregnancy and the planned dose regimen). Three breastfeeding women who had been advised by the IPIIC consultant to temporarily discontinue breastfeeding while taking the medication decided not to initiate the treatment in order to be able to continue breastfeeding. Others stated that they were no longer convinced that the treatment was necessary, sometimes since there was spontaneous improvement in their condition.

Provision of medication safety information

When asked whether the prescriber provided them with teratologic or breastfeeding medication safety information regarding their prescriptions, pregnant women reported that they received explicit and unequivocal information for 27 (50%) prescriptions, and breastfeeding women for 41 (55%) prescriptions. Moreover, for 12 (22%) prescriptions for pregnant women and 25 (33%) prescriptions for breastfeeding women, the patients reported not to have received any safety information. For 15 (28%) prescriptions for pregnant women and 9 (12%) for breastfeeding women, the patients stated that they received equivocal information by the prescriber.

Interruption of breastfeeding

Eight (11%) breastfeeding women stopped breastfeeding their babies, and 1(1%) reduced the breastfeeding frequency while taking the medication. Of those who stopped breastfeeding, 4 were advised to do so by their physician, two did not get any advice from the physician, one got equivocal advice, and for one the advice was not recorded. Only 1 of those 8 women were also advised to stop breastfeeding by the IPIIC consultant.

The prescriber advice, as recalled by the patient, regarding the safety of breastfeeding while taking the prescribed medication was often discordant from the IPIIC consultation. For 70 prescriptions with documented recommendations by both the IPIIC and the prescriber (as recalled by the patient), the advice regarding continuation of breastfeeding was concordant in 45 prescriptions (64%) and discordant in 25 (36%) prescriptions. For 11 of the 25 discordant recommendations, one party recommended interrupting breastfeeding while the other did not. For instance, 7 breastfeeding women (9%) receiving 9 prescriptions reported they were instructed by

Table 2. Bivariate analyses of variables associated with medication use by 59 pregnant women who received 62 prescriptions.

Variable	Prescribed and used (n = 55)	Prescribed and not used (n = 7)	p-value (Independent t-tests/Fisher's exact test)
Age (Years), Mean \pm SD	32.0 \pm 7.2	32.9 \pm 4.6	0.77
Age of pregnancy (weeks), Mean \pm SD	20.7 \pm 9.4	20.6 \pm 9.8	0.96
Numbers of pregnancies (including current), Mean \pm SD	3.1 \pm 2.1	3.1 \pm 0.9	0.97
Time from prescription to IPIC consultation (days)	1.3 \pm 2.6	0.9 \pm 1.2	0.69
Drug classes			
Antimicrobials	34 (62%)	4 (57%)	0.41
Systemic steroids	4 (7%)	0	
Antidepressants/anxiolytics	6 (11%)	0	
GI / anti-hemorrhoids	3 (6%)	0	
Asthma / allergy	4 (7%)	1 (14%)	
Other	4 (7%)	2 (29%)	
Tertiary Education	38 (69%)	5 (71%)	1.0
Previous abortion	17 (31%)	4 (57%)	0.21
Safety consult by prescribing physician ^a			
No consult	11 (23%)	1 (14%)	0.57
Equivocal recommendation	14 (30%)	1 (14%)	
Unequivocal recommendation	22 (47%)	5 (71%)	

^aData on provision of safety consult was missing for 8 prescriptions given to adherent women.

Table 3. Bivariate analyses of variables associated with medication use by 75 breastfeeding women who received 80 prescriptions.

Variable	Prescribed and used (N = 71)	Prescribed and not used (N = 9)	p-value (Independent t-tests/Fisher's exact test)
Age (Years)	31 \pm 4.6	32.4 \pm 4.3	0.61
Age of breastfed baby (months)	4.7 \pm 4.1	5.4 \pm 4.6	0.62
Drug classes			
Antimicrobials	40 (56%)	3 (33%)	0.036
Systemic steroids	3 (4%)	0	
Antidepressants/anxiolytics	1 (1%)	2 (22%)	
GI / anti-hemorrhoids	12 (17%)	0	
Asthma / allergy	5 (7%)	1 (11%)	
Analgesics	4 (6%)	1 (11%)	
Other	6 (9%)	2 (22%)	
Tertiary Education	59 (83%)	7 (78%)	0.65
Exclusive breastfeeding	33 (47%)	6 (67%)	0.31
Safety consult by prescribing physician ^a			
No consult	20 (30%)	5 (56%)	0.59
Equivocal recommendation	8 (12%)	1 (11%)	
Unequivocal recommendation	29 (44%)	3 (33%)	
Use medication and temporarily discontinue breast-feeding	9 (14%)	0	

^aData on provision of safety consult was missing for 5 prescriptions given to adherent women.

the prescriber to stop breastfeeding while using the medications (including *Helicobacter pylori* treatment [omeprazole, amoxicillin, clarithromycin], amoxicillin/clavulanic acid, azithromycin, prednisone, levofloxacin, and furosemide). Of those prescriptions, using the LactMed database as reference, only one (furosemide) was considered not compatible with breastfeeding of a neonate by the IPIC consultant. All others were advised by the IPIC to continue breastfeeding, sometimes with specific instructions for monitoring. For instance, for high doses of prednisone and levofloxacin, we recommended avoiding breastfeeding for the first few hours after the dosing [10]. Nonetheless, 3 of those 7 women stopped breastfeeding despite the IPIC consultant's reassurance.

Conversely, 5 women receiving 5 prescriptions were advised by the IPIC to stop breastfeeding if initiating the prescribed medications due to safety concerns or insufficient safety data. Only one of them recalled having been instructed by the prescriber to stop breast-feeding; 1 recalled receiving equivocal consult, and another 2 unequivocal reassurance, and one for one woman, lactation safety information provided by the prescriber was not recorded. Among these 5 women advised by the IPIC to interrupt

breastfeeding, two did not initiate the medication and continued breastfeeding, one stopped the medication that she had already initiated and continued breastfeeding, one initiated the medication and interrupted breastfeeding as advised, and only one continued breastfeeding against the IPIC recommendation while taking the medication (papaverine; the IPIC consultant advised against use during breastfeeding due to the lack of safety data).

Patient recall of IPIC consultation

When analyzing the recommendations given during the IPIC phone consultations, there was a high correlation between the recommendations recorded in the IPIC file with the recommendation understood and recalled by the study participants. In 91% of the women, the IPIC record and the patient-recalled IPIC recommendations were concordant. There were no cases in which IPIC said that the drug is unsafe and the women understood that it is safe to use. In 9%, the IPIC recommended to consider alternatives if possible, while the patient understood that the medication is safe, or vice versa. However, among the women who called

the IPIC TIS, 31% sought further reassurance through additional information sources (e.g. another TIS, internet websites, or pharmacist). This proportion was similar among adherent (30%) and non-adherent women (31%; $p = 1.0$).

Survey among postpartum women

We interviewed 49 postpartum women (median age, 32 years; interquartile range, 28–35 years). The distribution of religious affiliation (71% Jewish, 19% Muslim, and 10% Christian) was similar to that in Northern Israel, and 67% had tertiary education. For 10 women (20%), this had been the first pregnancy, 24 (49%) had 1 or 2 previous pregnancies, and 15 (31%) had more than 3 previous pregnancies. Eight (16%) recalled having taken prescription medications during their recent pregnancy, mainly a single antimicrobial medication. Only 15 (31%) were aware of TIS in Israel.

Discussion

In this study, we observed good adherence to prescription drug therapy among pregnant and breastfeeding women, with 89% of participants initiating the prescription medications, the majority of them within the first day after receiving the prescription. About two thirds of all prescriptions were for antimicrobial drugs, usually prescribed by a primary care physician. Only about half of the women reported receiving comprehensive drug safety information by the prescriber. Moreover, we found that only a minority of post-partum interviewees were aware of the teratology information services in Israel.

The rate of adherence in our study was higher than those previously reported. However, most previous studies evaluated the adherence to chronic treatments, reporting non-adherence to chronic medications for various conditions (cardiovascular, rheumatic and bowel disorders, asthma, diabetes, and epilepsy) ranging from 40 to 70% [11–15].

Less is known regarding adherence to medications for acute conditions, which represented the majority of prescriptions in our study. In a nationwide study from Denmark, the overall adherence to prescribed drugs during pregnancy was 43%, and was higher for chronic treatments: 100% for insulin-dependent diabetes mellitus, thyroid diseases, epilepsy, or hypertension, and 80% for depression, compared to 52% for antimicrobials and 59% for antihistamines [16]. Thus, the high adherence to medications for mostly acute conditions in our study was unexpected.

The high adherence in our cohort may reflect a selection bias resulting in a cohort that was not representative of pregnant or breastfeeding women in Israel: We recruited our study participants among women who initiated a telephone consultation with the IPIC and had received an in-depth consultation about the safety of their prescription medication during pregnancy or breastfeeding. The participants were therefore likely to be well-informed, motivated, and resourceful, which is likely to have improved adherence. This was also reflected by the demographic characteristics of our cohort: 68% of pregnant and 84% of breastfeeding women

had an academic degree, significantly higher than the average in the young adult population in Israel (46%) or in the OECD (42%) [17]. Moreover, almost all participants were Jewish (98.5%), although Jews comprise only 75% of the Israeli population. This may reflect a language barrier of the teratology and breastfeeding IPIC service, which does not provide consultations in the Arabic language. In non-Jewish segments of the Israeli population (mostly Arab Muslims and Christians, and Druze), fluency in Hebrew is not universal. The IPIC has therefore recently recruited more staff members who speak Arabic fluently.

Thus, the good adherence in our rather homogeneous and well-educated cohort is likely not to be representative of that in the general population of pregnant or breastfeeding Israeli women. In fact, our post-partum cohort, recruited among women hospitalized in the maternity ward, appeared more heterogeneous (30% non-Jewish).

Only about half of the prescriptions, the women reported receiving explicit and unequivocal information concerning drug safety by the prescriber. Even in these cases, the women contacted the IPIC to receive additional assurance about the safety of their prescription medication. Importantly, the women's perception was that the prescriber did not address at all the issue of medication safety in 33% of prescriptions for pregnant and 22% of prescriptions for breastfeeding women; the rest reported receiving equivocal advice or were referred to another physician or TIS. We cannot determine whether there were discrepancies between the prescribers' consultations and its perception by the patient. However, it appears that some physicians did issue a prescription to a pregnant or breastfeeding woman without verifying beforehand its safety for the fetus or the baby, and relied on the patient to do so. From the perspective of a concerned pregnant or breastfeeding mother, this prescriber behavior may increase anxiety and result in decreased adherence to therapy. Similarly, discordant recommendations from the prescriber and the TIS may be a source of doubt and anxiety, and may cause distrust in the health care system. For instance, despite of the reassurance by the TIS about the safety of breastfeeding during therapy, most women stopped breastfeeding if the prescriber – in their understanding – had previously recommended doing so.

In most cases where the prescriber provided unequivocal advice to discontinue breast-feeding during the medication course, the advice (as recalled by the women) was not competent. Fear of adverse medication effects on the nursing infant is a common cause of early breastfeeding cessation [18,19]. In fact, only few medications are contraindicated in breastfeeding mothers or associated with adverse effects on their infants. Thus, consultation by experts, for instance in the framework of TIS, or the use of reliable information sources such as LactMed [10], is essential.

The cohort of postpartum women surveyed about their knowledge of TIS differed in the distribution of religious affiliations from the women consulting the IPIC, and represented more closely the composition of the Israeli society in general and the population in Northern Israel in particular. Despite the existence of three TISs in Israel, one of which

(IPIC) provides service around the clock and 7 days a week, only about 31% of the post-partum women interviewed were aware of the existence of such services. On the other hand, a third of the women who called the IPIC TIS consulted additional information sources (e.g., another TIS, internet website or pharmacist), attesting to the enhanced need for reassurance in this anxious population.

Our study has some limitations. It was based on patient-reported data collected by a structured questionnaire, without access to medical records or prescription dispensing data. Thus, we could not verify the data accuracy and quality. We minimized recall bias by the short time lag between prescription and study interview. Moreover, patient understanding of the TIS recommendations were well correlated with the recorded TIS recommendation, giving credibility to the patient account. In addition, our cohort was rather small and did not allow subgroup and multivariate analyses.

Conclusions

In our study among pregnant or breastfeeding women seeking telephonic advice at our TIS, we observed high adherence to prescription medications, mostly antibiotics. Most patients reported that they did not receive adequate safety information by the prescriber, and if given, the recommendations were often inaccurate, emphasizing the importance of professional TISs. Moreover, many women were not aware of the existence of TIS. For optimal patient participation and medication adherence, in particular in the era of increasing patient empowerment, every patient, especially pregnant and breast-feeding women, should leave the physician's office feeling that all relevant issues were considered before issuing a prescription, while also being informed about the possibility to consult with specialized drug information services. Raising awareness of the importance of medication safety counseling during pregnancy and lactation among both physicians and patients may contribute to the quality of medical care of pregnant and breastfeeding women in Israel.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

- [1] Mitchell AA, Gilboa SM, Werler MM, et al. Medication use during pregnancy, with particular focus on prescription drugs: 1976–2008. *Am J Obstet Gynecol*. 2011;205(1):51.e1–51.e8.
- [2] Andrade SE, Gurwitz JH, Davis RL, et al. Prescription drug use in pregnancy. *Am J Obstet Gynecol*. 2004;191(2):398–407.
- [3] Bonari L, Koren G, Einarson TR, et al. Use of antidepressants by pregnant women: evaluation of perception of risk, efficacy of evidence based counseling and determinants of decision making. *Arch Womens Ment Health*. 2005;8(4):214–220.
- [4] Spiesser-Robelet L, Brunie V, de Andrade V, et al. Knowledge, representations, attitudes, and behaviors of women faced with taking medications while breastfeeding. *J Hum Lact*. 2017;33(1):98–114.
- [5] Baggeley A, Navioz Y, Maltepe C, et al. Determinants of women's decision making on whether to treat nausea and vomiting of pregnancy pharmacologically. *J Midwifery Womens Health*. 2004;49(4):350–354.
- [6] Naeye RL. Causes of the excessive rates of perinatal mortality and prematurity in pregnancies complicated by maternal urinary-tract infections. *N Engl J Med*. 1979;300(15):819–823.
- [7] Hartling L, Dryden DM, Guthrie A, et al. Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. *Ann Intern Med*. 2013;159(2):123–129.
- [8] Cooper ER, Charurat M, Mofenson L, et al. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr*. 2002;29(5):484–494.
- [9] Koren G, Pastuszak A. Prevention of unnecessary pregnancy terminations by counselling women on drug, chemical, and radiation exposure during the first trimester. *Teratology*. 1990;41(6):657–661.
- [10] Drugs and Lactation Database (LactMed). [cited 2019 Aug 18]. Available from: <https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>
- [11] Sawicki E, Stewart K, Wong S, et al. Medication use for chronic health conditions by pregnant women attending an Australian maternity hospital. *Aust NZ J Obstet Gynaecol*. 2011;51(4):333–338.
- [12] Lupattelli A, Spigset O, Nordeng H. Adherence to medication for chronic disorders during pregnancy: results from a multinational study. *Int J Clin Pharm*. 2014;36(1):145–153.
- [13] Gallinger ZR, Rumman A, Nguyen GC. Perceptions and attitudes towards medication adherence during pregnancy in inflammatory bowel disease. *J Crohns Colitis*. 2016;10(8):892–897.
- [14] Murphy VE, Gibson PG, Talbot PI, et al. Asthma self-management skills and the use of asthma education during pregnancy. *Eur Respir J*. 2005;26(3):435–441.
- [15] Bennett IM, Marcus SC, Palmer SC, et al. Pregnancy-related discontinuation of antidepressants and depression care visits among Medicaid recipients. *PS*. 2010;61(4):386–391.
- [16] Olesen C, Søndergaard C, Thrane N, et al. Do pregnant women report use of dispensed medications? *Epidemiology*. 2001;12(5):497–501.
- [17] OECD. 2016. Education at a glance 2016: OECD indicators. Paris: OECD Publishing; [cited 2019 Aug 18]. Available from: <http://dx.doi.org/10.187/eag-2016-en>.
- [18] Acevedo M, Pretini J, Micelli M, et al. Breastfeeding initiation, duration, and reasons for weaning in patients with systemic lupus erythematosus. *Rheumatol Int*. 2017;37(7):1183–1186.
- [19] Odom EC, Li R, Scanlon KS, et al. Reasons for earlier than desired cessation of breastfeeding. *Pediatrics*. 2013;131(3):e726–e732.