The concordance between self-reported medication use and pharmacy records in pregnant women

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ABSTRACT

Background and objectives: Several studies have been conducted to assess determinants affecting the performance or accuracy of self-reports. These studies are often not focused on pregnant women or medical records were used as a data source where it is unclear if medications have been dispensed. Therefore, our objective was to evaluate the concordance between self-reported medication data and pharmacy records among pregnant women, and its determinants.

Methods: We conducted a population-based cohort study within the Generation R study, in 2,293 pregnant women. The concordance between self-reported medication data and pharmacy records was calculated for different therapeutic classes using Yule's Y. We evaluated a number of variables as determinant of discordance between both sources through univariate and multivariate logistic regression analysis.

Results: The concordance between self-reports and pharmacy records was moderate to good for medications used for chronic conditions, such as selective serotonin reuptake inhibitors or anti-asthmatic medications (0.88 and 0.79, respectively). Medications that are used occasionally, such as antibiotics, had a lower concordance (0.51). Women with a Turkish or other non-western background were more likely to demonstrate discordance between pharmacy records and self-reported data, compared to women with a Dutch background (OR Turkish: 1.63, 95%CI: 1.16-2.29); OR other non-western: 1.33, 95%CI:1.03-1.71).

Conclusions: Further research is needed to assess how the cultural or ethnic differences may affect the concordance or discordance between both medication sources. The results of this study showed that the use of multiple sources is needed to have a good estimation of the medication use during pregnancy.

INTRODUCTION

Maternal medication use has increased over the past years with approximately 80% of women receiving at least one prescription medication during pregnancy [22, 23]. Knowledge about the medications used during pregnancy is crucial as it may affect the birth outcome. The risk of adverse perinatal outcomes or birth defects from medication exposure is often evaluated in observational studies, as pregnant women are often not enrolled in clinical trials. These studies mostly rely on exposure data collected by a self-reporting tool, as pharmacy records are often not available [24-26]. Self-reported data are considered to be an important source of information as it may also include over-the-counter medication data, which is not consequently registered in the pharmacy. However, patient self-reported data can be subject to errors caused by recall bias or social desirability bias, awareness and knowledge [27, 28]. Researchers of a previous study found that only 43% of the dispensed prescription medications were reported as actually used by pregnant women, but the factors that may have influenced this are not clear [29]. Another study showed that pregnant women may be more likely to recall and report medication use, because of their increased awareness of potential teratogenic effects of certain medications [30]. This may be different for women from ethnic minority groups as the literature shows that Hispanic and black women are less likely to seek for information about their health on the internet, but also cultural differences and language barriers may play a role [31, 32]. Other factors that may influence the accuracy of recalling the prescribed medications include age, educational level, alcohol use and general health [28, 33-35].
Currently, there is no 'golden standard' to assess maternal medication exposure, as each source is prone to bias, which may lead to misclassification of exposure. A number of studies have been conducted to assess the determinants that may affect the performance or accuracy of self-reports. However, these studies are often not focused on pregnant women in particular or the concordance is calculated with medical records and health insurance databases where it is not clear if medications have been dispensed [36-39]. Although pharmacy dispensations do not reflect patient compliance, a high medication possession ratio in case of chronic use is a good proxy indicator of compliance. Moreover, pharmacy records are not affected by patient recall. Therefore, pharmacy records can be used as an indicator of the validity of self-reported medication data.

In this study, we used self-reported data and pharmacy records collected from a population based cohort study in pregnant women to evaluate the concordance of medication use between self-reported data and pharmacy records for different therapeutic classes among pregnant women, and its determinants.

METHODS

Study population

This study was conducted within the Generation R study, a population-based prospective birth cohort in Rotterdam, the Netherlands [40]. The cohort included 9,778 mothers and their children who were born between April 2002 and January 2006. Of these mothers, 8,880 (91%) were enrolled in the study during pregnancy and 898 (9%) at birth of their child. Mothers were selected based on the availability of pharmacy records in our database. Dispensing records were obtained from pharmacies after permission to contact their pharmacy was given, which was obtained for the large majority (n=4,930). Furthermore, women with either no pharmacy records or self-reported data of the studied therapeutic classes were excluded (n=2,293). The flowchart for women included in the current study (n=2,637) is shown in Figure 1. The Generation R study was approved by the Medical Ethics Committee of the Erasmus Medical Centre, Rotterdam. Written informed consent was obtained from all parent-participants.

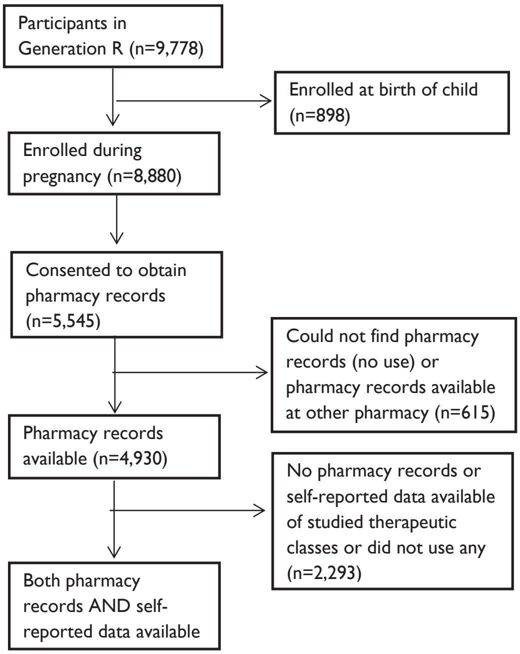

Figure 1. *Selection of mothers with both pharmacy records and self-report data available. The Generation R Study.*

Pharmacy records

All printed pharmacy records were stored and for each research hypothesis, the relevant drugs from each record were entered manually into an automated database. The following therapeutic classes were available electronically: Selective Serotonin Reuptake Inhibitors (SS-

RIs), benzodiazepines, folic acid, antibiotics, anti-asthmatics, antihistamines and non-steroidal anti-inflammatory drugs (NSAIDs), as used in earlier studies [41-45]. The medications were limited to 'prescription-only' medications, but folic acid and antihistamines were also included as these medications were relatively more often recorded at pharmacies compared to other medications which can also be obtained 'over-the-counter' (e.g. NSAIDs).Therefore, we did not include NSAIDs in our study. Details of dispensing date, product, number of units, daily prescribed number and strength were all available. Use of medication from other therapeutic classes was considered as 'no medication use' in our study as we focused on these six prescribed therapeutic classes.

Self-reported maternal medication use

Data on maternal medication use was collected using self-reported questionnaires that were sent by post to the mothers at each trimester: early pregnancy (gestational age < 18 weeks), mid-pregnancy (gestational age 18-25 weeks) and late pregnancy (gestational age >25 weeks). In the first trimester, we asked them to fill in the medicines that they had taken in the preceding six months. In the second and third trimester we asked which medications they had used in the preceding three months [40]. The questionnaires were available in Dutch (also comprehensible for Surinamese women), English and Turkish. If needed, women with a Moroccan ethnicity were assisted in the filling out of the questionnaires by Moroccan speaking research assistants.

Socioeconomic determinants

Other factors including maternal age at intake, alcohol use, smoking, ethnicity, education level, marital status and household income were also obtained using these questionnaires. Ethnicity of participating mothers was defined according to the classification of Statistics Netherlands [46]. All lifestyle and medication related questions included the question as to whether they were exposed to these factors before and/or during pregnancy to assess the period of exposure.

Statistical analysis

The concordance between self-reported medication data and pharmacy record data was calculated for different therapeutic classes using Yule's Y. This is a measure of agreement for dichotomous variables and is less dependent on the prevalence than kappa [47]. It has the same possible range of values as kappa (-1 to 1) and are interpreted as follows: <0 no agreement; 0.01-0.20 slight agreement; 0.21-0.40 fair agreement; 0.41-0.60 moderate agreement; 0.61-0.80 substantial agreement and 0.81-0.99 almost perfect agreement [48]. In addition, we calculated the sensitivity and specificity for self-reported medication use compared to pharmacy data. We calculated the Odds Ratio (OR), with 95% CI, as the chance of having discordance between self-reported data and pharmacy record data (presence pharmacy record/absence self-report or absence pharmacy record/ presence self-report). We evaluated the following variables as determinant of discordance (yes/no) between both sources through univariate logistic regression analysis: maternal age at intake, alcohol use and smoking during pregnancy, ethnicity, maternal education, marital status, net household income and the number of prior pregnancies. In addition, a multivariate analysis was performed. On average, 15.6% of data across these variables was missing. To avoid the bias of complete case analysis, we accounted for missing information on these determinants (data of self-reports and prescription records were not imputed) by using multiple imputation methods (n= 10 imputations). Results were considered statistically significant at $p < 0.05$. Finally, in a non-response analysis, we investigated whether any of the determinants was associated with non-response. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

RESULTS

Characteristics of the study population

A total of 2,637 women used medication during pregnancy according to their pharmacy records, self-reported data or both (Table 1). Mean maternal age was 29.8 years and the majority of the group never smoked during pregnancy (73.4%) or used alcohol while pregnant (48.3%). Furthermore, half of the study population was Dutch (50.5%) and only a small proportion of these women had a low educational level (5.2%). In addition, only a small percentage of the study population did not have a partner (16%) and almost half of these women were married (47.9%). The proportion of women with an average income (€900-€2200) was the same as the proportion of women with a high income (>€2200, 44.8%) and for the majority of women it was their first pregnancy.

Yule's Y, sensitivity and specificity

Table 2 shows the concordance between self-reported data and pharmacy records for different therapeutic classes. Among all classes reported, SSRIs showed the highest rate of concordance (0.88), whereas folic acid had the lowest concordance (0.48). Benzodiazepines, anti-asthmatics and antihistamines showed a substantial concordance (0.79; 0.68 and 0.61 respectively) and for antibiotics, the concordance was considered moderate (0.51). Overall, the specificity levels among these therapeutic classes are considered to be high (>90%), with the exception of antibiotics (83.9%). The sensitivity levels on the other hand, showed some greater differences among the different therapeutic classes. The sensitivity of SSRIs, benzodiazepines, antibiotics and anti-asthmatics ranged from 60.7% to 74.3%, indicating a moderate sensitivity. For the other therapeutic classes the sensitivity was somewhat lower (folic acid:36.4% and antihistamines:40.6%).

Table 1 *Characteristics of the mothers included in our study*

Characteristic	Mothers included in the study (n=2,637)
Age in years, mean (SD)	29.8 (5.2)
Alcohol use	
Never during pregnancy	48.3
Until pregnancy was known	13.9
Continued during pregnancy	37.8
Smoking	
Never during pregnancy	73.4
Until pregnancy was known	9.0
Continued during pregnancy	17.6
Ethnicity	
Dutch	50.5
Turkish	9.4
Surinamese	8.9
Moroccan	6.8
Other western	16.3
Other non-western	8.0
Maternal education [a]	
Primary education	5.2
Secondary education	46.8
Higher education	48.0
Marital status	
Married	47.9
Living together	36.1
No partner	16.0
Net household income	
<€900	10.4
€900-2200	44.8
>€2200	44.8
Number of prior pregnancies	
0	56.0
1	29.2
2 or more	14.8

All numbers are given in percentages or mean (SD). [a] *Highest education followed. Abbreviations: n; number of women, SD; standard deviation*

***Table 2** Concordance between self-reported data and pharmacy record data of maternal medication use, by therapeutic class (n=2637)*

Therapeutic class	Yule's Y [a]	FN rate, %	FP rate, %	Sensitivity [b], %	Specificity [b], %
SSRIs	0.88	33.3	0.8	66.7	99.2
Benzodiazepines	0.79	39.3	2.2	60.7	97.8
Folic acid	0.48	63.6	6.4	36.4	93.6
Antibiotics	0.51	34.9	16.1	65.1	83.9
Anti-asthmatics	0.68	25.7	9.5	74.3	90.5
Antihistamines	0.61	59.4	3.7	40.6	96.3

[a] Calculated using the following formula: Y=(√ad- √bc)/(√ad+√bc), a=pharmacy and self-report; b=only self-report; c=only pharmacy record; d=no pharmacy record and self-report. [b] Sensitivity and specificity of self-reported medication use compared to pharmacy records. Abbreviations: FN; false negatives, FP; false positives, n; number of women, SSRI; Selective Serotonin Reuptake Inhibitors

Factors associated with discordance between self-reported data and pharmacy records

Table 3 shows the results of the univariate analysis where discordance between both sources is associated with an age of 24 years and younger (OR:1.40, 95%CI: 1.05-1.85), a non-Western background (OR Turkish:1.91, 95%CI: 1.44-2.54; OR Surinamese:1.52, 95% CI: 1.13-2.04; OR Moroccan:1.66, 95%CI: 1.20-2.30 and OR other non-Western:1.49, 95%CI: 1.18-1.88), a lower education (OR primary:1.53, 95%CI: 1.05-2.21 and OR secondary:1.43, 95%CI: 1.20-1.70), a lower net household income (OR <€900:1.64, 95%CI: 1.19-2.25) and having two or more prior pregnancies (OR:1.34, 95%CI: 1.06-1.70). The results of the multivariate analysis only shows a significant association with a Turkish background (OR:1.63, 95%CI: 1.16-2.29), another non-western background (OR: 1.33, 95%CI:1.03-1.71) and having one or more prior pregnancies (OR 1 prior pregnancy:1.22, 95%CI: 1.00-1.49 and OR 2 or more prior pregnancies:1.32, 95%CI: 1.00-1.74).

***Table 3** Determinants that are associated with discordance between self-reported data and pharmacy records (n=2,637)*

		Univariate analysis		**Multivariate analysis**	
Characteristic	N (%)	OR	95% CI	OR	95% CI
Age				0.98	0.96-1.00
<25 years	533 (20.2)	1.40	1.05-1.85	-	
25-35 years	1711 (64.9)	1.01	0.79-1.29	-	
>35 years	393 (14.9)	1 (ref)		-	
Alcohol					
Never during pregnancy	1279 (48.5)	1 (ref)		-	
Until pregnancy was known	359 (13.6)	0.80	0.61-1.03	0.99	0.75-1.31
Continued during pregnancy	1001 (37.9)	0.76	0.63-0.91	1.00	0.81-1.23

Table 3 *Determinants that are associated with discordance between self-reported data and pharmacy records (n=2,637)* (*continued*)

		Univariate analysis		**Multivariate analysis**	
Smoking					
Never during pregnancy	1939 (73.5)	1 (ref)		-	
Until pregnancy was known	234 (8.9)	0.78	0.57-1.07	0.79	0.57-1.10
Continued during pregnancy	465 (17.6)	1.11	0.89-1.38	1.01	0.80-1.29
Ethnicity					
Dutch	1332 (50.5)	1 (ref)		-	
Turkish	249 (9.4)	1.91	1.44-2.54	1.63	1.16-2.29
Surinamese	236 (8.9)	1.52	1.13-2.04	1.30	0.94-1.79
Moroccan	180 (6.8)	1.66	1.20-2.30	1.38	0.94-2.01
Other non-western	429 (16.3)	1.49	1.18-1.88	1.33	1.03-1.71
Other western	212 (8.0)	0.59	0.41-0.86	0.58	0.39-0.84
Maternal education [a]					
Primary education	152 (5.8)	1.53	1.05-2.21	0.96	0.63-1.46
Secondary education	1207 (45.8)	1.43	1.20-1.70	1.10	0.88-1.36
Higher education	1280 (48.5)	1 (ref)		-	
Marital status					
Married	1268 (48.1)	1 (ref)		-	
Living together	948 (35.9)	0.82	0.68-0.99	0.98	0.79-1.20
No partner	422 (16.0)	1.17	0.92-1.47	1.03	0.77-1.38
Net household income					
<€900	414 (15.7)	1.64	1.19-2.25	1.21	0.84-1.73
€900-2200	864 (32.8)	1.16	0.90-1.49	0.93	0.72-1.21
>€2200	1360 (51.6)	1 (ref)		-	
Number of prior pregnancies					
0	1479 (56.1)	1 (ref)		-	
1	768 (29.1)	1.19	0.99-1.44	1.22	1.00-1.49
2 or more	391 (14.8)	1.34	1.06-1.70	1.32	1.00-1.74

[a]*Highest education followed. Abbreviations: CI; confidence interval, n; number of women , OR; odds ratio, P; p-value*

DISCUSSION

Pharmacy records are often used as the source of medication exposure information [49-51]. However, not all medications are dispensed through pharmacies and therefore, questionnaire data are also an important source of information. In this study, we compared the self-reported information on prescribed medication use during pregnancy with the presence of medication use in pharmacy records for different therapeutic classes of medications. In addition, we evaluated the potential factors that are associated with discordance between self-reported medication use and pharmacy records.

Overall, we found that medications required for managing chronic conditions (SSRIs and anti-asthmatics) had a good or substantial concordance between maternal self-reports and pharmacy records. This finding is in line with the results of another study where the authors compared self-reports with prescription data in medical records [52]. However, a higher concordance for benzodiazepines was observed in our study compared to the results of a study in older adults (0.58), which can be explained by age as studies have shown that older people are less likely to recall their medication use [38, 53]. Medications taken for acute conditions (antibiotics, folic acid, antihistamines) had a substantial to moderate concordance. Sarangarm et al. observed similar results for the concordance of antibiotics, but for folic acid and antihistamines we found a lower concordance in the available literature [37, 52, 53]. This can be explained by recall bias, which is less likely to occur in chronic medication than in acute medication use [29, 54]. Furthermore, the number of drugs that were used during pregnancy may also contribute to discordance between both sources. However, we were not able to study this as the number of women who used more than one drug during their pregnancy was very small (n=97). Another possible explanation of the low concordance of folic acid and antihistamines is that these medications are available over the counter. Therefore, the use of these medications is not always captured in the pharmacy databases and thus contributing to discrepancy between both sources.

The sociodemographic and economic characteristics may have influenced the probability of concordance. In our study, the number of prior pregnancies was associated with discordance between both medication sources, which is not in line with a previous study [37]. The group of women with no prior pregnancies was larger (57.1%) compared to those who had 1 to 2 (28.6%) or more prior pregnancies (14.3%) when it comes to 'not reporting' medication use. However, the number of women who did not report medication use in the concerning study was quite low (n=7) which may explain these differences compared to our study. Furthermore, the concordance was lower in women with a Turkish and other non-western background. The ethnic differences between self-reported data and data based on medical records from general practitioners has been examined in a previous study by Uiters E. et al [39]. They report that the level of concordance did not differ between the ethnic groups, implying that the validity of self-reported data and medical records did not differ among different ethnic groups. However, another study, based on data from a survey and health insurance register, found lower concordance rates on health care utilization (including prescription medication) for immigrants [55]. This finding is in line with the current results, where women with a non-western background were more likely to have a discordance between self-reported and pharmacy data. Other studies showed that adherence to medication may be lower in the ethnic minority groups, which means that the prescribed medications are not always taken by these patients [56-58]. Non-adherence and lack of persistence should therefore also be taken into consideration.

Moreover, the question remains as to how much this discordance between self-reported data and pharmacy data is due to cultural or religious factors as they may have different beliefs about the use of medication during pregnancy. Finally, a possible explanation is that ethnic minorities may face language barriers as Dutch is not their native language and potentially did not understand all questions. However, the questionnaires in our study were also available in Turkish, which means that language barrier should not have hampered these women completing the questionnaires. Further research is needed to assess how the cultural or ethnic differences may affect the concordance or discordance between both medication sources.

Strengths and Limitations

One of the strengths of this study is that maternal medication use was determined based on pharmacy record data, which is more accurate than prescribed medication according to medical records, because medication can be prescribed but never collected from pharmacies [59]. Furthermore, our study population comprises almost 50% of women with a non-Dutch ethnic background, thus we were able to study the patterns of concordance among women with different ethnic backgrounds. Despite the strengths of our study, we also had some limitations. First, the period of recall was three months, which can be considered as long. Therefore, it is likely that women do not recall all medications that have been used in that period. However, we believe that pregnant women are more likely to remember what they have used as they may be more aware of the risks and safety of medication use during pregnancy [30, 60]. Second, the time frames of pharmacy records and self-reported data did not perfectly overlap for all participants as there was no possibility to fill out the exact dates of use in the questionnaire. Participants who were enrolled in the study during the third trimester of pregnancy may have used medications in the first trimester and discontinued medication use during the third trimester of pregnancy. Therefore, these women may not have reported use of medications during pregnancy. However, given that the specificity is high for all therapeutic classes and the proportion of women enrolled at this stage was low (~10%), this scenario is unlikely. Third, the majority of our study population was highly educated, which may have affected our results in terms of external validity, showing higher concordance rates compared to the general population. However, in our study we were not able to see a significant association between maternal education and discordance. Finally, for a large number of women information on medication use of both sources was not available, which may increase the likelihood that these women did not complete the questionnaire or did not give consent to obtain pharmacy records for certain reasons that are related to the demographic and socio economic factors. The results of the non-response analyses did not show significant differences between both groups for ethnicity, net household income, number of prior pregnancies, smoking and alcohol. However, for marital status (p-value:0.03) and education (p-value:<0.001) we did see some differences between both groups. Despite these differences, we did observe similar results in our study compared to the existing literature showing an association between marital status and education as determinants and discordance between both sources [37, 55, 61, 62]. There is also a possibility that the pharmacy records were not available, because the medication was dispensed at another pharmacy. Furthermore, some mothers did not receive one or more questionnaires due to a variety of logistical reasons and were therefore not able to complete the questionnaires [40]. These data are missing completely at random and therefore it does not influence our results.

Conclusion

In conclusion, the results of our study indicate that the concordance between self-reports and pharmacy records was moderate to good for medications used for chronic conditions, such as antidepressants or anti-asthmatic medications. Medications that are used occasionally, such as antibiotics had a lower concordance. The concordance could be explained by the accuracy of recall, which may be influenced by factors such as the level of education and prior pregnancies. Furthermore, as some of the investigated medications (e.g. folic acid) are also available over the counter, the pharmacy records may represent a selection and this may also influence the concordance and should be taken into account. Finally, we found that ethnic background may play a role in self-reporting the use of medications. Different cultural beliefs about medication use during pregnancy, non-adherence and lack of persistence may be an explanation of the observed discrepancy among the different ethnic groups. Further research is needed to assess how the cultural or ethnic differences may affect the concordance or discordance between both medication sources. The results of this study showed that the use of multiple sources on medication use is needed to have a good estimation of the medication use during pregnancy.