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Investigation of the Frequency and Nature of Medication Related Problems in the Women's Health Unit of an Australian Tertiary Teaching Hospital

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Conflict of Interest

The authors declare that they have no conflict of interest.

Abstract

Background: Despite the large burden medication related morbidity and mortality places on the Australian healthcare system, there is little known about the extent of this problem in a women's health (obstetric and gynaecology) setting.

Objective: Determine the frequency and nature of medication related problems (MRPs) occurring in a women's health unit (WHU) of an Australian teaching hospital.

Methods: A prospective audit of consecutive cases of patients treated in the Women's Health Unit at a tertiary level teaching hospital was undertaken by a clinical pharmacist over a five week period. Data collected included: patient characteristics, type of MRP (using a modified version of the Hepler-Strand classification system), medication involved (according to the World Health Organisation Anatomical Therapeutic Chemical classification system) and clinical significance (using a two-level severity index).

Results: A total of 454 potential MRPs identified over the five week period among 241 patients. A total of 39 MRPs (8.6%) identified were deemed to be of moderate/high clinical significance. The highest number of MRPs (221; 49%) were identified amongst women admitted following a caesarean delivery, with 83 of 85 women in this group experiencing at least one MRP. Additional factors associated with an increased likelihood of patient's experiencing a MRP included increased age, length of hospital stay and number of regular medications taken prior to and during admission($p<0.05$).

Conclusion: The widespread nature of identified MRPs in this setting suggest various approaches to minimising these problems and mitigating the associated burden on the healthcare system are warranted.

Introduction

An Australian landmark study undertaken almost two decades ago reported that 16.6% of admissions to hospitals were associated with an iatrogenic adverse event, with medication-related adverse events being large contributors to this figure.[1] Such medication related adverse events are commonly delineated in terms of a framework proposed by Hepler and Strand, which defined a Medication Related Problem (MRP) as "an event or circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care".[2] While MRP prevalence rates vary significantly across different populations and different studies, likely owing to differing study designs and the lack of a universal definition of MRPs, there remains a clear consensus from all studies that MRPs are not only common but also of significant concern to the healthcare system.[3-5]

A recognised approach to counteracting MRPs and reducing their associated negative burden has been the expanded role of ward based clinical pharmacy services.[6] Studies have demonstrated that increased staffing levels for clinical pharmacists and pharmacist-provided admission histories were associated with a statistically significant reduction in medication errors and subsequently patient morbidity and mortality.[5, 7-9] A particularly unique challenge within the women's health setting is that of medication use during pregnancy and lactation. Prescribing medications to women during pregnancy and lactation is often a complex multifactorial scenario, with the need to balance the associated benefits and risks to both the mother and child.[10] Furthermore, the numerous physiological changes that occur during pregnancy can alter medication pharmacokinetics.[11] In addition, obstetric patients are certainly not exempt from experiencing conditions that may require medication therapy, with chronic health conditions, obstetric related conditions and complications arising in labour and delivery each affecting an estimated proportion of between 30 and 40% of obstetric patients

each year.[12] Further to this, medication use appears to be almost ubiquitous amongst pregnant women with Australian studies reporting that up to 97% of women use at least one medication (non-prescription medications more commonly used than prescription medications) and 26.5% of women were using at least one prescribed medication during pregnancy.[13, 14]

Few studies have investigated the nature and prevalence of MRPs occurring within a women's health setting.[15-20] Three previous studies have focused on the evaluation of self-reporting error databases,[17-19] and while these reports may be useful in highlighting examples of medication errors, they are unable to determine the true frequency with which they occur. An additional three studies have focused on evaluating medication errors associated at the point of medication orders (e.g. point of prescribing/dispensing)[15, 16, 20], demonstrating variability in the extent to which errors occur, with errors ranging from 0.4/100 orders[20], up to 4.2/100 orders[16]. Notably, as none of these previous studies involved the identification of MRPs following the completion of a detailed pharmacist-provided medication history and clinical evaluation, they are likely to represent an underestimate of the true number of MRPs. Therefore, the aim of this study was to examine the frequency and nature of MRPs occurring in an obstetrics and gynaecology hospital inpatient setting.

Methods

Ethics approval was obtained from the University of South Australia and the Lyell McEwin Hospital/Queen Elizabeth Hospital/Modbury Hospital Human Research and Ethics Committees.

A prospective clinical audit of consecutive cases of patients treated in the Women's Health Unit (WHU) at the Lyell McEwin Hospital (LMH) was undertaken over a five week study period in June and July 2013. The LMH is a tertiary level public teaching hospital with a 39 bed WHU and is currently the second largest provider of obstetric services in South Australia (SA), accounting for 15.6% of hospital births in SA in 2010.[12] The model of care provided at the LMH differs somewhat from other maternity units in SA. Women having a vaginal delivery give birth in the labour ward and if there are no complications with the mother or baby, they are discharged as soon as six hours after delivery. Midwives then undertake a series of home-visits to ensure that the mother and baby are doing well. Therefore the clinical case-mix of obstetric patients admitted to the WHU is mainly comprised of the more complicated vaginal deliveries in addition to caesarean deliveries and antenatal patients. Moreover, some uncomplicated vaginal deliveries are admitted to the WHU if the labour ward is over capacity or in the case that the neonate requires observation or treatment in the Special Care Nursery.

During the study period the WHU was serviced by a ward-based clinical pharmacist during the hours of 9am to 1pm on Mondays to Fridays. As part of routine clinical care, the clinical pharmacist was responsible for undertaking a process of medication reconciliation for each obstetric/gynaecology patient admitted to the ward. Medication reconciliation is defined as the formal process of obtaining and verifying a complete and accurate list of a patient's current medications, comparing the medications the patient has actually been prescribed to what they should be prescribed and discussing any discrepancies with the prescriber.[21] In addition, medication chart reviews were undertaken for each patient on first contact with the pharmacy service and were repeated on subsequent days if time permitted. Any MRPs considered by the clinical pharmacist to require urgent action were brought to the attention of

the Resident Medical Officer (RMO) on the ward immediately. Other less urgent issues were recorded, along with recommendations, on a separate report as they were identified and discussed with the RMO at the end of the clinical pharmacist's shift. Patients in which medication reconciliation was not possible (i.e. interpreter unavailable, patient discharged prior to pharmacy review) were not included.

All MRPs identified by the clinical pharmacist were recorded using a purpose built data collection instrument. Data were then entered into a spread sheet, including: type of patient (caesarean delivery, vaginal delivery, antenatal or gynaecology), the number of regular medications taken prior to admission and during hospital stay and length of hospital stay. The type of MRP was classified based on a modified version of the Hepler-Strand classification system. This system is based upon eight fundamental classes of MRPs and although first published some 23 years ago, is still widely used in studies internationally and serves to facilitate a greater understanding surrounding the circumstances in which various MRPs might develop.[22] Medications involved in MRPs were classified according to the World Health Organisation Anatomical Therapeutic Chemical classification system. For simplicity, the clinical significance of each MRP was classified according to a modified version of the three level scale originally published by Cornish et al., which originally classified MRPs according to whether they had low, moderate, or severe potential to cause patient harm.[23] We collapsed the three levels into two levels, with clinical significance classified either as being of low potential to result in patient deterioration or discomfort (level one) or of moderate or severe potential to result in patient deterioration or discomfort (level two). The clinical significance was initially assessed by the pharmacist recording the MRP and was subsequently discussed and reviewed by the remaining study authors, with consultation and review by a senior medical representative within the hospital. Inter-rater

agreement was not evaluated between those assessing the clinical significance of each MRP. Medication-related discrepancies deemed not to be of clinical significance prior to commencing the study (i.e. the omission of pregnancy multi-vitamins in a patient who had taken them prior to admission) were not recorded as MRPs.

Descriptive statistics were used to describe patient characteristics and the frequency and nature of identified MRPs. Non-parametric analyses were undertaken with multiple independent samples compared with a Kruskal-Wallis one-way analysis of variance (reporting adjusted significance using the Bonferroni correction) and two groups being compared with a Mann-Whitney-U Test. To compare categorical data, a Chi-Square Test was undertaken if values in each cell were more than or equal to five. In other cases a Fisher's Exact Test was performed. Binary logistic regressions were used to calculate odds ratios (OR) with 95% confidence intervals for particular variables. Statistical analyses were undertaken using Statistical Package for the Social Sciences (SPSS, Chicago, IL) version 22.0. Statistical significance was defined as a two-sided p-value of < 0.05.

Results

Data from a total of 241 patients was included in the study including 32 (13%) antenatal, 85 (35%) caesarean delivery, 88 (37%) vaginal deliveries and 36 (15%) gynaecology patients. Of the 32 antenatal patients, 10 eventually proceeded to parturition during their hospital stay; seven had a caesarean section and three had a vaginal delivery. Significant differences were evidence across the four patient groups in relation to age, number of regular medications taken prior to and during admission, obesity and length of hospital stay (**Table 1**).

A total of 454 discrete medication related problems were identified. The highest number of MRPs (221; 49%) were identified amongst women admitted following a caesarean delivery, with 83 of 85 women in this group experiencing at least one MRP (**Table 1**). Amongst postnatal women, those with a normal vaginal delivery were significantly less likely to experience a MRP than those with a caesarean delivery (OR 0.06, 95% CI 0.02-0.28). Additional factors associated with an increased likelihood of patient's experiencing a MRP included increased age, length of hospital stay and number of regular medications taken prior to and during admission (**Table 2**). Within the obstetric cohort, advanced maternal age (>35 years) was associated with a significantly increased likelihood of experiencing a MRP (OR 7.75, 95% CI 1.30-infinity), whereas obesity (defined as Body Mass Index (BMI) > 30) was not (OR 1.71, 95% CI 0.75-3.90).

The types of MRPs identified are presented in **Table 3** which includes an example of each MRP category. When classified according to medication type, the most common therapeutic group implicated in MRPs was alimentary tract and metabolism, mainly aperients and vitamins (32%) (**Figure 1**). Medications for the nervous system, largely analgesics and antidepressants were also a large contributor to MRPs in the study, accounting for 30% of all MRPs. A total of 39 (8.6%) of all MRPs were considered to be of moderate to high clinical significance (classified as level two MRPs). Despite being associated with the highest number of total MRPs, caesarean delivery was associated with the lowest proportion of level two MRPs, although this was not statistically significant (P=0.86; **Table 1**). A total of 136 (30%) MRPs were identified in the process of completing medication reconciliation, whilst the remaining 318 (70%) were identified whilst undertaking daily medication chart reviews. A higher number of daily medication chart reviews was associated with the identification of at least MRP, as compared to no MRP (p=0.003).

A total of 92 hours was spent on the ward by the clinical pharmacist over the five week period. The 241 patients in the study had a total length of stay of 941 days, with 0.44 level one MRPs and 0.041 level two MRPs identified per patient day.

Discussion

This study suggests that MRPs are prevalent in the area of women's health, with an average of 0.482 MRPs identified per patient day, highlighting the importance of clinical pharmacy services in identifying, managing and preventing MRPs. With a paucity of existing data available on MRPs, the results of this study are important in highlighting the types of MRPs and medications likely to be involved in MRPs in this setting. While the majority of issues identified were of relatively modest clinical significance, the sheer frequency of some of these MRPs is suggestive of possible system problems inherent in day to day practices on the unit, potentially improved via simple systems changes.

Few studies have investigated the nature and prevalence of MRPs occurring within a women's health setting, with none undertaken in an Australian setting. A number of previous studies have focused on medication errors identified by error reporting systems or retrospective chart reviews.[17-19] While such self-reported notifications are useful in providing potential insight into the nature of MRPs in this setting, they are likely to result in an underestimation of the total number of medication errors. Subsequent prospective studies also have their own limitations, such as focusing on medication errors associated with prescribed orders only, rather than the detailed range of MRPs explored in this present study.[15, 16, 20] Therefore, while the incidence of MRPs may appear approximately 10-fold higher in our present study compared with that reported previously (1.88 /woman vs. 0.20/woman[16]), this is

likely to reflect methodological differences between studies. For example, the process of medication reconciliation as undertaken by the pharmacist proved crucial to the identification of many issues identified in our study. Previous research has reviewed the value of medication reconciliation in terms of reducing the incidence of both medication errors and subsequent ADRs.[24] In the present study, medication reconciliation assisted in the identification of 136 MRPs (including six level two MRPs) over the five week period, 30% of the overall total. A further benefit of a detailed medication history is in identifying regular medications that have not been charted during hospital admission, this accounted for 112 (28%) of MRPs identified in obstetric patients. Many of these involved the use of medications in the management of identified vitamin D deficiency (37%), asthma (35%) and depression (11%). It is important to be aware of a patient's medical and medication history as these can have an impact on clinical care and the continued use of regular medications (e.g. antiepileptics) may be vital in ensuring adequate continued management of certain conditions. Furthermore, the charting of regular medications provides opportunities to discuss and support their use in the clinical setting (e.g. use of medications while breastfeeding).

The identification of factors associated with an increased risk of experiencing a MRP are useful to determine what patients are at most risk of experiencing a MRP and therefore use this as a guide to prioritising work load on the ward. Factors associated with a significantly increased risk of experiencing a MRP included increased length of hospital stay, number of regular medications taken prior to and during admission, age and caesarean delivery. A number of these factors are likely to be closely correlated. For example, advancing age, which is more common amongst gynaecology patients than obstetric patients, is often associated with an increased occurrence of co-morbidities and subsequent medication use.

In this study, within the obstetric setting, advanced maternal age (>35 years) was associated with a significantly increased likelihood of experiencing a MRP. This is probably not surprising given advanced maternal age has been associated with an increased risk of pre-existing medical conditions (e.g. hypertension), obstetric complications (e.g. gestational diabetes) and adverse labour and birth outcomes (e.g. caesarean section).[25] Like advanced maternal age, obesity also increases the risk of numerous pregnancy related complications.[26] However, despite obese women being more likely to have undergone caesarean section and be older compared to non-obese women, no difference was observed in relation to the presence of MRPs.

Of note, while a number of risk factors were identified, the presence of a clinical significant level two MRP could not clearly be predicted based on any specific patient characteristic. This makes it difficult when prioritising clinical pharmacy service delivery, as only examining MRPs among patients considered to be at high risk could lead to missing clinical significant MRPs among other patients.

In this study caesarean section patients experienced significantly more MRPs ($p<0.001$) and were significantly more likely to experience at least one MRP compared to those who had vaginal deliveries (OR 0.06, 95% CI 0.02-0.28), although they were not more likely to experience a level two MRP. In the South Australian public health system, patients are usually only eligible for an elective caesarean section if there is a medical reason (e.g. hypertension, antepartum haemorrhage or multiple pregnancy) for this to occur and emergency caesarean sections are performed for similar reasons in addition to foetal distress and failure to progress during labour.[12] Further, a caesarean procedure is associated with increased maternal morbidity due to the invasive nature of the procedure, with complications

including increased risk of thrombosis and post-partum haemorrhage.[27] This increased complexity of caesarean section patients was evident in the present study in view of the significantly longer hospital stay, number of medications taken prior to admission and greater number of medications charted for caesarean patients as compared to those with vaginal deliveries. However, it should be noted that the vaginal delivery patient group in the present study are not necessarily representative of all vaginal births in the facility, and may in fact be skewed toward more medically complex cases, given the model of care implemented on the ward, which affects the ability to draw generalisations from these comparisons. This may help to explain the similar observed distribution of severity of MRPs amongst the vaginal and caesarean delivery patients.

This study has a number of limitations. Firstly, MRPs were only assessed within the WHU, not the labour ward. Previous research suggests that these areas are not exempt from MRPs with one study reporting that half of errors reported in their study occurred here.[18] Secondly, the generalisability of these results is influenced by the short study period and single-site methodology. While many aspects of clinical care remain constant (i.e. senior medical staff, nursing/midwifery staff), much of the ward based clinical care is undertaken by junior doctors on rotating placements, and therefore the presence of MRPs could differ according to their varying levels of experience in obstetrics and gynaecology. Furthermore, it is possible that the frequency and nature of MRPs identified within this setting may not be reflective of other hospitals due to differences in clinical staff, patient characteristics and/or differing clinical management protocols. Thirdly, the assignment of severity classifications to MRPs was not validated. While the severities were assigned by an experienced group of clinical pharmacists and reviewed by a senior medical representative within the hospital, inter-rater agreement was not evaluated. Finally, while the utility of a pharmacist in this setting is likely

to extend beyond the identification and resolution of MRPs (e.g. the provision of information on the safety of medications in pregnancy and breastfeeding, as well as discharge counselling) these activities were not systematically recorded or analysed over the study period. Future research might reasonably include a more formal investigation into the overall value of a clinical pharmacist in this specialised context.

In conclusion, this study demonstrates that MRPs are widespread within a women's health setting. Future research should address whether clinical pharmacy services have the potential to reduce the frequency and significance of MRPs in this setting and whether this leads to improvements in patient health outcomes.

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Table 1: Patient Characteristics and Number of MRPs by patient type

Characteristic[‡]	**Total**	**Obstetrics**			**Gynaecology**	**Overall Comparison P Value** [#]
		Antenatal	**Postnatal**			
			Caesarean Delivery	**Vaginal Delivery**		
Number of women, n	241	32	85	88	36	
Age (years), median (range)	29 (17-83)	27 (18-39)[a]	29 (18-41)[a]	27 (17-41)[a]	45 (18-83)[b]	P<0.001
Number of medicines prior to admission, median (range)	1 (0-14)	2 (0-10)[b]	2 (0-9)[a,b]	1 (0-6)[a]	1.5 (0-14)[a,b]	P=0.015
Obese (BMI>30), n (%)[^]	86 (39%)	16 (53%)[a]	35 (41%)[a,b]	24 (28%)[b]	11 (55%)[a]	P=0.021
Length of stay (days), median (range)	4 (1-16)	4 (1-16)[a, b]	4 (3-10)[a]	3 (1-6)[b, c]	2 (1-16)[c]	P<0.001
Number of medicines during admission, median (range)[*]	2 (0-13)	2 (0-12)[a]	3 (2-7)[a]	0 (0-6)[b]	2 (0-13)[a]	P<0.001
Number of chart reviews performed, median (range)	1 (1-9)	1 (1-9) [a, b]	2 (1-4) [a]	1 (1-3)[b]	1 (1-3) [b]	P<0.001
Number of MRPs identified, n	454	74	221	105	54	
Median number of MRPs	2 (0-14)	2 (0-14)[a,b]	3 (0-6)[a]	1 (0-5)[b]	1 (0-4)[b]	P<0.001

identified (range)						
Number of patients with ≥ 1 MRP, n (%)	201 (83%)	24 (75%)[b]	83 (98%)[a]	64 (73%)[b]	30 (83%)[b]	P<0.001
Level two MRPs, n (%)	39 (8.6%)	7 (9%)	11 (5%)	14 (13%)	7 (13%)	P=0.864

Abbreviations: MRP, medication related problem; BMI, body mass index;

[‡] Groups with different superscripts (e.g. a, b, c) are significantly different ($p<0.05$), while groups with the same superscript are not significantly different

[#] Continuous variables were analysed with Kruskal-Wallis. Categorical variables were analysed with Chi-square tests or where the count in a cell was less than 5, by Fisher's Exact test.

[^] Percentages are calculated from non-missing values (i.e. $n_{obese}/n_{BMI\ recorded}$)

[*] Number of regular medications charted as an inpatient was recorded at the point of initial review and updated if noted during a chart review that additional regular medicines were charted

Table 2: Characteristics of Patients with ≥ 1 MRP compared to those who experienced no MRPs

Characteristic	No MRPs	≥ 1 MRP	P Value [#]
Number, n	40	201	
Age, median (range)	24.5 (18-69)	30 (17-83)	P=0.002
Length of stay, median (range)	3 (1-6)	4 (1-16)	P=0.001
Regular medications prior to admission, median (range)	1 (0-5)	2 (0-14)	P<0.001
Regular medications as inpatient, median (range) [^]	0 (0-6)	3 (0-13)	P<0.001
Obese (BMI>30), n (%) [*]	12 (32%)	74 (40%)	P=0.462

Abbreviations: MRP, Medication Related Problem; BMI, body mass index

[#] Continuous variables were analysed with Mann-Whitney U Tests. Categorical variables were analysed with Chi-square tests or where the count in a cell was less than 5, by Fischer's Exact test

[^] Number of regular medications charted as an inpatient was recorded at the point of initial review and updated if noted during a chart review that additional regular medicines were charted

[*] Percentages are calculated from non-missing values (i.e. $n_{obese}/n_{BMI\ recorded}$)

Table 3: Types of MRPs identified

Type of MRP	n (%)	Example
Incomplete medications charted on admission	128 (28%)	Patient's asthma inhalers not charted for duration of stay.
Dose too high	104 (23%)	Patient's receiving >4 g of paracetamol within 24 hours post caesarean delivery.
Incomplete drug order	75 (17%)	Patient charted for fluticasone/salmeterol however no strength specified. Patient usually uses 250 micrograms /50 micrograms.
Additional medication required	55 (12%)	Patient experienced significant blood loss in delivery and subsequently has a low haemoglobin (<10 g/dL), which is currently not being treated (require iron therapy).
Therapeutic duplication	22 (5%)	Patient is charted for paracetamol regularly and when required paracetamol/codeine, with no mention of maximum allowable dose in 24 hours.
Incorrect medication choice	18 (4%)	Patient has moderate to severe asthma and is prescribed labetalol for management of gestational hypertension.
Drug-drug or drug-food interaction	10 (2%)	Patient usually takes thyroxine on an empty stomach, however as an inpatient it has been prescribed and administered with breakfast.
Dose too low	9 (2%)	Patient received 20 mg daily of prophylactic enoxaparin post caesarean section. Guidelines recommend 40 mg. Patient weighed approximately 60 kg.
Failure to receive medication	9 (2%)	Patient charted to receive levetiracetam dose post caesarean section, was not administered and thus

		patient went > 24 hours without receiving her anti-epileptic medication.
Unnecessary medication	8 (2%)	Patient still charted for benzyl penicillin, for Group B Streptococci prophylaxis, in the postnatal period.
Adverse drug reaction not documented	7 (2%)	Patient had a prior reaction to iron polymaltose (rash and difficulty breathing), which was not documented on her chart during her admission for anaemia.
Allergy to drug prescribed	6 (1%)	Patient has a documented history of anaphylaxis to cephalosporins, and received one dose of cephazolin following caesarean delivery.
Need for additional laboratory test	3 (1%)	Patient underwent vaginal delivery, despite potentially active vaginal herpetic lesions. Neonate required IV antivirals and herpes swabs.

Abbreviations: MRP, medication related problem

Figure 1: Types of medication involved in medication related problems (MRP) according to Anatomical Therapeutic Chemical (ATC) classification