Adverse Drug Reactions in Pregnant People with Hypertension and/or Diabetes: Temporal Profile and Associated Factors

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ABSTRACT

Background: Pregnant people, especially those with diabetes mellitus or hypertension, are particularly vulnerable to adverse drug reactions (ADRs).

Objective: To determine the incidence of and factors associated with ADRs in hospitalized pregnant people with diabetes and/or hypertension.

Methods: This prospective cohort study involved pregnant people with diabetes and/or hypertension admitted to a maternity hospital in Natal, Brazil, between August 2019 and July 2022. Data for various patient characteristics and the occurrence of ADRs were collected by means of interviewing patients and searching their medical charts. Multivariate logistic regression was used to identify and analyze the association of ADRs with various patient characteristics and other factors.

Results: A total of 571 pregnant people met the inclusion criteria. Over the study period, the incidence rate of ADRs was 634.4 (95% confidence interval [CI] 522.7–787.1) per 1000 patient-days, with 123 (21.5%) of the patients experiencing at least 1 incident. ADRs occurred predominately in the first 24 hours, with a marked decrease in frequency to the seventh day of admission. Methyldopa was identified as the cause in 42.1% (8/19) of cases of headache and 39.5% (17/43) of cases of sedation. Systemic corticosteroids were responsible for almost all cases of hyperglycemia (97.0% [32/33]). Blurred vision (82.4% [14/17]) and sedation (14.0% [6/43]) were related to the administration of antiemetics and antinauseants, especially scopolamine. Longer hospitalization time (OR 1.052, 95% CI 1.010–1.097, $p = 0.016$) and greater number of prescribed medications (OR 1.200, 95% CI 1.099–1.310, $p < 0.001$) were related to the occurrence of ADRs.

Conclusions: In this study, 1 of every 5 hospitalized pregnant people had at least 1 ADR, most often in the first 24 hours, with a decrease in incidence in the following days. Pregnant people with longer hospital stays and a greater number of medications had a higher risk of ADRs.

Keywords: adverse drug reaction, high-risk pregnancy, clinical pharmacy service, patient safety

RÉSUMÉ

Contexte : Les personnes enceintes, en particulier celles qui souffrent de diabète sucré ou d'hypertension, sont particulièrement vulnérables aux effets indésirables des médicaments.

Objectif : Déterminer l'incidence des effets indésirables et les facteurs qui y sont associés chez les personnes enceintes hospitalisées et souffrant de diabète et d'hypertension.

Méthodologie : Cette étude de cohorte prospective portait sur des personnes enceintes atteintes de diabète ou d'hypertension admises dans une maternité de Natal, au Brésil, entre août 2019 et juillet 2022. Les données relatives à diverses caractéristiques de la patientèle et à la survenue d'effets indésirables ont été recueillies au moyen d'entretiens et de recherches dans les dossiers médicaux de celle-ci. Une régression logistique multivariée a été utilisée pour recenser et analyser l'association des effets indésirables avec diverses caractéristiques de la patientèle et d'autres facteurs.

Résultats : Au total, 571 personnes enceintes répondaient aux critères d'inclusion. Au cours de la période d'étude, le taux d'incidence des effets indésirables se chiffrait à 634,4 pour 1000 jours-patients (intervalle de confiance [IC] à 95 % 522,7-787,1), 123 (21,5 %) de la patientèle ayant eu au moins un incident. Les effets indésirables prédominaient dans les 24 premières heures, avec une diminution marquée de la fréquence jusqu'au septième jour d'admission. La méthyldopa a été identifiée comme cause dans 42,1 % (8/19) des cas de céphalées et 39,5 % (17/43) des cas de sédation. Les corticostéroïdes systémiques étaient responsables de presque tous les cas d'hyperglycémie (97,0 % [32/33]). La vision floue (82,4 % [14/17]) et la sédation (14,0 % [6/43]) étaient liées à l'administration d'antiémétiques et d'antinauséeux, en particulier de scopolamine. Une durée d'hospitalisation prolongée (rapport de cotes [RC] 1,052, IC à 95 % 1,010-1,097, $p = 0,016$) et un plus grand nombre de médicaments prescrits (RC 1,200, IC à 95 % 1,099-1,310, $p < 0,001$) étaient liés à la survenue d'effets indésirables.

Conclusions : Dans cette étude, 1 personne enceinte hospitalisée sur 5 présentait au moins un effet indésirable, le plus souvent dans les 24 premières heures, avec une diminution de l'incidence dans les jours suivants. Les personnes enceintes ayant séjourné plus longtemps à l'hôpital et ayant pris un plus grand nombre de médicaments présentaient un risque plus élevé d'effets indésirables.

Mots-clés : réaction indésirable aux médicaments, grossesse à haut risque, service de pharmacie clinique, sécurité des patients

INTRODUCTION

Gestational hypertension and gestational diabetes mellitus are considered some of the main causes of maternal–fetal morbidity and mortality, and their occurrence is increasing worldwide.[1-4] It is estimated that the prevalence of gestational hypertension is 5%–10%, whereas the prevalence of gestational diabetes is approximately 2%–5%.[5] In recent decades, there has been a notable rise in the hospitalization of pregnant people due to complications related to these conditions, particularly in low- and middle-income countries.[6] Pregnant people with high blood pressure are about 6 times more likely than those without hypertension to be hospitalized for related care.[6,7] In these cases, pharmacological therapy based on antihypertensive drugs, insulin therapy, and hypoglycemic agents is considered the first choice.[8-10] However, the use of medication during pregnancy is associated with a higher frequency of adverse events.[11]

Physiological changes significantly modify pharmacokinetic and pharmacodynamic variables during pregnancy, which can lead to an inadequate therapeutic response, as well as toxicity or even fetal death.[12,13] Modification of the pharmacokinetic profile, characterized by the processes of drug absorption, distribution, metabolism, and excretion, may be related to physiological changes, such as nausea/vomiting, increase in body weight, alteration in hepatic metabolism, increase in blood flow, and accumulation of amniotic fluid.[12-14] Conversely, the pharmacodynamic profile is responsible for the mechanism of action and pharmacological effects of a drug.[14] In this context, clinical trials with pregnant women are scarce due to ethics criteria[15]; thus, information on the safety of drug use in these patients is insufficient, and off-label use is common.[16] Such peculiarities make drug therapy in high-risk pregnant women more complex due to the lack of consistent information in certain cases, specifically with regard to adverse drug reactions (ADRs).

The occurrence of ADRs in the hospital environment is associated with prolonged hospitalization and increased morbidity and mortality, as well as health problems after the hospital stay.[17] The prevalence of ADRs in hospitalized pregnant women is about 10%.[18] However, little is known about the occurrence of ADRs in hospitalized pregnant women who have diabetes and/or hypertension. The objective of this study was to characterize ADRs in pregnant people with diabetes and/or hypertension according to temporal profile, the main drugs involved, and the factors associated with ADR occurrence in the hospital setting.

METHODS

Study Design and Population

This prospective cohort study involved pregnant people with diabetes and/or hypertension who were admitted to a teaching maternity hospital in Natal, Brazil, from August 2019 to July 2022. The study focused on the high-risk wards of the hospital, which had a combined capacity of 22 beds. Included in the study were consecutive pregnant people of all ages who were admitted for 24 hours or longer during the study period, who provided written informed consent, and for whom at least 1 medication was prescribed. Excluded from the study were patients who were readmitted and those for whom only non-drug therapy (electrolyte solutions, blood and blood products, oxygen therapy, diagnostic agents, and vitamin/mineral supplements) was prescribed. Also excluded were patients with non-adherence to treatment, accidental or intentional overdose, treatment failure, and medication errors, as these occurrences were not classified as ADRs. Patients remained part of the study until their discharge from hospital or transfer to another ward.

The study was approved by the Research Ethics Committee of the Federal University of Rio Grande do Norte (No. 3,301,330).

The STROBE guidelines for reporting observational studies, recommended by the EQUATOR Network (https://www.equator-network.org/strobe/), were consulted and adhered to in reporting the results of this study, to ensure transparency and adherence to established standards in scientific research.

Data Collection

Daily data collection involved interviews with pregnant people and review of their medical records. Recruitment occurred consecutively upon admission, with a maximum of 12 participants for simultaneous evaluation, based on a pilot study, aligning with the research team's capacity to ensure high-quality data collection. Clinical and demographic variables, including admission diagnosis, gestational age in weeks, comorbidities, allergies, maternal age in years, number of previous deliveries, and medical history (complete blood count, C-reactive protein, electrolytes, total proteins, and protein fractions) were gathered. Additionally, glycemic, hepatic, and renal profiles were recorded.

Admission diagnoses and medications were categorized using the *International Statistical Classification of Diseases and Related Health Problems,* 10th revision,[8] and the Anatomical Therapeutic Chemical (ATC) classification system,[9] respectively. In accordance with the World Health Organization's definition, an ADR was defined as any harmful or undesired response to a drug, which was unintentional and which occurred at normal doses during prophylaxis, diagnosis, or treatment of disease or for the modification of physiological function.[19]

The process of identifying ADRs was conducted daily throughout the entire hospital stay of pregnant people with diabetes and/or hypertension in the high-risk wards and involved 3 sequential steps: identification of trigger drugs followed by daily interviews, active searching in patients'

medical records, and application of the Naranjo algorithm.[20] The detailed description of these steps is provided below.

- Step 1—Identification of trigger drugs followed by daily interviews: In accordance with prior studies,[7,11] eligible drugs that prompted the search for ADRs included scopolamine, methyldopa, insulin, ferrous sulfate, betamethasone, nifedipine, hydralazine, paracetamol (acetaminophen), cephalexin, lithium, acetylsalicylic acid, carbamazepine, and sertraline. Once a trigger drug was identified in a patient's regimen, the patient was questioned about the presence of symptoms potentially indicative of ADRs. These inquiries were tailored according to initial assessment of the prescription.
- Step 2—Active searching in the medical records: Following identification of trigger drugs, a comprehensive examination of the patient's medical records was undertaken to identify any changes in clinical or laboratory parameters. During this investigative process, alterations, substitutions, and/or discontinuations of medications were regarded as potential indicators of an ADR.
- Step 3—Application of Naranjo algorithm: The suspected ADR was evaluated using the Naranjo algorithm,[20] a straightforward and practical assessment scale designed to evaluate the causality between a specific drug and a potential ADR. This score reflects the likelihood that a specific drug caused the ADR and that the observed event was not a manifestation of the underlying disease. The algorithm consists of 10 questions, each with empirical scoring options (no, yes, I don't know). The cumulative score ranges from −4 to +13, with higher values indicating greater strength of the causal relationship. Causality scores according to the Naranjo algorithm are categorized as follows: ≥ 9, definite ADR; 5–8, probable ADR; 1–4, possible ADR; and < 1, doubtful ADR.

The active search for ADRs was conducted collaboratively by 2 pharmacists (J.E.C.C., P.K.V.B.), with support from 4 pharmacy students who had undergone prior training.

The Naranjo algorithm was applied independently by the same 2 researchers (J.E.C.C., P.K.V.B.). In instances of disagreement, a third researcher (R.R.M.) was consulted to reach a consensus. To ensure precision in data collection, a pilot project involving 15 patients was conducted before the study began. This pilot served to fine-tune the data collection forms and familiarize the team with the process.

We implemented rigorous strategies during data collection to minimize interviewer and recall biases in detecting ADRs among hospitalized patients. The 2 experienced clinical pharmacists who conducted the interviews underwent rigorous training to ensure consistency and accuracy. Detailed protocols guided each stage, including approaching participants, formulating neutral questions, and accurately recording responses. Structured questionnaires with clear, objective questions were used to minimize interviewer bias.

Statistical Analysis

Patient characteristics are presented as means with standard deviations (SDs) or relative/absolute frequencies, according to the type of variable under analysis. The ADRs were quantified in terms of incidence rates (number of ADRs per 1000 patient-days) and incidence proportions (number of ADRs per 1000 patients), along with their respective 95% confidence intervals (CIs). Risk factors for ADR occurrence were assessed with univariate logistic regression, whereby each variable was associated separately with the incidence of ADR. Variables with a p value less than 0.10 in the association test were included in a multivariate logistic regression model employing the stepwise backward approach. A significance level of p less than 0.05 was then adopted to identify factors independently associated with ADR occurrence in pregnant people. Multicollinearity was tested by calculating variance inflation factors (VIFs) for all explanatory variables in the full and minimal multivariate models. The full model had all values of VIF less than 4.5, and the minimal model had all values of VIF less than 2.0; hence, no problems were displayed. The statistical analysis was conducted using Stata 15 software (Stata Corporation).

RESULTS

During the study period, 5607 high-risk pregnant people were admitted to the study institution between August 2019 and July 2022. However, due to the COVID-19 pandemic, data collection was temporarily suspended between the months of March 2020 to April 2021 (during which a total of 2152 pregnant people attended). In the non-pandemic periods, the institution admitted 3455 pregnant people, of whom 30 refused to participate and 2854 exceeded the capacity of the research team (Figure 1). The study sample therefore consisted of 571 patients with a mean age of 30.5 (SD 6.8) years and gestational age at the time of delivery of 30.9 (SD 7.0) weeks. This sample size ensured a maximum

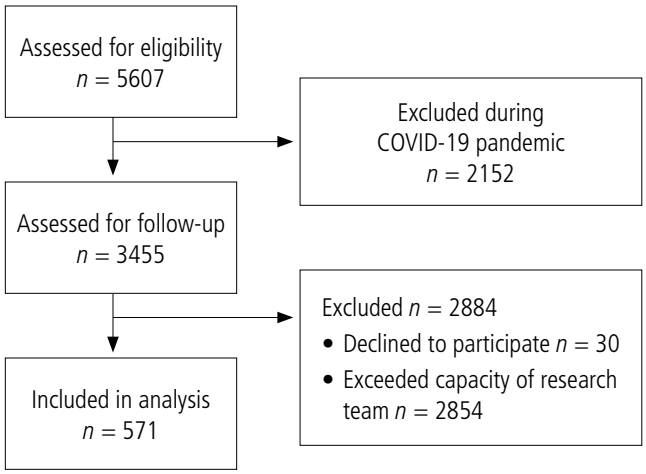

FIGURE 1. Participant flow diagram.

error of estimates of ±4 percentage points with 95% confidence. The main admission diagnoses were hypertensive syndromes (n = 398, 69.7%) and gestational diabetes (n = 326, 57.1%). Of the 570 patients for whom number of pregnancies was known, 172 (30.2%) were experiencing their first pregnancy and 305 (53.5%) had already had 1 or 2 previous deliveries. The mean length of hospital stay and associated treatment was 6.0 (SD 5.1) days (Table 1).

The patients included in the study sample experienced a total of 216 ADRs. Regarding the types and prevalences of these ADRs (Table 2), sedation (19.9%,), dizziness and nausea (17.6%), hyperglycemia (15.3%), and headache (8.8%) were most common throughout the study period. More precisely, these 4 reactions represented 61.6% (95% CI 54.7%–68.1%) of all identified ADRs. Regarding the duration of ADRs, they lasted a median of 3 days, except for xerostomia (which had a median duration of 8 days).

Table 3 details the occurrence of the most common ADRs (n = 165, 76.4%) in relation to the main pharmacological classes, according to the ATC system. Methyldopa and centrally acting antiadrenergics (class C02A) were identified as the cause of 42.1% (95% CI 20.3%–66.5%) of headache cases and 39.5% (95% CI 25.0%–55.6%) of cases of sedation. Systemic corticosteroids (class H02A), especially parenteral betamethasone, were responsible for almost all cases of hyperglycemia (97.0%, 95% CI 84.2%–99.9%). Blurred vision (82.4%, 95% CI 56.6%–96.2%) and sedation (14.0%, 95% CI 5.3%–27.9%) were related to the administration of antiemetics and anti-nauseants (class A04A), especially scopolamine. Antipsychotics (class N05A), especially levomepromazine, were associated with the occurrence of sedation (30.2%, 95% CI 17.2%–46.1%).

Over the entire study period, we observed an incidence rate of 634.4 (95% CI 522.7–787.1) ADRs per 1000 patient-days; however, there was greater detection of ADRs in the first 24 hours, with a marked decrease up to the seventh day of hospitalization. Figure 2 presents the ADR incidence proportions during the first 7 days, highlighting the most commonly implicated drugs. The overall incidence of ADRs was 189.1 (95% CI 159.1–223.3) cases per 1000 patients in the first 24 hours, decreasing to 44.1 (95% CI 29.8–64.8) and 67.1 (95% CI 47.1–94.2) cases per 1000 patients on the second and third days, respectively. The values continued to decline, reaching an incidence of 5.6 (95% CI 0.9–30.9) cases per 1000 patients on the seventh day. With regard to the main drugs involved, methyldopa had an incidence of 49.0 (95% CI 34.1–69.9) cases per 1000 patients on the first day of hospitalization, decreasing to 3.7 (95% CI 1.0–13.3) cases per 1000 patients on the second day. On the fourth day, we detected the last ADRs to be associated with methyldopa (2.9 [95% CI 0.5–16.0] cases per 1000 patients). Showing a similar pattern, injectable scopolamine had a peak incidence on day 1 of treatment (31.5 [95% CI 20.0–49.3] cases per 1000 patients), declining to 7.4 (95% CI 2.0–26.4) cases per 1000 patients on day 5. Despite lower incidence values, the occurrence of ADRs associated with betamethasone and levomepromazine was also higher in the first 24 hours: 22.8 (95% CI 2.0–26.4) and 14.0 (95% CI 2.0–26.4) ADRs per 1000 patients, respectively. Subsequently, there was a decrease in the incidence proportions for both drugs.

Univariate analysis showed that the diagnosis of a urinary tract infection (OR 2.085, 95% CI 1.053–4.127), more days of treatment (OR 1.102, 95% CI 1.061–1.144), and a greater number of prescribed drugs (OR 1.264, 95% CI 1.171–1.365) were associated with higher occurrence of ADRs. However, after multivariate analysis, only the longest treatment time (OR 1.052, 95% CI 1.010–1.097, p = 0.016) and the number of drugs prescribed (OR 1.200, 95% CI 1.099–1.310, p < 0.001) were related to the occurrence of ADRs.

TABLE 1. Characteristics of the Study Population

Characteristic	No. (%) of Patients[a] (n = 571)
Age (years) (mean ± SD)	30.5 ± 6.8
Gestational age (weeks) (mean ± SD)	30.9 ± 7.0
Report of drug hypersensitivity	
Analgesics and antipyretics	47 (8.2)
Metoclopramide	15 (2.6)
Penicillins	9 (1.6)
NSAIDs	8 (1.4)
Other	11 (1.9)
Admission diagnosis	
Arterial hypertension	398 (69.7)
Gestational diabetes	326 (57.1)
Urinary tract infections and vaginosis	40 (7.0)
Fetal and placental changes	32 (5.6)
Parity (no. of previous deliveries) (n = 570)	
First gestation	172 (30.2)
1 or 2	305 (53.5)
≥ 3	93 (16.3)
Previous miscarriage	169 (29.6)
Length of hospital stay (days) (mean ± SD)	6.0 ± 5.1
Patients with ≥ 1 ADR	123 (21.5)

ADR = adverse drug reaction, NSAID = nonsteroidal anti-inflammatory drug, SD = standard deviation.
[a]Except where indicated otherwise.

DISCUSSION

In this prospective cohort study, 1 of every 5 hospitalized pregnant people experienced an ADR, with the highest incidence on the first day of treatment and decreases in the following days. With a median duration of 3 days, the main ADRs observed were methyldopa-associated sedation, nausea, and headache; scopolamine-related blurred vision;

betamethasone-induced hyperglycemia; and sedation caused by levomepromazine. Longer hospitalization time and a greater number of medications were factors associated with the occurrence of ADRs.

Despite the characterization of ADRs as a widely explored topic, few studies have addressed their occurrence in hospitalized pregnant women, especially those with diabetes and hypertension. A study involving pregnant women in Ethiopia[21] showed an ADR prevalence of only 0.6%; however, the women evaluated in that study had much shorter hospitalization times (more than 60% stayed no more than 3 days) and younger age (mean 25 years), in addition to there being a low occurrence of diabetes and hypertensive syndromes. Two Brazilian studies evaluated populations of hospitalized pregnant women with profiles similar to that of the current study, although with a lower prevalence of ADRs than we observed: 8.8%[7] and 10.7%.[11] Contrary to the methods of our study, the previous studies[7,11,21] did not investigate the occurrence of ADRs on a daily basis through active searches in the medical records and interviews with

TABLE 2. Adverse Drug Reactions (ADRs) According to Occurrence, Frequency, and Duration

Adverse Drug Reaction	Occurrence during Hospital Stay		Duration of Reaction (days) (Median and IQR)
	No. (%) of ADR Cases	95% CI[a]	
Sedation	43 (19.9)	14.8–25.9	5 (2–8)
Dizziness and nausea	38 (17.6)	12.8–23.3	4 (2–7)
Hyperglycemia	33 (15.3)	10.8–20.8	2 (2–3)
Headache	19 (8.8)	5.4–13.4	3 (2–6)
Blurred vision	17 (7.9)	4.7–12.3	3 (1–4)
Transaminase elevation	8 (3.7)	1.6–7.2	2.5 (2–4)
Xerostomia	7 (3.2)	1.3–6.6	8 (2–10)
Hypersensitive reactions	7 (3.2)	1.3–6.6	2 (1–2)
Hypoglycemia	2 (0.9)	0.1–3.3	1 (1–1)
Other	42 (19.4)	14.7–25.8	3 (2–4)
Total	216 (100.0)	–	3 (2–5)

CI = confidence interval, IQR = interquartile range.
[a]Confidence interval for the percent of cases.

TABLE 3. Adverse Drug Reactions According to Frequency and ATC Drug Class

ATC Drug Class[b]	Adverse Drug Reaction; No. (%) of Cases[a]						
	Sedation	Dizziness and Nausea	Hyperglycemia	Headache	Blurred Vision	Other	Total
C02A	17 (39.5)	6 15.8)	0 (0.0)	8 (42.1)	0 (0.0)	11 (16.7)	42 (19.4)
H02A	0 (0.0)	0 (0.0)	32 (97.0)	0 (0.0)	0 (0.0)	2 (3.0)	34 (15.7)
A04A	6 (14.0)	3 (7.9)	0 (0.0)	0 (0.0)	14 (82.4)	9 (13.6)	32 (14.8)
N05A	13 (30.2)	3 (7.9)	1 (3.0)	0 (0.0)	1 (5.9)	4 (6.1)	22 (10.2)
C08C	2 (4.7)	4 (10.5)	0 (0.0)	4 (21.1)	1 (5.9)	2 (3.0)	13 (6.0)
B03A	0 (0.0)	11 (28.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	12 (5.6)
C02D	1 (2.3)	0 (0.0)	0 (0.0)	2 (10.5)	0 (0.0)	7 (10.6)	10 (4.6)
Other	4 (9.3)	11 (28.9)	0 (0.0)	5 (26.3)	1 (5.9)	30 (45.5)	51 (23.6)
Total	43 (100.0)	38 (100.0)	33 (100.0)	19 (100.0)	17 (100.0)	66 (100.0)	216 (100.0)

ATC = Anatomical, Therapeutic and Chemical (drug classification system).[9]
[a]For each adverse drug reaction, the percentage of cases associated with each ATC class was calculated in relation to the total number of cases of that reaction.
[b]C02A = centrally acting anti-adrenergic agents,\ H02A = corticosteroids for systemic use, A04A = antiemetics and antinauseants, N05A = antipsychotics C08C = selective calcium-channel blockers with mainly vascular effects, B03A = iron preparation, C02D = agents acting on arteriolar smooth muscle.

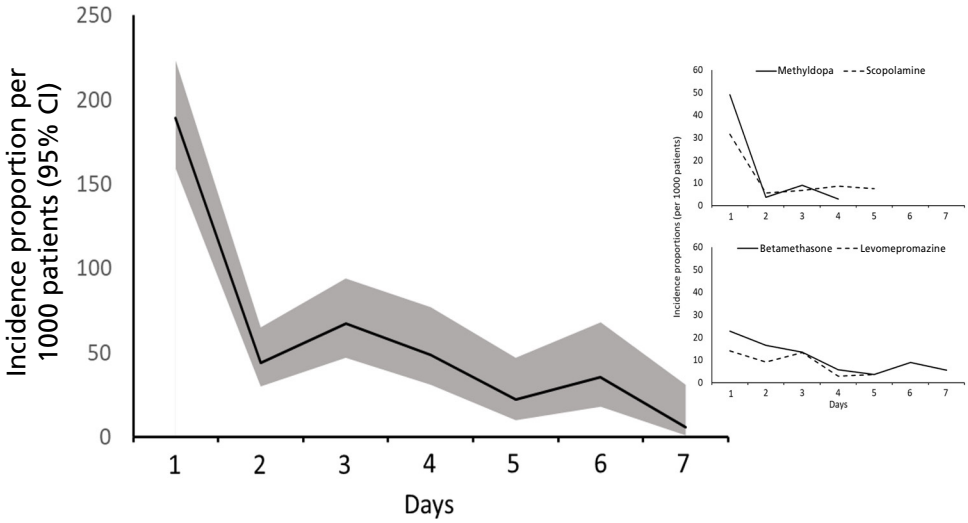

FIGURE 2. Incidence proportions of adverse drug reactions in relation to day of occurrence: overall (at left) and according to the 4 principal drugs (smaller charts at right). CI = confidence interval.

patients. A cross-sectional study carried out in 2 Norwegian maternity hospitals[17] detected a prevalence similar to ours (20.0%); however, the data were obtained only from self-reports by the pregnant women themselves, without other search strategies. None of the cited studies characterized ADRs in terms of their frequency on different days of the hospital stay.

In addition to the daily active search in medical records, another important aspect of our methodology was questioning the patients about suspected ADRs. Less serious ADRs tend not to be described in medical records and, consequently, are underreported.[22] An illustrative example detected in our study was headache related to methyldopa: if a detailed investigation had not been carried out, this ADR might have been attributed to an increase in blood pressure.

The occurrence of ADRs was markedly frequent in the first 24 hours of hospitalization, with a decrease in the following days. Our sample consisted primarily of people admitted with hypertensive peaks and hyperglycemia. About 7.2% of pregnant women manifest at least 1 episode of hypertensive crisis resulting in hospitalization,[18] and among women with gestational diabetes, the proportion of hospital admissions due to hyperglycemia reaches 48%.[23] High blood pressure and high glycemic values can result in pre-eclampsia, hemorrhage, prematurity, and risk of death for the mother and the fetus.[24,25] Therefore, it is a priority to normalize these parameters as soon as possible, which can lead to optimization of doses at the beginning of the hospital stay and thus a lower risk of ADRs. In this context, we highlight the ADR profiles associated with the prescription of methyldopa and scopolamine as examples.

In the first 24 hours, we observed that sedation and headache associated with the use of methyldopa, as well as the anticholinergic effects of scopolamine, were the most common ADRs, similar to what others have reported.[26-28] Methyldopa (ATC class C02A), a first-line antihypertensive drug for gestational hypertension, is commonly associated with sympathetic depression, typically manifesting as a low-severity ADR.[26] We found similar incidences of diplopia, xerostomia, and constipation associated with scopolamine for the treatment of nausea and vomiting (ATC class A04A).[28,29] Therefore, the occurrence of these dose-dependent ADRs is associated with the severity of the condition on admission (peak pressure and gastrointestinal discomfort) and the need for higher doses to control symptoms. As blood pressure values normalized, lower doses were used in the following days and the occurrence of ADRs declined. Also common was excessive sedation related to levomepromazine used as an anxiolytic, as well as hyperglycemia induced by corticosteroids for systemic use (ATC class H02A).[30,31] However, the incidence of these ADRs showed a uniform distribution profile in the first 5 days, probably due to the lower need for higher doses during treatment.

As already observed in other scenarios,[32] as well as with hospitalized pregnant women,[33] we found that longer hospitalization time and a greater number of medications were risk factors for the occurrence of ADRs. Other risk factors reported in the literature, such as older age[7] and multimorbidity,[34,35] were not observed in our study.

Our findings point to the need for greater monitoring of ADRs in the first days of admission, especially in situations where pregnant people need extensive use of antihypertensives and antiemetics to control their symptoms. Despite the predominance of less severe ADRs, as previously observed by other authors,[7,11] these effects manifest for a considerable period of the hospital stay (a median of 3 days) and cause substantial discomfort. It is important to highlight that a hospital stay is a delicate moment for the pregnant person and their family, so optimizing pharmacovigilance actions

and effectively identifying ADRs, with the goal of alleviating discomfort, are essential.

The main limitation of the current study was the collection of data in a single institution. Another limitation relates to the prior selection of drugs commonly associated with ADRs, to direct the active surveillance (step 3 of data collection). This approach may have compromised the detection of less frequent ADRs associated with other drugs. However, some methodological features validated the results, such as the prospective cohort design and the detection of ADRs through daily active search in a substantial sample of patients. Although the ADRs detected were of low severity, potential negative outcomes related to the health of the newborn should be investigated.

CONCLUSION

In this study, 1 out of every 5 hospitalized pregnant people had at least 1 ADR, especially in the first 24 hours, with a decrease in incidence in the following days. ADRs were primarily of low severity and lasted a median of 3 days; the most common ADRs were sedation and headache associated with methyldopa and the anticholinergic effects of scopolamine. Finally, pregnant people with longer hospital stays and those using more medications had a higher risk of ADRs.

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