Title:

Accuracy of information on medication use and adverse drug reactions recorded in pregnancy handheld records

Short Title:

Medication Use and Pregnancy Handheld Records

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Abstract

Background: Pregnancy handheld records (PHR) are a personally controlled health record utilised in the promotion of continuity of care across pregnancy by providing a single resource for the recording of pregnancy related health information.

Aims: To determine the accuracy of the PHR in relation to information on medications and adverse drug reactions (ADRs) and to examine the frequency and nature of any identified discrepancies.

Method: A 12 week prospective clinical audit of 300 women admitted to either the antenatal or postnatal ward at a tertiary level maternity hospital. A detailed medication history was completed for each woman by a pharmacist, with women interviewed about medication use prior to and during their pregnancy as well as any ADRs. The medication history and PHR were compared to identify discrepancies.

Results: Medication discrepancies were extremely common, with 254 (84.7%; 95% CI 80.6-88.8%) women having at least one or more medication related discrepancy involving 686 (55%; 95% CI 52.2–57.8%) prescription and non-prescription medications. Most common reasons for prescription medication discrepancies included the medication details being incomplete (44%), missing (29%), or incorrect (17%). ADR and allergy discrepancies were also common, identified among 59 (20%; 95% CI 15.5-24.5%) women.

Conclusions: The PHR is of low accuracy in relation to the recording of medications and ADRs. This warrants further research to examine the impact of these discrepancies on patient care and outcomes. The identification of strategies for improving the recording of information on medications and ADRs in the PHR are also required.

Manuscript Text

Background

The pregnancy handheld record (PHR) was developed to support collaboration and co-ordination of treatment efforts across the healthcare team.[1, 2] During antenatal visits healthcare providers complete relevant information in the PHR pertinent to patient care during pregnancy and birth, with an aim to increase health professional communication and reduce clinical errors.[3]

While the PHR format varies across settings, the amount of space and prominence provided to recording information on medications and ADRs is less than ideal. This is despite medication use during pregnancy being extremely common, with recent studies reporting that eight out of ten women use at least one medication during pregnancy.[4, 5] Coupled with this is the fact that chronic medical conditions are common during pregnancy, with a recent Australian study reporting that 39.3% of surveyed pregnant women had at least one medical condition and 26.5% of them were taking medications for those conditions.[5] This is in addition to the knowledge that pregnancy not only has a unique effect on decisions relating to medication use, largely due to concerns regarding medication safety, but can also influence medication pharmacokinetics and therefore alter treatment efficacy or toxicity.[6] Further complicating this is that evidence regarding medication use in pregnancy is often lacking, contradictory or difficult to interpret and apply to clinical practice.[7, 8]

While a number of studies have examined the broad benefits of using a PHR, no specific studies have assessed the accuracy of a PHR in areas such as information recorded on medication use and ADRs. Therefore, the aim of this study was to determine the accuracy of the PHR in relation to information on medications and ADRs and examine the frequency and nature of any identified discrepancies.

Method

Prospective clinical audit of antenatal and postnatal women admitted to Flinders Medical Centre (FMC), South Australia, between 1 April and 23 June 2014. Each year, approximately 3,000 births occur at FMC, a university-affiliated tertiary level teaching hospital, which has a 14 bed antenatal ward and 18 bed postnatal ward. Ethics approval was obtained from the Southern Adelaide Local Health Network Ethics Committee (HREC/14/SAC/48).

Inclusion/Exclusion Criteria

As the study was dependant on a detailed medication history interview being undertaken by a pharmacist, only women who could be seen during standard clinical pharmacy working hours *(Monday to Friday – 0845 to 1700)* were eligible. Women were not included in the study in situations where a language barrier was present and no interpreter was available, or in sensitive situations where the treating midwife deemed it inappropriate to enter the woman's room at that point in time.

Data collection

In accordance with the routine clinical pharmacy service provided within the hospital, each woman underwent a detailed medication history interview with a pharmacist. The medication history interview was undertaken using a structured medication history taking instrument developed specifically for this study. The instrument consisted of two main parts including medications and allergies or ADRs. Women were asked to specify all use of prescription or non-prescription medications prior to and during their pregnancy with information recorded on: commencement and cessation dates, medication name, strength, dose, form, route, administration schedule, and the indication for use. Prescription medications were defined as medications only available by prescription from a doctor, while non-prescription medications were defined as medications available without a prescription from a community pharmacy or alternative location (e.g. supermarket or health food store). Non-prescription medicines

included the use of complementary medicines, including herbal and dietary supplements. While some medications may be available both with and without a prescription (e.g. paracetamol, Non-steroidal anti-inflammatory drugs [NSAIDs], folic acid, iron supplements), these were classified as non-prescription medicines for the purposes of this study. Initiation of medications or allergies or ADRs experienced during the woman's current hospital admission were not included in the study, as these would not have been routinely recorded in the PHR. Women were also asked about any allergies or ADRs, with data collected on the medication involved (or other trigger), reaction type, reaction date, and whether this has subsequently been confirmed through allergy testing. Allergies were defined as non-medication related reactions, for example food allergies, whereas ADRs were defined as adverse reactions to medications.

Demographic information including employment status, age, height, weight, medical conditions and ethnicity, obstetric history, and obstetric complications, were collected based on data recorded in the medical records.

For the purpose of identifying discrepancies, the pharmacist completed medication history was classified as the 'gold standard' and used as a point of comparison with the PHR. Any discrepancies that were identified by the pharmacist in the PHR were subsequently recorded. Discrepancies identified were categorised as prescription or non-prescription discrepancies and categorised into four groups (**Table 1**). ADRs were categorised using a similar concept, however they were only categorised into three different groups (**Table 1**). All medications were categorised according to the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) Classification System.

Sample Size Calculation

In the absence of previous literature, anecdotal evidence was used to hypothesise a 70% level of accuracy of information of medication use recorded in PHR; that is for 7 out of 10 women

the PHR would correctly identify medication use during pregnancy. To estimate the prevalence within 5 percentage points of the true value (65-75%) with 95% confidence, a sample size of approximately 300 participants was required.

Statistical Analysis

Differences were examined using a Chi-squared test for nominal variables and Chi-squared test for trend for ordinal variables. Analyses were undertaken using Statistical Package for Social Sciences (SPSS) version 22.0, with a p-value < 0.05 considered statistically significant.

Results

A total of 300 women were included in the study, with 29 (10%) being antenatal and 271 (90%) postnatal. Mean age and BMI was 30 years (±6 SD) and 28 kg/m^2 (±7 SD) respectively. The majority of women were of Caucasian ethnicity (n=258: 87%), non-smokers (n=266: 89%), and currently employed (n=202: 68%). Pre-existing medical conditions were reported for 149 (50%) women and included conditions such as asthma (n=72; 24%), anxiety or depression (n=65; 22%), thyroid disorder (n=13; 4%), neurological disorder (n=9; 3%), polycystic ovary syndrome (n=8; 3%) gastrointestinal disorder (n=4; 1%), Type 1 or Type 2 diabetes (n=4; 1%), and hypertension (n=4; 1%). Obstetric complications were recorded for 107 (36%) women and included gestational diabetes (n=44; 15%), pregnancy induced hypertensive disorders (n=26; 9.0%), gestational thrombocytopaenia (n=4; 1%), and gestational hypothyroidism (n=4; 1%).

Use of prescription and non-prescription medications was extremely common during pregnancy, with a total of 276 prescription and 972 non-prescription medications reported by a total of 297 (99%) women. A total of 145 women (48%) used at least one prescription medication during pregnancy, while 296 women (99%) used at least one non-prescription medication. The most commonly used prescription and non-prescription medications included

those in the alimentary tract and metabolism (n=667), blood and blood forming organs (n=189) and nervous system (n=125) ATC categories (Appendix 1). Of all medications that were reported, 971 (78%) were initiated during pregnancy and over half of these medications (55%) were used on a regular basis. Of the 277 medications (22%) initiated prior to pregnancy, 207 (75%) were used intermittently whilst a further 70 (25%) medications were used regularly. ADRs and allergies were reported in 115 women (38%), with a total of 153 ADRs and 64 allergies identified. It was found that 91 women (30%) reported at least one ADR, whilst another 45 women (15%) reported at least one allergy.

Medication discrepancies were prevalent, with a total of 686 (55.0%; 95%CI 52.2–57.8%) non-prescription and prescription medication discrepancies. A total of 254 (84.7% 95%CI 80.6-88.8%) women had a least one discrepancy in their PHR, and of these, 177 women (70.0%; 95%CI 64.4-75.7%) had two or more discrepancies. A total of 87 (29%) women had at least one prescription discrepancy recorded in their PHR, with 132 of 276 (48%) prescription medications associated with a discrepancy. In contrast, a total of 240 (81%) women were found to have at least one non-prescription discrepancy, with 554 of 972 (57%) non-prescription medications associated with a discrepancy. The majority of women were more likely to have two or more non-prescription discrepancies in their PHR (62%). The difference between the proportion of prescription and non-prescription discrepancies was found to be statistically significant (*P-value* <0.001).

Of the discrepancies that were identified, the majority of prescription medication discrepancies were likely to be incomplete (44%) and missing (29%), whereas for non-prescription medication discrepancies, 302 (55%) were missing and 166 (30%) were incomplete (**Figure 1**).

The most common prescription medications with discrepancies were medications for alimentary tract and metabolism (n=46), which includes medications such as insulin and metoclopramide (Appendix 1). The next most common discrepancies were found with respiratory medications such as those for asthma (n=18), as well as medications for the nervous system including anti-epileptics, anti-psychotics and anti-depressants (n=18). The most common non-prescription medications that contained discrepancies involved medications for alimentary tract and metabolism (n=283) such as pregnancy multivitamins and vitamin D, as well as medications for blood and blood forming organs (n=111) which includes iron preparations.

For women reporting 1, 2, 3, or ≥4 medications, a significant trend was observed in relation to an increasing proportion of a medication discrepancy being identified (25%, 71%, 90%, and 97% respectively; $p<0.0001$).

Of the women who reported an ADR or allergy, a total of 59 (51%; 95% CI 41.8-60.0%) were identified as having a discrepancy, which accounted for 101 discrepancies in total. The majority of these discrepancies were associated with ADRs (58; 57%). Of the women who had a discrepancy, 65% had one discrepancy and 35% having two or more discrepancies. For both ADRs and allergies, the most common discrepancy type was "missing" (66% and 72% respectively) (**Figure 1**).

Discussion

These findings demonstrate that discrepancies related to medication use and ADRs are common in PHRs, with the potential to contribute towards prescribing errors and patient harm.

While no previous studies have examined the accuracy of the PHR when it comes to medication use and ADRs, the reported prevalence of medication discrepancies is similar to that reported in previous studies undertaken within other clinical areas, where medication discrepancies were identified in up to 70% of patients at hospital admission or discharge.[9-13]

The strongest factor associated with the likelihood of a medication discrepancy appeared to be the number of medications reported in the interview. One potential explanation for this is that the fact that the amount of space for medications in the PHR is small and therefore does not allow enough room for all medications to be recorded, or for medications to be accurately recorded with sufficient detail.

Non-prescription medication discrepancies were more common than prescription medication discrepancies. This could be explained by the fact that patients under-report their use of non-prescription medications, with a previous study showing that 53.2% of patients did not report non-prescription medication use to their general practitioner.[15] Another study suggested that women use complementary medicines to avoid taking prescription medications during their pregnancy and that many women perceive complementary medication use as natural and without risk or the occurrence of side effects.[16]

Strengths of this study include the use of a detailed medication history to determine medication use during pregnancy. This systematic process of undertaking a detailed medication history provides much stronger methodological rigour then relying on alternative methods, such as maternal self-reporting in a questionnaire. Highlighting this point is the finding that 99% of women reported using at least one medication during pregnancy in our study, whereas in a recent Australian study 83.1% of women self-reported use of at least one medication through a questionnaire. Limitations are that this study was only conducted at one hospital site, making

it difficult to evaluate the generalizability of these findings to other hospital settings, especially where different PHRs may be in use. Participant recall could be another limitation of this study, despite prompting women about medications as part of the detailed medication history, there may still be a potential for recall issues. Another potential limitation may include the fact that we did not reconcile each woman's medication history with general practitioners or community pharmacies, unless patients were unsure about what they were taking.

In summary, the PHR appears to be of low accuracy in relation to the recording of medications and ADRs, warranting further research to examine the impact of these discrepancies on patient care and outcomes. Furthermore, these findings suggest the need for strategies to improve the accuracy of information on medication use and ADRs to enhance continuity of care in the obstetric setting.

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Figure 1. Types of Discrepancies Identified

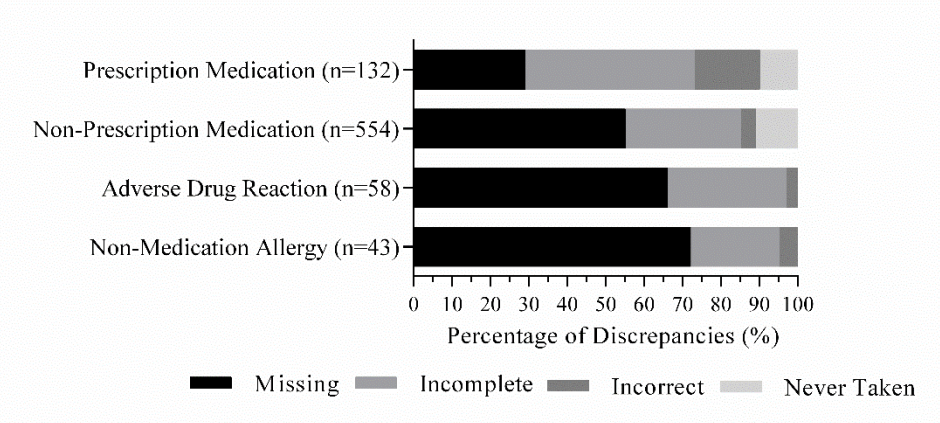

Table 1: Classification Types of Medication and Adverse Drug Reaction or Allergy Discrepancies

Classification Type	**Medication**	**ADR or Allergy**
Incomplete	Medication recorded in PHR, however vital information such as dose and frequency are missing (e.g. levetiracetam recorded in PHR without a dose or frequency)	ADR or allergy documented in part in PHR, but with incomplete details (e.g. penicillin allergy recorded without any details specifying the reaction).
Incorrect	Medication details provided in PHR are incorrect with respect to the documented dose or frequency, for example (e.g. phenytoin dose increased during pregnancy but not updated in PHR)	ADR or allergy documented in PHR is incorrect when compared to that identified during the interview (e.g. penicillin reaction recorded as patient not experiencing shortness of breath when they actually did)
Missing	Medication identified during interview but not documented in PHR (e.g. patient reported taking sertraline with no record of use in PHR)	ADR or allergy identified during interview but not documented in PHR (e.g. NSAID sensitive asthma not recorded in PHR)
Never Taken/Non-compliant	Medication recorded in PHR, however, according to the interview this medication was not actually used during pregnancy (e.g. PHR	*Not Applicable*

	documentation that patient taking low-dose aspirin for pre-eclampsia prophylaxis, but patient reported never actually taking it)	

Abbreviations: ADR, adverse drug reaction; PHR, pregnancy handheld record; NSAID, non-steroidal anti-inflammatory drug

Appendix 1: Medication Discrepancies According to ATC Code and Prescription Type							
	Prescription Medication Discrepancy			**Non-prescription Medication Discrepancy**			
	Yes	**No**	**Medication Example**	**Yes**	**No**	**Medication Example**	**Total**
	N (%)	**N (%)**		**N (%)**	**N (%)**		
A - Alimentary Tract and Metabolism	46 (54)	39 (46)	Omeprazole	283 (49)	299 (51)	Cholecalciferol, multivitamin	667
B - Blood and Blood Forming Organs	1 (17)	5 (83)	Enoxaparin	111 (61)	72 (39)	Iron supplement	189
C - Cardiovascular System	2 (20)	8 (80)	Labetalol	22 (88)	3 (12)	Omega-3 triglycerides	35
D - Dermatologicals	2 (100)	0 (0)	Betamethasone cream	9 (82)	2 (18)	Aciclovir	13
G - Genitourinary System and Sex Hormones	4 (67)	2 (33)	Progesterone pessaries	7 (64)	4 (36)	Clotrimazole pessaries	17
H - Systemic Hormonal Preparations excluding Sex Hormones and Insulins	5 (23)	17 (77)	Thyroxine	0	0	-	22
J - Anti-Infectives for Systemic Use	35 (81)	8 (19)	Amoxycillin	0	0	-	43
L - Antineoplastic and Immunomodulating Agents	0	1 (100)	Azathioprine	0	0	-	1
M - Musculoskeletal System	1 (100)	0	Sulphasalazine	1 (50)	1 (50)	Ibuprofen	3
N - Nervous System	18 (50)	18 (50)	Sertraline	58 (65)	31 (35)	Paracetamol	125
P - Anti-parasitic Products, Insecticides and Repellents	0	0	-	1 (100)	0	Pyrantel	1
R - Respiratory System	18 (28)	46 (72)	Fluticasone and Salmeterol	15 (94)	1 (6)	Loratadine	80
Other†	N/A	N/A	-	47 (90)	5 (10)	Raspberry leaf tea	52
Total	132 (48)	144 (52)		554 (57)	418 (43)		1248

N/A: not applicable
†Indicates medications not covered under the ATC codes