

**Drug use according to risk classification and associated factors among pregnant women:
results from NISAMI cohort**

**Uso de medicamentos segundo classificação de risco e fatores associados entre gestantes:
resultados da coorte NISAMI**

**Utilización de medicamentos según clasificación de riesgo y factores asociados en
embarazadas: resultados de la cohorte NISAMI**

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Abstract

This study aimed to investigate the factors associated with drug use in pregnancy by risk categories in pregnant women from Santo Antônio de Jesus, Bahia. It is a cross-sectional cohort study with 1,091 pregnant women attended in primary health care between 2012 and 2014. Drug use during pregnancy was classified according to the FDA's pregnancy risk classification. Prevalence ratios and respective 95% confidence intervals were adjusted by Poisson regression with robust error variance. The prevalence of drug use was more pronounced in risk categories A, B, C, D, and X, respectively. The use of safe medication was associated with education,

number of prenatal consultations, and health problems after data adjustment. Age greater than 24 years, onset of prenatal care during the first trimester, and have any health problem were factors associated with the use of risk medication. Quality prenatal care is important to ensure the safe and conscious use of drugs. Furthermore, investments in continuing vocational education that promote rational antenatal drug use are needed.

Keywords: Drug utilization; Pregnancy; Prenatal care; Brazil; Pharmacoepidemiology.

Resumo

Este estudo teve como objetivo investigar os fatores associados ao uso de medicamentos na gestação por categorias de risco em gestantes do município de Santo Antônio de Jesus, Bahia. Trata-se de um estudo transversal aninhado à coorte prospectiva com 1.091 gestantes atendidas na atenção primária à saúde entre 2012 e 2014. A utilização de medicamentos durante a gestação seguiu a classificação dos medicamentos segundo critérios de risco da FDA. As razões de prevalência e seus respectivos intervalos de confiança de 95% foram ajustados por regressão de Poisson com variância robusta. A prevalência do uso de medicamentos foi mais pronunciada nas categorias de risco A, B, C, D e X, respectivamente. Após o ajuste, o uso de medicamentos seguros foi associado à escolaridade, número de consultas pré-natal e problemas de saúde. Idade superior a 24 anos, início do pré-natal no primeiro trimestre e ter algum problema de saúde foram fatores associados ao uso de medicamentos de risco. O pré-natal de qualidade é importante para garantir o uso seguro e consciente dos medicamentos. Além disso, são necessários investimentos em educação profissional continuada que promova o uso racional de medicamentos no período pré-natal.

Palavras-chave: Uso de medicamentos; Gravidez; Cuidado pré-natal; Brasil; Farmacoepidemiologia.

Resumen

Este estudio tuvo como objetivo investigar los factores asociados al uso de medicamentos en el embarazo por categorías de riesgo en gestantes del municipio de Santo Antônio de Jesus, Bahía. Se trata de un estudio transversal anidado en la cohorte prospectiva con 1.091 gestantes atendidas en atención primaria de salud entre 2012 y 2014. El uso de medicamentos durante el embarazo siguió la clasificación de medicamentos según los criterios de riesgo de la FDA. Las razones de prevalencia y sus respectivos intervalos de confianza del 95% se ajustaron mediante regresión de Poisson con varianza robusta. La prevalencia del uso de medicamentos fue más pronunciada en las categorías de riesgo A, B, C, D y X, respectivamente. Después del ajuste, el

uso de medicamentos seguros se asoció con educación, número de consultas prenatales y problemas de salud. Tener más de 24 años, iniciar la atención prenatal en el primer trimestre y tener un problema de salud fueron factores asociados al uso de medicamentos de riesgo. La atención prenatal de calidad es importante para garantizar el uso seguro y consciente de los medicamentos. Además, se necesitan inversiones en educación profesional continua para promover el uso racional de los medicamentos en el período prenatal.

Palabras clave: Utilización de medicamentos; Embarazo; Atención prenatal; Brasil; Farmacoepidemiología.

1. Introduction

The use of medications during pregnancy is a phenomenon that has been described by pharmacoepidemiological studies worldwide, due to its increasing prevalence and insufficient evidence about its effects on the fetus (Daw et al., 2011; Stanley et al., 2019). Its utilization is frequent, as shown in one research carried out in Brazil, in which 94.7% of pregnant women used at least one medication during pregnancy (Kassada et al., 2015). The concern regarding drug use by pregnant women is based on their harmful implications since most drugs cross the placental barrier and consequently expose the embryo to pharmacological effects (Guerra et al., 2008).

Due to the frequent need for drug interventions, the North American Food and Drug Administration (FDA) proposed the classification of drugs according to risk criteria, in an attempt to direct and make the prescription safer. This classification is limited and has been updated because it does not take into account an individual analysis of the drugs used during pregnancy (Andrade et al., 2014; Feibus, 2008; Holmes, 2011), however, it continues to be used, as few studies adopt other risk classifications, thus preventing comparability. In Brazil the percentage of use of drugs included in categories D and X, considered potentially teratogenic, varies from 0.3% to 3.0% (Carmo & Nitrini, 2004; Guerra et al., 2008); concerning category C, in which risk, the probability that a drug will produce adverse effects on a given population (Paumgarten, 1993), cannot be excluded, there is a variation between 17.5% and 33.6% (Brum et al., 2011; Lunardi-Maia et al., 2014).

The effect of drug use during pregnancy is often unpredictable, which is why pharmacoepidemiological studies are developed to look for associations between drug consumption and the development of diseases in childhood and gestational outcomes. In this perspective, the present study aimed to investigate the factors associated with drug use during

pregnancy according to risk classification in women in the municipality of Santo Antônio de Jesus, Bahia, Brazil.

2. Methodology

The present study used data from the research project Maternal Risk Factors for Low Birth Weight, Prematurity and Intrauterine Growth Retardation, in Recôncavo da Bahia, carried out by the Center for Research in Maternal and Child Health (NISAMI) of the Health Sciences Center, Federal University of Recôncavo da Bahia, Brazil. This is a cross-sectional study nested in the prospective cohort of pregnant women who underwent prenatal care at the Unified Health System (SUS) basic health units in the municipality of Santo Antônio de Jesus, from June 2012 to February 2014 (Costa et al., 2017).

The city of Santo Antônio de Jesus, located in the Bahia state, had 90,985 inhabitants, 48,020 females, in 2010 (Instituto Brasileiro de Geografia e Estatística, 2011). The provision of health services took place in 26 primary care units, 38 clinics/specialty centers, five hospitals, two polyclinics, and also attends the 4th Regional Health Directorate.

The research was carried out in all basic health units in the urban area. Basic health units in the rural area were excluded due to the difficulty of access and distance. Thus, all pregnant women aged 18 years or over, residing in the urban area of the municipality, at any gestational age, enrolled in the Monitoring System of the Humanization Program for Prenatal and Birth (SISPRENATAL), and who performed at least one prenatal consultation were included in this study.

The sample size was calculated to provide estimates of the prevalence of some characteristics of interest, the maximum acceptable error was 4 percentage points, adopting the 95% confidence level. To ensure this occurred, the sample was dimensioned considering the prevalence of medication use is in the order of 50%. This is the safest estimate because it corresponds to the largest sample size that can be calculated. The minimum sample required to guarantee statistical significance was 600 pregnant women, given the power of the test equal to 80%.

As other associations were investigated, the largest number of pregnant women was adopted to find an association with the variable prenatal consultations, which totaled 891 women. Adding 10% more pregnant women to compensate for non-responses and losses, the total sample was 1,091 women.

All completed questionnaires were reviewed by the team of supervisors, data validation

was adopted by comparing the information obtained by the questionnaires with those recorded on the prenatal cards. The interviewer, whenever necessary, returned to the patient's home to correct imperfections in the interview. Twenty percent of the pregnant women interviewed were revisited by the field supervisors, who partially reapplied the interview. The data were compared with the original interviews to assess their quality, aiming to identify any inaccuracies, systematic errors, or even fraud. The questionnaires with inaccuracies that could not be corrected were considered a loss.

The data was entered in an entry screen created in the Epidata program, version 3.0 (Epidata Association, Odense, Denmark), with an automatic consistency and amplitude checking system. After reviewing the questionnaires, the information was compiled into a computerized database for further statistical analysis using the Stata program, version 12.0 (StataCorp LP, College Station, United States). Then, the information bank was edited to assess the quality of the data entry process and correct the detected errors. This was done by examining the frequency distribution of each variable to identify out-of-limits values, check for invalid values, identify duplicate entries, and check incompatible or contradictory data.

The use of risk medications and the use of safe medications were considered as dependent variables. Risk medications were those classified as C, D, and X by the FDA, as these include drugs that had adverse effects on the fetus in experimental work on animals, regardless of the evidence in humans. Drugs classified as safe were those placed in categories A and B (Feibus, 2008).

The exposure variables were: maternal age (18 to 24, 25 to 29, 30 to 45 years), education (≤ 8 , 9 to 11, > 11 years of study), skin color (non-black, black), marital status (without a partner, with a partner), family income (> 1 minimum wage, ≤ 1 minimum wage), economic class (A/B, C/D/E), number of previous pregnancies (≥ 2 , <2), onset of prenatal care (during the 1st trimester, after the 1st trimester), number of prenatal consultations (≤ 3 , > 3), history of miscarriage (yes, no), smoking (yes, no), having any health condition (yes, no) – this variable was obtained by grouping the self-reported variables having or not the following pathologies: anemia, asthma, tuberculosis, pneumonia, diabetes, hypertension, kidney disease, urinary tract infection, and bleeding.

The prevalence and frequency of use of risk medications and safe medications during pregnancy were estimated using the total number of pregnant women and the total number of medicines, respectively, according to demographic, socioeconomic, and health characteristics.

A bivariate analysis was carried out to investigate the association between independent variables and the use of risk medications and safe medications during pregnancy. The outcome

measure was expressed by the prevalence ratio (PR) with a 95% confidence interval (95% CI). Variables with $p \leq 0.20$ in the crude analysis were introduced in the Poisson regression model using the stepwise selection. The final model was composed of the variables that remained significant after adjustment for the other variables ($p \leq 0.05$).

Multivariate models were adjusted to calculate the adjusted PR (aPR) estimated by Poisson regression with robust variance, with 95% CI (Barros & Hirakata, 2003). Stata version 12.0 (Stata Corporation, College Station, USA) was used for data analysis.

The research Maternal Risk Factors for Low Birth Weight, Prematurity and Intrauterine Growth Retardation, in Recôncavo da Bahia was submitted and approved by the Ethics and Research Committee of the Adventist Physiotherapy Faculty of Bahia (FAFIS) (Protocol No. 4369.0.000.070-10). Pregnant women were instructed on the purposes of the research and its methodology and informed about the confidentiality of the data by the Informed Consent Form, which contained explicit information about the nature and objectives of the study. The interviews were conducted only after signing the Informed Consent Form.

3. Results

A total of 1,091 pregnant women participated in this study. The age of the pregnant women ranged between 18 and 45 years, with an average of 25.5 years ($SD \pm 6.21$) and a median of 25 years. Approximately 50,00% of pregnant women had less than nine years of study, 84.70% were black, and 23.50% earned less than one minimum wage. Half of the women in this study had no previous pregnancy ($n = 547$), 61.10% ($n = 662$) reported not having planned their pregnancy, and 24.00% had a history of miscarriage. Eight-three percent of pregnant women started prenatal care in the 1st trimester with an average of 3.30 ± 3.02 consultations (Table 1). At the time of the interview, 44.00% ($n = 466$) of the women were between the 13th and 24th weeks of gestation.

Table 1. General characteristics of the population and distribution of drugs consumed during pregnancy according to risk classification criteria. Santo Antônio de Jesus, Bahia, 2012-2014 (n = 1,091)*.

Socioeconomic and health characteristics	n = 1,091		Drug risk categories A/B		Drug risk categories C/D/X	
	n	%	n	%	n	%
Maternal age (years)						
≤ 24	509	46.65	396	77.80	100	19.65
25 to 29	290	26.58	231	79.66	84	28.97
≥ 30	292	26.76	237	81.16	90	30.82
Education (years)						
≤ 8	539	49.54	403	74.77	100	19.65
9 to 11	487	44.76	404	82.96	84	28.97
> 11	62	5.70	55	88.71	90	30.82
Skin color						
Non-black	162	15.31	132	81.48	44	27.16
Black	896	84.69	705	78.68	217	24.22
Marital status						
Without a partner	189	17.34	723	80.24	232	25.75
With a partner	901	82.66	140	74.07	42	22.22
Family income						
≤ 1 minimum wage	245	23.54	191	77.96	53	21.63
> 1 minimum wage	796	76.46	634	79.65	212	26.63
Economic class						
A/B	110	14.77	84	76.36	27	24.55
C/D/E	635	85.23	475	74.80	143	22.52
Previous pregnancies						
< 2	854	78.49	687	80.44	208	24.36
≥ 2	234	21.51	175	74.79	66	28.21
Onset of prenatal care						
During the 1st trimester	860	83.01	711	82.67	232	26.98
After the 1st trimester	176	16.99	124	70.45	27	15.34
Prenatal consultations						
≤ 3 consultations	669	61.32	470	70.25	167	24.96
> 3 consultations	422	38.68	394	93.36	107	25.36
History of miscarriage						
No	714	75.48	566	79.27	177	24.79
Yes	232	24.52	182	78.45	63	27.16
Smoking						
No	1040	96.56	822	79.04	257	24.71
Yes	37	3.44	30	81.08	13	35.14
Health problems**						
No	535	49.68	401	74.95	152	28.04
Yes	542	50.32	452	83.39	117	21.87

* There are losses in some variables ** Anemia, asthma, tuberculosis, pneumonia, diabetes, hypertension, kidney disease, urinary tract infection, and bleeding.
Source: own study.

According to the FDA's risk classification, pregnant women used drugs from all categories, with distribution described in Figure 1. The drugs most used by pregnant women in category A were folic acid (62.60%, n = 683) and ferrous sulfate (49.30%, n = 538), in category B were paracetamol (19.00%, n = 207) and dimenhydrinate (6.05%, n = 71), in category C were the drugs that contained in their formulation scopolamine (15.9%, n = 174) and metamizole (7.70%, n = 84), in category D was progesterone (2.65%, n = 29), and in category X were the combined oral contraceptives (0.18%, n = 2). A total of 275 pregnant women (25.21%) used some type of medication considered to be high risk and 71 (25.70%) reported self-medication.

Figure 1. Distribution of medication use by pregnant women according to the FDA's risk classification system, Santo Antônio de Jesus, 2012 - 2014.

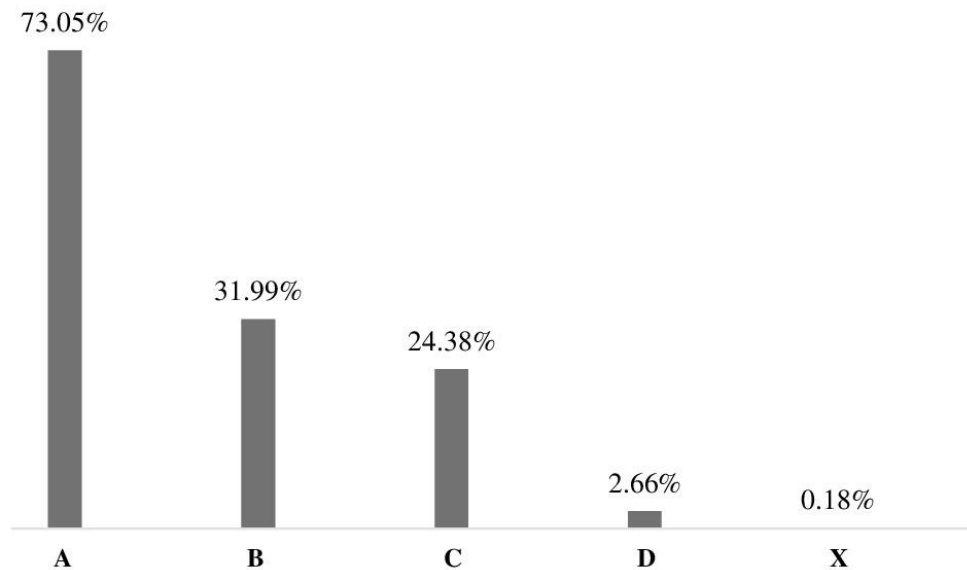


Figure 1 shows the distribution of medication use in the population according to the FDA's risk classification system. A: No risk in controlled human studies; B: No risk in animal reproduction studies; C: Adverse effect on the fetus in animal reproduction studies; D: Positive evidence of risk; X: Fetal abnormalities in animal or human studies. Source: own study.

The factors associated with the use of risk medications, both in the crude analysis and in the final adjustment of the model, were age older than 24 years, onset of prenatal care during the first trimester, and having some health condition (Tables 2 and 3).

Table 2. Crude prevalence ratios for the use of drugs consumed during pregnancy according to risk classification criteria. Santo Antônio de Jesus, Bahia, 2012-2014 (n = 1,091)*.

	Drug risk categories A/B			Drug risk categories C/D/X		
	cPR	95% CI	P-value	cPR	95% CI	P-value
Maternal age (years)						
≤ 24	1.00			1.00		
25 to 29	1.02	0.95 – 1.10	0.539	1.47	1.14 – 1.89	0.002
≥ 30	1.04	0.97 – 1.12	0.260	1.56	1.22 – 2.00	0.003
Education (years)						
≤ 8	1.00			1.00		
9 to 11	1.10	1.04 – 1.18	0.001	1.19	0.96 – 1.47	0.096
> 11	1.18	1.07 – 1.31	0.014	1.12	0.71 – 1.75	0.621
Skin color						
Non-black	1.00			1.00		
Black	0.96	0.89 – 1.04	0.420	0.89	0.67 – 1.17	0.424
Marital status						
Without a partner	1.00			1.00		
With a partner	1.08	0.98 – 1.18	0.057	1.15	0.86 – 1.54	0.309
Family income						
≤ 1 minimum wage	1.00			1.00		
> 1 minimum wage	1.02	0.94 – 1.10	0.568	1.23	0.94 – 1.60	0.116
Economic class						
A/B	1.02	0.91 – 1.14	0.727	1.08	0.76 – 1.55	0.640
C/D/E	1.00			1.00		
Previous pregnancies						
< 2	0.92	0.85 – 1.00	0.058	1.15	0.91 – 1.46	0.229
≥ 2	1.00			1.00		
Onset of prenatal care						
During the 1st trimester	1.00			1.00		
After the 1st trimester	1.17	1.06 – 1.29	0.000	1.75	1.22 – 2.53	0.001
Prenatal consultations						
≤ 3 consultations	1.00			1.00		
> 3 consultations	1.32	1.25 – 1.40	0.000	1.01	0.82 – 1.25	0.884
History of miscarriage						
No	1.00			1.00		
Yes	0.98	0.91 – 1.06	0.788	1.09	0.85 – 1.40	0.472
Smoking						
No	1.00			1.00		
Yes	1.02	0.87 – 1.20	0.763	1.42	0.90 – 2.23	0.150
Health problems**						
No	1.00			1.00		
Yes	1.11	1.04 – 1.18	0.000	1.28	1.04 – 1.58	0.019

* There are losses in some variables ** Anemia, asthma, tuberculosis, pneumonia, diabetes, hypertension, kidney disease, urinary tract infection, and bleeding.
Source: own study

More than 9 years of study, onset of prenatal care during the first trimester, having had more than three prenatal consultations, and having some health condition were associated with the use of safe drugs in the crude analysis; however, after adjusting, only education, number of prenatal consultations, and having some health condition remained in the model (Tables 2 and 3).

Table 3. Adjusted prevalence ratios for the use of drugs consumed during pregnancy according to risk classification criteria. Santo Antônio de Jesus, Bahia, 2012-2014 (n = 1,091)*.

	Drug risk categories A/B			Drug risk categories C/D/X		
	aPR	95% CI	p-value	aPR	95% CI	p-value
Maternal age (years)						
≤ 24				1.00		
25 to 29				1.43	1.09 – 1.86	0.008
≥ 30				1.49	1.15 – 1.93	0.002
Education (years)						
≤ 8	1.00					
9 to 11	1.08	1.02 – 1.15	0.009			
> 11	1.18	1.07 – 1.31	0.001			
Onset of prenatal care						
During the 1st trimester				1.00		
After the 1st trimester				1.61	1.11 – 2.34	0.011
Prenatal consultations						
≤ 3 consultations	1.00					
> 3 consultations	1.31	1.24 – 1.38	0.000			
Health problems**						
No	1.00			1.00		
Yes	1.08	1.02 – 1.15	0.006	1.36	1.09 – 1.68	0.005

* There are losses in some variables ** Anemia, asthma, tuberculosis, pneumonia, diabetes, hypertension, kidney disease, urinary tract infection, and bleeding.
 Source: own study.

4. Discussion

The prevalence of medication use was more frequent in risk category A (73.05%), followed by B (31.99%), C (24.38%), D (2.66%), and X (0.18%). Similar to our findings, the prevalence of use of medicines of risk category A reported were 42.70% in the northeast of Brazil, 53.40% in a municipality in the state of Rio Grande do Sul, and 69.30% in the state of Acre (Andrade et al., 2014; Brum et al., 2011; Guerra et al., 2008). The data in the international literature is still controversial, while some studies show greater use of drugs in risk category A (Alema et al., 2020; Molla et al., 2017; Mosha et al., 2014; Odalovic et al., 2012), others point

to higher consumption of drugs in classes B and C (Cleary et al., 2010; Irvine et al., 2010; Leke et al., 2018; Zhang et al., 2019).

Although the methodological differences between the studies, it appears that in Santo Antônio de Jesus the consumption of class A drugs during pregnancy was greater than that found in the cited studies. Considering anemia during pregnancy was reported by 27.84% of the study participants, there is high prophylactic consumption of antianemic drugs, which increases the prevalence of the use of class A drugs.

It was found that about 25.00% of pregnant women used one or more drugs in the FDA risk categories C, D, or X during pregnancy. These data are similar to most studies carried out in Brazil, in which the prevalence varies from 17.50% to 29.00% (Brum et al., 2011; Carmo & Nitrini, 2004; Guerra et al., 2008; Maeda & Secoli, 2008; Osorio-de-Castro et al., 2004). In the international literature, an Ethiopian study found a prevalence of drug dispensing of these risk classes of 20.00% (Alema et al., 2020). In an Irish pilot study, the observed prevalence of use of these drugs was 32.40% (Dillon et al., 2015).

Most of the risk medications used belong to the FDA's category C, including scopolamine and metamizole in combination or alone. Metamizole is the analgesic most consumed by pregnant women in Brazil; however, its commercialization is prohibited in some European countries and the United States due to associations with serious adverse events, for this reason, the literature recommends the use of acetaminophen for analgesia during pregnancy (Couto et al., 2015; Dathe et al., 2019; Toda, 2017).

Only 2.74% of pregnant women used medications in classes D and X, with progesterone being the most prescribed medication in these classes. Possibly, the prescription of this drug may have been done intentionally in early pregnancy, in an attempt to prevent miscarriage. A systematic review and meta-analysis concluded that the use of progesterone in the first trimester of pregnancy may be effective in women with a history of recurrent spontaneous abortions (Saccone et al., 2017).

In the present study, being over 24 years-old had a positive effect on the use of risk medications during pregnancy. Research conducted in the city of Rio Branco, in the state of Acre, found an odds ratio of 2.07 for the association between the use of risk medications and pregnant women between 25 and 43 years old (Andrade et al., 2014). In the Rio Grande do Sul state, an odds ratio of 1.63 was observed for pregnant women over 20 years old (Geib et al., 2007). In a study conducted in Ireland, in which only the use of risk medications included in classes D/X was evaluated, an association with maternal age greater than 25 years was also found (Cleary et al., 2010).

Pregnant women with more than nine years of education had an increased prevalence of safe medication use. This may suggest that those women are following prescriptions more closely or pregnant women with less education may be neglecting treatment, exposing themselves to pathologies such as anemia or folic acid deficiency. Although category A/B medications are considered to be risk-free, supervision by health professionals is necessary to ensure adequate therapy for pregnant women with less education, as the lack of understanding of the prescriptions can influence adherence and treatment effectiveness (Ferreira et al., 2011).

A greater number of prenatal consultations was associated with a higher prevalence of risk-free medication consumption, which highlights the importance of health professionals monitoring in preventing pregnancy complications, fetal impairment, and relieving symptoms related to early pregnancy, especially given this class being constituted of antianemic drugs, vitamins, analgesics, and medicines for nausea (Geib et al., 2007).

In contrast with what was found in the present study, in which there was no association between prenatal care and the use of risk medications, a Brazilian research observed that having performed more than 6 prenatal consultations was associated with the use of risk medications (aOR 1.78 CI 95% 1.33-2.38) (Andrade et al., 2014). However, in our study, early onset of prenatal care increased the prevalence of risk medications use. This suggests that pregnant women who seek health care at the beginning of pregnancy may already have health problems or some gestational complications that expose them to greater use of risk medications.

Having health problems during pregnancy was associated with the use of risk and safe medications. A study performed in Cameroon indicated that the consumption of medications is higher among pregnant women with health problems (Leke et al., 2018). Regarding the use of safe medications, this may have been driven by a need for pharmacological treatment (Nordeng et al., 2001), confirming once again the importance of monitoring pregnant women to ensure adequate treatment of their chronic or acute pathologies (Narayan & Nelson-Piercy, 2017; Osorio-de-Castro et al., 2004).

The association between having health problems and the use of risk medications is corroborated by the literature, in which problems during pregnancy also increased this prevalence. In a study carried out in Canada, pregnant women with chronic diseases were four times more likely to be exposed to these drugs when compared to women without chronic diseases (Yang et al., 2008). In an American study, an association between problems in pregnancy and the use of risk medications (aOR 2.5; 95% CI 0.70-8.50) was found (Lee et al., 2006). Also, it was observed that health complications during pregnancy were associated with a greater risk of using drugs in risk category C (aOR 3.04, 95% CI 2.29-4.04) and category D

(aOR 5.78; 95% CI 1.36-24.62) (Geib et al., 2007).

The current study presents as possible limitations the recall bias concerning the use of medications throughout pregnancy, which can lead to an underestimation in the prevalence of outcomes. To minimize the problem, procedures were adopted, such as the use of a standardized and tested questionnaire, well-trained staff, standardization of data collection, and data validation by comparing the information obtained from the questionnaires with those recorded on the prenatal cards.

Considering the study was carried out only in the urban area of the city, due to the difficulties faced for collection in the rural area, and captured only pregnant women who attended basic health units, this work does not represent the totality of pregnant women in the city.

5. Conclusion

The use of risk medications was associated with pregnant women over 24 years old, with the beginning of prenatal care in the first trimester, and with the presence of health problems, indicating the importance of quality prenatal care to ensure the safe and conscious use of these drugs. Furthermore, it is necessary to develop scientific evidence capable of promoting continuous improvement in the quality of maternal and child care, in addition to investments in continuing professional education that promote the rational use of medications in the prenatal period.

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References

Alema, N. M., Semagn, G., Melesse, S., Araya, E. M., Gebremedhin, H., Demsie, D. G., Asgedom, S. W., & Weldekidan, E. (2020). Patterns and determinants of prescribed drug use

among pregnant women in Adigrat general hospital, northern Ethiopia: a cross-sectional study. *BMC Pregnancy and Childbirth*, 20(1). <https://doi.org/10.1186/s12884-020-03327-7>

Andrade, A. M., Ramalho, A. A., Koifman, R. J., Dotto, L. M. G., Cunha, M. A., & Opitz, S. P. (2014). Fatores associados ao uso de medicamentos na gestação em primigestas no Município de Rio Branco, Acre, Brasil. *Cadernos de Saúde Pública*, 30(5), 1042–1056. <https://doi.org/10.1590/0102-311X00172412>

Barros, A. J., & Hirakata, V. N. (2003). Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. *BMC Medical Research Methodology*, 3(1), 21. <https://doi.org/10.1186/1471-2288-3-21>

Brum, L. F. da S., Pereira, P., Felicetti, L. L., & da Silveira, R. D. (2011). Utilização de medicamentos por gestantes usuárias do sistema único de saúde no município de Santa Rosa (RS, Brasil). *Ciencia e Saude Coletiva*, 16(5), 2435–2442. <https://doi.org/10.1590/s1413-81232011000500012>

Carmo, T. A., & Nitrini, S. M. O. O. (2004). Prescrições de medicamentos para gestantes: um estudo farmacoepidemiológico. *Cadernos de Saúde Pública*, 20(4), 1004–1013. <https://doi.org/10.1590/S0102-311X2004000400015>

Cleary, B. J., Butt, H., Strawbridge, J. D., Gallagher, P. J., Fahey, T., & Murphy, D. J. (2010). Medication use in early pregnancy-prevalence and determinants of use in a prospective cohort of women. *Pharmacoepidemiology and Drug Safety*, 19(4), 408–417. <https://doi.org/10.1002/pds.1906>

Costa, D. B., Coelho, H. L. L., & Santos, D. B. dos. (2017). Utilização de medicamentos antes e durante a gestação: prevalência e fatores associados. *Cadernos de Saúde Pública*, 33(2). <https://doi.org/10.1590/0102-311x00126215>

Couto, A. C., Ferreira, J. D., Pombo-de-Oliveira, M. S., & Koifman, S. (2015). Pregnancy, maternal exposure to analgesic medicines, and leukemia in Brazilian children below 2 years of age. *European Journal of Cancer Prevention : The Official Journal of the European Cancer*

Prevention Organisation (ECP), 24(3), 245–252.
<https://doi.org/10.1097/CEJ.0000000000000070>

Dathe, K., Hultsch, S., Pritchard, L. W., & Schaefer, C. (2019). Risk estimation of fetal adverse effects after short-term second trimester exposure to non-steroidal anti-inflammatory drugs: a literature review. *European Journal of Clinical Pharmacology*. <https://doi.org/10.1007/s00228-019-02712-2>

Daw, J. R., Hanley, G. E., Greyson, D. L., & Morgan, S. G. (2011). Prescription drug use during pregnancy in developed countries: a systematic review. *Pharmacoepidemiology and Drug Safety*, 20(9), 895–902. <https://doi.org/10.1002/pds.2184>

Dillon, P., O'Brien, K. K., McDonnell, R., Donnelly-Swift, E., Galvin, R., Roche, A., Cronin, K., Walsh, D. R., Schelten, R., Smith, S., & Fahey, T. (2015). Prevalence of prescribing in pregnancy using the Irish primary care research network: a pilot study. *BMC Pregnancy and Childbirth*, 15(1), 67. <https://doi.org/10.1186/s12884-015-0489-0>

Feibus, K. B. (2008). FDA's Proposed Rule for Pregnancy and Lactation Labeling: Improving maternal child health through well-informed medicine use. *Journal of Medical Toxicology*, 4(4), 284. <https://doi.org/10.1007/BF03161214>

Ferreira, V. D. O. G., Melnikov, P., & Kadri, M. C. T. (2011). Nível de entendimento de prescrições medicamentosas pediátricas em Unidades Básicas de Saúde. *Revista Brasileira Saúde Materno Infantil*, 11(3), 249–256.

Geib, L. T. C., Vargas Filho, E. F., Geib, D., Mesquita, D. I., & Nunes, M. L. (2007). Prevalência e determinantes maternos do consumo de medicamentos na gestação por classe de risco em mães de nascidos vivos. *Cadernos de Saúde Pública*, 23(10), 2351–2362. <https://doi.org/10.1590/S0102-311X2007001000010>

Guerra, G. C. B., Silva, A. Q. B. da, França, L. B., Assunção, P. M. C., Cabral, R. X., & Ferreira, A. A. de A. (2008). Utilização de medicamentos durante a gravidez na cidade de Natal, Rio Grande do Norte, Brasil. *Revista Brasileira de Ginecologia e Obstetrícia*, 30(1), 12–18. <https://doi.org/10.1590/S0100-72032008000100003>

Holmes, L. B. (2011). Human teratogens: Update 2010. *Birth Defects Research Part A: Clinical and Molecular Teratology*, 91(1), 1–7. <https://doi.org/10.1002/bdra.20748>

Instituto Brasileiro de Geografia e Estatística. (2011). Censo Demográfico - 2010: Características da população e dos domicílios. <http://cidades.ibge.gov.br/painel/painel.php?lang=&codmun=292870&search=bahia%7Csant%7Cantonio-de-jesus%7Cinfograficos:-dados-gerais-do-municipio>

Irvine, L., Flynn, R. W. V., Libby, G., Crombie, I. K., & Evans, J. M. M. (2010). Drugs dispensed in primary care during pregnancy: A record-linkage analysis in tayside, Scotland. *Drug Safety*, 33(7), 593–604. <https://doi.org/10.2165/11532330-000000000-00000>

Kassada, D. S., Miasso, A. I., Waidman, M. A. P., Marcon, S. S., Kassada, D. S., Miasso, A. I., Waidman, M. A. P., & Marcon, S. S. (2015). Prevalence and factors associated with drug use in pregnant women assisted in primary care. *Texto & Contexto - Enfermagem*, 24(3), 713–721. <https://doi.org/10.1590/0104-07072015002770013>

Lee, E., Maneno, M. K., Smith, L., Weiss, S. R., Zuckerman, I. H., Wutoh, A. K., & Xue, Z. (2006). National patterns of medication use during pregnancy. *Pharmacoepidemiology and Drug Safety*, 15(8), 537–545. <https://doi.org/10.1002/pds.1241>

Leke, A. Z., Dolk, H., Loane, M., Casson, K., Maboh, N. M., Maeya, S. E., Dibo Ndumbe, L., Nyenti, P. B., Armstrong, O., & Etiendem, D. (2018). First trimester medication use in pregnancy in Cameroon: a multi-hospital survey. *BMC Pregnancy and Childbirth*, 18(450). <https://doi.org/10.1186/s12884-018-2081-x>

Lunardi-Maia, T., Schuelter-Trevisol, F., Galato, D., Lunardi-Maia, T., Schuelter-Trevisol, F., & Galato, D. (2014). Uso de medicamentos no primeiro trimestre de gravidez: avaliação da segurança dos medicamentos e uso de ácido fólico e sulfato ferroso. *Revista Brasileira de Ginecologia e Obstetrícia*, 36(12), 541–547. <https://doi.org/10.1590/So100-720320140005051>

Maeda, S. T., & Secoli, S. R. (2008). Use and cost of medication in low risk pregnant women. 16(2).

Molla, F., Assen, A., Abrha, S., Masresha, B., Gashaw, A., Wondimu, A., Belete, Y., & Melkam, W. (2017). Prescription drug use during pregnancy in Southern Tigray region, North Ethiopia. *BMC Pregnancy and Childbirth*, 17(1), 170. <https://doi.org/10.1186/s12884-017-1359-8>

Mosha, D., Mazuguni, F., Mrema, S., Abdulla, S., & Genton, B. (2014). Medication exposure during pregnancy: a pilot pharmacovigilance system using health and demographic surveillance platform. *BMC Pregnancy and Childbirth*, 14(1), 322. <https://doi.org/10.1186/1471-2393-14-322>

Narayan, B., & Nelson-Piercy, C. (2017). Medical problems in pregnancy. *Clinical Medicine*, 17(3), 251–257.

Nordeng, H., Eskild, A., Nesheim, B.-I., Aursnes, I., & Jacobsen, G. (2001). Drug use during early pregnancy. *European Journal of Clinical Pharmacology*, 57(3), 259–263. <https://doi.org/10.1007/s002280100304>

Odalovic, M., Vezmar Kovacevic, S., Ilic, K., Sabo, A., & Tasic, L. (2012). Drug use before and during pregnancy in Serbia. *International Journal of Clinical Pharmacy*, 34(5), 719–727. <https://doi.org/10.1007/s11096-012-9665-8>

Osorio-de-Castro, C. G. S., Paumgarten, F. J. R., & Silver, L. D. (2004). O uso de medicamentos na gravidez. *Ciência & Saúde Coletiva*, 9(4), 987–996. <https://doi.org/10.1590/S1413-81232004000400019>

Paumgarten, Francisco J. R.. (1993). Risk assessment for chemical substances: the link between toxicology and public health. *Cadernos de Saúde Pública*, 9(4), 439-447. <https://doi.org/10.1590/S0102-311X1993000400004>

Saccone, G., Schoen, C., Franasiak, J. M., Scott, R. T., & Berghella, V. (2017). Supplementation with progestogens in the first trimester of pregnancy to prevent miscarriage in women with unexplained recurrent miscarriage: a systematic review and meta-analysis of

randomized, controlled trials. *Fertility and Sterility*, 107(2), 430-438.e3.
<https://doi.org/10.1016/j.fertnstert.2016.10.031>

Stanley, A. Y., Durham, C. O., Sterrett, J. J., & Wallace, J. B. (2019). Safety of Over-the-Counter Medications in Pregnancy. *MCN, The American Journal of Maternal/Child Nursing*, 44(4), 196–205. <https://doi.org/10.1097/NMC.0000000000000537>

Toda, K. (2017). Is acetaminophen safe in pregnancy? *Scandinavian Journal of Pain*, 17(1), 445–446. <https://doi.org/10.1016/j.sjpain.2017.09.007>

Yang, T., Walker, M. C., Krewski, D., Yang, Q., Nimrod, C., Garner, P., Fraser, W., Olatunbosun, O., & Wen, S. W. (2008). Maternal characteristics associated with pregnancy exposure to FDA category C, D, and X drugs in a Canadian population. *Pharmacoepidemiology and Drug Safety*, 17(3), 270–277. <https://doi.org/10.1002/pds.1538>

Zhang, J., Ung, C. O. L., Guan, X., & Shi, L. (2019). Safety of medication use during pregnancy in mainland China: Based on a national health insurance database in 2015. *BMC Pregnancy and Childbirth*, 19(1). <https://doi.org/10.1186/s12884-019-2622-y>

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