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Evaluation of the Use of Anti-Inflammatory, Analgesics, and Antipyretics during Pregnancy: A Population Cohort Study in a Capital City of the North Region of Brazil

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: To analyze the use of anti-inflammatory drugs and the associated factors, including educational level, number of prenatal visits, and food insecurity, during pregnancy.
Study Desing: Population-based cross-sectional study.
Place and Durationof Study: The sample were recruited in two maternity hospitals of Rio Branco, Acre, Brazil. The Santa Juliana Hospital and Maternity (HSJ) and the Bárbara Heliodora Maternity in April 6 and July 10, 2015
Methodology: Demographic, socioeconomic, reproductive, maternal habits, prenatal care, and newborn status were investigated. Multivariate analysis with logistic regression was performed, considering $p<0.05$ for association.
Results: 1190 postpartum women were interviewed. Anti-inflammatories were not used by only 13.2% of pregnant women. The prevalence of dipyrone use was 72.7%, paracetamol 50.3%, nimesulide 16.1%, and diclofenac 5.2%. Women with lower educational levels (up to high school OR=1.55, 95% CI 1.07-2.25), those who consumed alcohol (OR=1.96, 95% CI 1.03-3.73), and those with a higher number of living children (more than 4 children OR=1.6, 95% CI 1.06-2.24, 2 to 3 children OR=1.52, 95% CI 1.10-2.27) had a higher chance of using anti-inflammatories during pregnancy. Primiparous women (OR=0.66, 95% CI 0.47-0.93), those with more than eight prenatal visits (OR=0.55, 95% CI 0.35-0.85), and those experiencing moderate to severe food insecurity (OR=0.42, 95% CI 0.25-0.69) had a lower chance of using anti-inflammatories during pregnancy. After adjusted analysis, alcohol consumption and the number of living children lost statistical significance and were not included in the final model as independent variables.
Conclusion: The prevalence of anti-inflammatory use was high. Alternative therapies and restricting prescriptions to necessary cases could be proposed to reduce the use of non-steroidal anti-inflammatory drugs (NSAIDs) during pregnancy.

Keywords: Anti-inflamatórios; gestantes; pré-natal, pregnancy.

1. INTRODUCTION

Medications with anti-inflammatory, analgesic, and antipyretic properties serve multiple physiological functions, often overlapping in their efficacy. While certain drugs may excel in one aspect over another, their shared mechanism of action—primarily the inhibition of cyclooxygenases (COX-1 and COX-2) and subsequent suppression of prostaglandin synthesis allow them to effectively address pain, inflammation, and fever across the spectrum [1].

In the context of pregnancy, where ensuring the safety of both the mother and the developing fetus is paramount, the decision to utilize such medications demands a careful, personalized approach. Factors such as the specific risks associated with the medication, the gestational period, optimal dosage, and duration of therapeutic intervention must be meticulously considered. Recognizing the inherent risks accompanying the use of any pharmacological agent, a thorough evaluation of the potential benefits against these risks becomes imperative [2].

Conditions during pregnancy that may necessitate the use of these therapeutic agents are commonplace, including complaints such as lower back pain, headaches, leg pain, and fever resulting from infections [3]. Importantly, it should be noted that alternative therapies exist for some of these conditions, offering a medication-free approach that also prepares the body for the anticipated changes associated with pregnancy. This approach becomes crucial in minimizing exposure to medications, as their potential adverse effects on the reproductive cycle warrant further in-depth exploration [4].

Non-steroidal anti-inflammatory drugs (NSAIDs), including ibuprofen and aspirin, are commonly used analgesics and antipyretics. Their mechanism involves the inhibition of

prostaglandin synthesis, which, while effective in managing symptoms, can pose significant risks during pregnancy. For instance, NSAIDs are known to affect the fetal cardiovascular system, particularly causing premature closure of the ductus arteriosus, a vital part of fetal circulation [5]. Additionally, the use of these medications during the third trimester is associated with an increased risk of prolonged labor and postpartum hemorrhage due to their effect on platelet function and uterine contractility [6].

Paracetamol, also known as acetaminophen, is another widely used analgesic and antipyretic considered safer for use during pregnancy. However, recent studies have raised concerns about its potential association with neurodevelopmental disorders in children when used extensively during pregnancy. Despite being a first-line treatment for fever and mild to moderate pain, its use should be carefully monitored and limited to the lowest effective dose [7].

The prevalence of self-medication during pregnancy is a significant public health concern. Many pregnant women opt to self-medicate due to the ease of access to over-the-counter medications and the commonality of ailments such as headaches and back pain. This behavior underscores the need for better education and counseling regarding the risks and safe practices associated with medication use during pregnancy. Healthcare providers play a crucial role in guiding pregnant women to make informed decisions about their health and the health of their unborn children [8-10].

In Brazil, the use of medications during pregnancy is influenced by various factors, including socioeconomic status, access to healthcare, and cultural practices. Studies have shown that women with lower educational levels and those with limited access to healthcare services are more likely to self-medicate. This highlights the disparities in healthcare access and the need for targeted interventions to educate and support these vulnerable populations [9].

This article seeks to delve into the prevalence of anti-inflammatory, analgesic, and antipyretic use during pregnancy, along with the associated factors, focusing on data from the municipality of Rio Branco/AC in the year 2015. Understanding the patterns of medication use and the underlying factors can inform public health strategies to improve maternal and fetal health outcomes.

The decision-making process regarding medication use during pregnancy is complex and multifaceted. It involves not only the clinical assessment of the benefits and risks but also the social, cultural, and economic contexts in which pregnant women live [9]. Therefore, a comprehensive approach that includes medical guidance, patient education, and supportive policies is essential to ensure the safe use of medications during pregnancy [10,11].

The primary aim of this study is to analyze the utilization of anti-inflammatory drugs and associated factors among pregnant women in Rio Branco, AC. By examining demographic, socioeconomic, reproductive, and maternal health variables, we aim to identify the determinants of medication use and the potential risks involved. This knowledge is crucial for developing targeted interventions to promote safe medication practices and ultimately improve the health of mothers and their babies. The findings of this study are crucial for the development of public policies and clinical practices aimed at reducing the inappropriate use of anti-inflammatory drugs during pregnancy. Understanding the factors associated with their use can guide health education strategies and interventions to promote safer practices.

2. METHODOLOGY

2.1 Study Design

This study employs a cross-sectional, population-based design.

2.2 Population and Sample

Rio Branco, the capital of the state of Acre, had an estimated population of 377,057 inhabitants in 2015, with the majority residing in the urban area (89.4%). The city hosts two maternity hospitals: the Santa Juliana Hospital and Maternity (HSJ) and the Bárbara Heliodora Maternity, the latter serving only the public system. The sample was based on 6,943 deliveries in these hospitals in 2014. With a 3% sampling error, 80% test power, and an estimated odds ratio of 2.0, 926 pregnant women were initially required. The final sample included 1,190 postpartum women. The inclusion criteria was who gave birth between April and July 2015, residing in the urban area of Rio Branco/AC, were included. However, women

with cognitive conditions that prevented them from understanding the instrument were excluded.

2.3 Instruments

Data were collected through interviews with postpartum women and medical record reviews. A standardized and semi-structured research questionnaire was used. Interviews were conducted by trained interviewers, including undergraduate students and/or professionals in health-related fields, who underwent prior training and were financially supported during the data collection period. The questionnaire used in this study was developed based on instruments validated in previous research on medication use during pregnancy called “Nascer no Brasil” after transcultural validation. The content validity was reviewed by experts in maternal health, ensuring the relevance and appropriateness of the questions for the study context.

2.4 Data Collection Procedures

Data collection occurred between April 6 and July 10, 2015, at the two maternity hospitals in the municipality, specifically among parturients residing in the urban area. Pregnant women were identified through the hospital admission record, invited to participate in the research, and asked to sign an informed consent form. Interviews took place within 24 hours after delivery. The collected information was reviewed, coded, and entered into the database. Inconsistencies were addressed through questionnaire review and/or telephone contact with the parturients.

2.5 Statistical Procedures

Data analysis was performed using IBM SPSS 22.0 for Windows. The study began with a description of the study population using prevalence for each independent variable. The outcome's prevalence was measured according to the studied variables. Both crude and adjusted analyses were conducted using logistic regression to calculate odds ratios and 95% confidence intervals (95% CI). Variables with a p-value < 0.05 in Wald tests were considered associated with the outcome.

3. RESULTS

Of the 1,190 pregnant women in the sample, the majority were aged between 25 and 34 years (38.7%), had completed high school (51.3%), had an income above 1.5 minimum wages (56.4%), belonged to economic classes C, D, or E (79.4%), and reported having a partner (84.0%) (Table 1). Regarding prenatal care, most pregnant women received it in the public health system (85.1%), with six or more consultations (60.7%), and 63.4% reported unplanned pregnancies. The majority of pregnant women were multiparous (60.7%) and reported having 2 to 3 living children (31.1%). Smoking was reported by 9.6% of these women, 12.3% reported alcohol consumption, and only 10.7% engaged in physical activity during pregnancy. The prevalence of cesarean section was 48.0% (Table 1).

Only 13.2% of the respondents did not use anti-inflammatory drugs during pregnancy. The prevalence of dipyrone use was 72.7%, paracetamol 50.3%, nimesulide 16.1%, and diclofenac 5.2%. It is noteworthy that 46.0% of the women reported using two or more of these drugs during pregnancy (Table 1).

The frequency of anti-inflammatory drug use varied according to the type of medication. For dipyrone, the proportion was higher when the pregnant woman had completed lower secondary and upper secondary education, belonged to economic classes C, D, or E, had fewer prenatal consultations, consumed alcoholic beverages during pregnancy, did not engage in physical activity, was not a primipara, and had a higher number of living children. The use was higher among those who had prenatal care in the public health system (Table 2).

The proportion of paracetamol consumption was higher when pregnancy was unplanned and lower among pregnant women with one living child (Table 2).

For nimesulide, the highest proportion of use occurred in women aged 25 or older, with lower educational attainment, experiencing food insecurity, having fewer prenatal consultations, reporting smoking during pregnancy, and receiving prenatal care in the public service (Table 2).

Diclofenac showed a higher proportion of use by pregnant women with lower educational attainment, experiencing food insecurity, having fewer prenatal consultations, and reporting smoking during pregnancy (Table 2).

The prevalence of any anti-inflammatory drug use during pregnancy was 86.8%. In bivariate analysis, women with lower educational attainment, up to complete high school (Crude OR = 1.55, 95% CI 1.07-2.25), with reference to those with a higher education level, those who consumed alcoholic beverages (Crude OR = 1.96, 95% CI 1.03-3.73), and those with a higher number of living children (more than 4 children, Crude OR = 1.6, 95% CI 1.06-2.24, and 2 to 3 children, Crude OR = 1.52, 95% CI 1.10-2.27), had a higher chance of using anti-inflammatory drugs. Primiparous women (Crude OR = 0.66, 95% CI 0.47-0.93), those who had more than eight prenatal consultations (Crude OR = 0.55, 95% CI 0.35-0.85), and those in a situation of moderate to severe food insecurity (Crude OR = 0.42, 95% CI 0.25-0.69) had a lower chance of using anti-inflammatory drugs during pregnancy. After adjusted analysis, alcohol consumption and the number of living children lost statistical significance and did not remain in the final model as independent variables associated with the use of anti-inflammatory drugs (Table 3).

4. DISCUSSION

Our manuscript aimed to analyze the use of anti-inflammatory drugs and the associated factors, including educational level, number of prenatal visits, and food insecurity, during pregnancy. The data shown a prevalent overall use of these medications during pregnancy at 86.8%. Dipyrone was the most commonly used medication (72.7%), followed by paracetamol (50.3%) and nimesulide (16.1%), while 5.2% of pregnant women reported using diclofenac. Comparing these results with the scientific literature proved challenging, as studies classifying analgesics, anti-inflammatories, and antipyretics in the same group were scarce. However, prevalence results from publications analyzing medication use during pregnancy were obtainable.

The prevalence of using anti-inflammatories, analgesics, and antipyretics during pregnancy (86.8%) can be considered high compared to various studies analyzing the use of this therapeutic class. A population-based study analyzing medication consumption among 5,564 pregnant women in six Brazilian cities reported a prevalence of analgesic/anti-inflammatory use at 22.2% [10,11]. In Santa Rosa/RS, a population-based study with 470 pregnant women found a prevalence of 17.6% for non-opioid analgesics [12]. Another population-based study with 1,091 pregnant women in Santo Antônio de Jesus/BA reported a prevalence of analgesic use at 21.9% [13].

In Maceió/AL, a study with 130 pregnant women treated at the university hospital reported that 19.0% of pregnant women used analgesics, anti-inflammatories, and antipyretics [14]. Another study with a convenience sample of military pregnant women (n=100) in Belo Horizonte/MG reported that 4.6% reported using analgesics and anti-inflammatories [15].

Observing studies from other countries also indicates that the percentage of usage is lower than found in this research. It is essential to consider the diverse study designs. but prevalence for the use of these medications in each respective group could be extracted. In a historical cohort study involving 65.547 women in Israel. exposure to anti-inflammatories was 6.9%. with the analysis including the use of ibuprofen. diclofenac. naproxen. etodolac. indomethacin. lornoxicam. or nabumetone [16]. In Canada. a case-control study with 4.705 women diagnosed with spontaneous abortion reported a prevalence of anti-inflammatory use at 7.5% among cases and 2.6% among controls [17]. In Norway. a cohort study with 69.929 women found that 4.32% of women reported using anti-inflammatories early in pregnancy [4]. Another cohort study. also in Norway. with 90.417 pregnant women. reported that 7.2% of them used at least one of the four analyzed anti-inflammatories [18]. In Quebec. Canada. in a case-control study with 36.387 pregnant women.

Table 1. Socioeconomic, demographic, maternal and prenatal care habits characteristics of the study population in the municipality of Rio Branco - AC, 2015. (N=1190)

Variable	N	%
Age (years)		
13 -18	221	18,6
19 – 24	386	32,4
25 – 34	460	38,7
≥ 35 anos	123	10,3
Education		
Elementary school I	77	6,5
Elementary school II	232	19,5

Variable	N	%
High school	611	51,3
Higher education	270	22,7
Family income (minimum wages) *		
Up to 1.5 MW	444	43,6
≥ 1.5 MW	574	56,4
ABEP Class**		
	242	20,6
A and B	935	79,4
Receipt of Bolsa Família		
No	914	80,9
Yes	216	19,1
Marital status		
No partner	190	16,0
With partner	999	84,0
Self-declared skin color		
White	125	10,5
Non-white	1064	89,5
Food and Nutritional Security		
Mild Security and Insecurity	777	65,3
Moderate and severe insecurity	413	34,7
Prenatal Care		
Public	982	85,1
Private	172	14,9
Number of Prenatal Consultations		
None	17	1,4
1 to 5	450	37,8
6 to 8	494	41,5
> 8	229	19,2
Planned pregnancy		
No	751	63,4
Yes	434	36,6
Primigravida		
No	718	60,7
Yes	464	39,3
Number of living children (including newborns)		
One	466	39,3
2 or 3	369	31,1
4 or more	352	29,7
Smoked during pregnancy		
No	1076	90,4
Yes	114	9,6
Drank alcoholic beverages during pregnancy		
No	1035	87,7
Yes	145	12,3
Practicipated physical activities		
No	1046	89,3
Yes	125	10,7
Type of delivery		
Normal	618	52,0
Cesarean section	570	48,0
Use of anti-inflammatory medication by pregnant woman		
Did not take	157	13,2
Took one type	485	40,8
Took two types	427	35,9
Took three types	105	8,8
Took four types	16	1,3
Dipyrone		
No	325	27,3
Yes	865	72,7
Paracetamol		
No	591	49,7
Yes	599	50,3
Nimesulide		
No	998	83,9
Yes	192	16,1
Diclofenac		
No	1128	94,8
Yes	62	5,2

Note: ** Minimum wage in force at the time (R$ 788,00); **ABEP – Brazilian Association of Research Companies*

Table 2. Distribution of the absolute and relative frequency of use of the main anti-inflammatory drugs according to socioeconomic and demographic characteristics, maternal habits and prenatal care in the city of Rio Branco - AC, 2015.

	Dipyrone			Paracetamol			Nimesulide			Diclofenac		
Age (years)	**No (%)**	**Yes (%)**	**p-value**	**No (%)**	**Yes (%)**	**p-value**	**No (%)**	**Yes (%)**	**p-value**	**No (%)**	**Yes (%)**	**p-value**
13 - 18	53 (24.0%)	168 (76.0%)	0.387	110 (49.8%)	111 (50.2%)	0.275	181 (81.9%)	40 (18.1%)	0.016	210 (95.0%)	11 (5.0%)	0.064
19 – 24	108 (28.0%)	278 (72.0%)		178 (46.1%)	208 (53.9%)		311 (80.6%)	75 (19.4%)		358 (92.7%)	28 (7.3%)	
25 – 34	124 (27.0%)	336 (73.0%)		235 (51.1%)	225 (48.9%)		393 (85.4%)	67 (14.6%)		445 (96.7%)	15 (3.3%)	
≥ 35 years	40 (32.5%)	83 (67.5%)		68 (55.3%)	55 (44.7%)		113 (91.9%)	10 (8.1%)		115 (93.5%)	8 (6.5%)	
Education												
Fundamental I	24 (31.2%)	53 (68.8%)	**0.014**	38 (49.4%)	39 (50.6%)	0.385	62 (80.5%)	15 (19.5%)	0.002	70 (90.9%)	7 (9.1%)	0.044
Fundamental II	60 (25.9%)	172 (74.1%)		127 (54.7%)	105 (45.3%)		197 (84.9%)	35 (15.1%)		217 (93.5%)	15 (6.5%)	
High School	148 (24.2%)	463 (75.8%)		294 (48.1%)	317 (51.9%)		494 (80.9%)	117 (19.1%)		577 (94.4%)	34 (5.6%)	
College	93 (34.4%)	177 (65.6%)		132 (48.9%)	138 (51.1%)		245 (90.7%)	25 (9.3%)		264 (97.8%)	6 (2.2%)	
Family Income												
Up to 1.5 SM	108 (24.3%)	336 (75.7%)	0.181	215 (48.4%)	229 (51.6%)	0.739	365 (82.2%)	79 (17.8%)	0.259	414 (93.2%)	30 (6.8%)	0.248
≥ 1.5 SM	161 (28.0%)	413 (72.0%)		284 (49.5%)	290 (50.5%)		487 (84.8%)	87 (15.2%)		545 (94.9%)	29 (5.1%)	
ABEP Class												
A and B	90 (37.2%)	152 (62.8%)	**0.001**	120 (49.6%)	122 (50.4%)	0.961	209 (86.4%)	33 (13.6%)	0.206	229 (94.6%)	13 (5.4%)	0.935
C. D. and E	230 (24.6%)	705 (75.4%)		462 (49.4%)	473 (50.6%)		776 (83.0%)	159 (17.0%)		886 (94.8%)	49 (5.2%)	
Receives Bolsa Família												
No	258 (28.2%)	656 (71.8%)	0.074	456 (49.9%)	458 (50.1%)	0.735	774 (84.7%)	140 (15.3%)	0.070	863 (94.4%)	51 (5.6%)	0.578
Yes	48 (22.2%)	168 (77.8%)		105 (48.6%)	111 (51.4)		172 (79.6)	172 (79.6)		206 (95.4)	206 (95.4)	
Marry situation												
No marryed	45 (23.7)	145 (76.3)	0.218	99 (52.1)	91 (47.9)	0.455	160 (84.2)	30 (15.8)	0.884	178 (93.7)	12 (6.3)	0.456
Married	280 (28.0)	719 (72.0)		491 (49.1)	508 (50.9)		837 (83.8)	162 (16.2)		949 (95.0)	50 (5.0)	
Skin collor												
Branca	30 (24.0)	95 (76.0)	0.377	59 (47.2)	66 (52.8)	0.554	107 (85.6)	18 (14.4)	0.574	123 (98.4)	2 (1.6)	**0.050****
Não Branca	295 (27.7)	769 (72.3)		532 (50.0)	532 (50.0)		890 (83.6)	174 (16.4)		1004 (94.4)	60 (5.6)	
Food security												
Safe	225 (29.0)	552 (71.0)	0.080	383 (49.3)	394 (50.7)	0.725	664 (85.5)	113 (14.5)	**0.041**	744 (95.8)	33 (4.2)	**0.040**
Non-safe	100 (24.2.)	313 (75.8)		208 (50.4)	205 (49.6)		334 (80.9)	79 (19.1)		384 (93.0)	29 (7.0)	
Number of prenatal are consultancy												
1 a 5	113 (25.1)	337 (74.9)	**0.009**	215 (47.8)	235 (52.2)	0.342	358 (79.6)	92 (20.4)	**0.004**	415 (92.2)	35 (7.8)	**0.007**
6 a 8	126 (25.5)	368 (74.5)		247 (50.0)	247 (50.0)		423 (85.60	71 (14.4)		478 (96.8)	16 (3.2)	
> 8	81 (35.4)	148 (64.6)		123 (53.7)	106 (46.3)		203 (88.60	26 (11.4)		218 (95.2)	11 (4.8)	
Smokyng												
No	297 (27.6)	779 (72.4)	0.448	538 (50.0)	538 (50.0)	0.476	916 (85.1)	160 (14.9)	**0.001**	1026 (95.4)	50 (4.6)	**0.007**
Yes	28 (24.6)	86 (75.4)		53 (46.5)	61 (53.5)		82 (71.9)	32 (28.1)		102 (89.5)	12 (10.5)	
Alcoholic Drink												
No	292 (28.2)	743 (71.8)	**0.057**	522 (50.4)	513 (49.6)	0.115	874 (84.4)	161 (15.6)	0.116	980 (94.7)	55 (5.3)	0.806

	Dipyrone			**Paracetamol**			**Nimesulide**			**Diclofenac**		
Yes	30 (20.7)	115 (79.3)		63 (43.4)	82 (56.6)		115 (79.3)	30 (20.7)		138 (95.2)	7 (4.8)	
Physical activity												
No	277 (26.5)	769 (73.5)	**0.039**	526 (50.3)	520 (49.7)	0.322	877 (83.8)	169 (16.2)	0.964	994 (95.0)	52 (5.0)	0.761
Yes	44 (35.2)	81 (64.8)		57 (45.6)	68 (54.4)		105 (84.0)	20 (16.0)		118 (94.4)	7 (5.6)	
First Pregnancy												
No	180 (25.1)	538 (74.9)	**0.025**	342 (47.6)	376 (52.4)	0.083	602 (83.8)	116 (16.2)	0.769	676 (94.2)	42 (5.8)	0.246
Yes	144 (31.0)	320 (69.0)		245 (52.8)	219 (47.2)		392 (84.5)	72 (15.5)		444 (95.7)	20 (4.3)	
Planed pregnancy												
No	202 (26.9)	549 (73.1)	0.652	355 (47.3)	396 (52.7)	**0.027**	618 (82.3)	133 (17.7)	0.064	706 (94.0)	45 (6.0)	0.122
Yes	122 (28.1)	312 (71.9)		234 (53.9)	200 (46.1)		375 (86.4)	59 (13.6)		417 (96.1)	17 (3.9)	
Prenatal care												
Public	253 (25.8)	729 (74.2)	**0.002**	490 (49.9)	492 (50.1)	0.760	817 (83.2)	165 (16.8)	**0.057**	928 (94.5)	54 (5.5)	0.155
Privit	64 (37.2)	108 (62.8)		88 (51.2)	84 (48.8)		153 (89.0)	19 (11.0)		167 (97.1)	5 (2.9)	
Number of living children												
One	145 (31.1)	321 (68.9)	**0.010**	246 (52.8)	220 (47.2)	**0.050**	394 (84.5)	72 (15.5)	0.543	446 (95.7)	20 (4.3)	0.164
2 or 3	103 (27.9)	266 (72.1)		164 (44.4)	205 (55.6)		313 (84.8)	56 (15.2)		352 (95.4)	17 (4.6)	
4 or more	76 (21,6)	276 (78,4)		178 (50,6)	174 (49,4)		289 (82,1)	63 (17,9)		327 (92,9)	25 (7,1)	

Note: ** p-Value: Pearson Qui-quadrado; ** Exact Fisher Test; *** Minimum wage in force at the time (R$ 788,00); ***** ABEP – Associação Brasileira de Empresas de Pesquisa*

Table 3. Independent variables associated with the use of anti-inflammatory drugs

Variable	Yes (n/%)	OR (Crude)	95% CI	p-value	OR (Adjusted)	95% CI
Age (years)						
Up to 35 years	931 (87.3%)	1		0.179		
≥ 35 years	102 (82.9%)	0.71	(0.42-1.17%)			
Education						
College	223 (82.6%)	1		**0.021**	1	
Up to complete high school	810 (88.0%)	**1.55**	**(1.07-2.25%)**		**1.46**	**(0.99-2.17)**
Family Income (minimum wages)						
Up to 1.5 SM	392 (88.3%)	1		0.374		
≥ 1.5 SM	496 (86.4%)	0.84	(0.58-1.22%)			
ABEP Class						
A and B	203 (83.9%)	1		0.107		
C. D. and E	821 (87.8%)	1.38	(0.93-1.05%)			
Receives Bolsa Família						
No	792 (86.7%)	1		0.608		
Yes	190 (88.0%)	1.12	(0.71-1.76%)			
Marital Status						
No partner	163 (85.8%)	1		0.655		
With partner	869 (87.0%)	1.10	(0.70-1.73%)			
Skin Color						
White	114 (91.2%)	1		0.128		
Non-White	918 (86.3%)	0.60	(0.31-1.15%)			
Food and Nutrition Security						
Mild insecurity	937 (87.7%)	1		**0.011**	1	
Moderate and severe insecurity	96 (79.3%)	**0.54**	**(0.33-0.87%)**		**0.421**	**(0.25-0.69)**
Number of Prenatal Consultations						
1 to 5	398 (88.4%)	1		**0.014**	1	
6 to 8	434 (87.9%)	0.95	(0.63-1.40%)		0.95	(0.63-1.42)
> 8	185 (80.8%)	**0.55**	**(0.35-0.85%)**		**0.57**	**(0.36-0.90)**
Smoked during pregnancy						
No	932 (86.6%)	1		0.553		
Yes	101 (88.6%)	1.2	(0.65-2.19%)			
Consumed alcohol during pregnancy						
No	891 (86.1%)	1		0.038		
Yes	134 (92.4%)	**1.96**	**(1.03-3.73%)**			
Praticant of physical activity						
No	914 (87.4%)	1		0.073		
Yes	102 (81.6%)	0.64	(0.39-1.04%)			
First pregnancy						
No	636 (88.6%)	1		**0.019**	1	
Yes	389 (83.8%)	**0.66**	**(0.47-0.93%)**		**0.65**	**(0.45-0.92)**

Variable	Yes (n/%)	OR (Crude)	95% CI	p-value	OR (Adjusted)	95% CI
Planed pregnancy						
No	659 (87.7%)	1		0.221		
Yes	370 (85.3%)	0.80	(0.57-1.13%)			
Prenatal care						
No	855 (87.1%)	1		0.326		
Yes	145 (84.3%)	0.79	(0.50-1.25%)			
Number of living children						
One	390 (83.7%)	1		**0.035**		
2 or 3	327 (88.6%)	**1.52**	**(1.10-2.27%)**			
4 or more	314 (89.2%)	**1.61**	**(1.06-2.44%)**			

Note: ** p-Value Wald Test; ** Minimum wage in force at the time (R$ 788,00); *** ABEP – Associação Brasileira de Empresas de Pesquisa*

the prevalence of anti-inflammatory use was 2.9% in the first trimester of gestation [19]. and in San Francisco. USA. a cohort with 1.055 pregnant women. 5% reported using anti-inflammatories during pregnancy and around conception [3]. Dipyrone was the most used analgesic in this study. reported by 72.7% of pregnant women. Dipyrone has been cited as the drug of choice in some other studies in Brazil [10,20,21]. There is controversy regarding dipyrone's general use. as the Food and Drug Administration (FDA) prohibited it in 1977 in the United States. citing the potential risk of irreversible agranulocytosis [22]. This American initiative has been widely debated. but given the global influence of the FDA. other countries (England. Canada. Denmark. Norway. Sweden. Japan. and Australia) follow this guidance [23,24]. In Brazil. in 2001. the National Health Surveillance Agency (ANVISA) conducted an "International Panel for the Assessment of Dipyrone Safety." recognizing its undeniable effectiveness as an analgesic and antipyretic. The reported risks were deemed low and insufficient to remove the drug from the market. The recommendation was not to withdraw it [23,25].

Caution is required in the use of this medication among pregnant groups. as the risk of developing agranulocytosis cannot be the sole attribution. Literature reports suggest an association of dipyrone with cases of childhood acute leukemia [20,26,27]. orofacial clefts in newborns [28]. Wilms tumor [29]. spontaneous abortion. and congenital malformation [30].

Paracetamol. the second most commonly reported medication among pregnant women in Rio Branco/AC. was mentioned by 50.3%. The literature designates this drug as the preferred choice for prescription during pregnancy. considering the strong controversies surrounding dipyrone. The FDA classifies paracetamol as low risk for pregnant women based on studies in animals and humans. In Brazil. it is widely used [31,32]. Even though it presents a lower prevalence than observed for dipyrone. it is still considerably high when compared to other research in the country. A study in Rio de Janeiro/RJ found a prevalence of 35.5% [20]. and in a study analyzing medication use in six Brazilian capitals. the prevalence was 18.3% [10]. In a population-based study in Santa Rosa/RS. paracetamol had the highest prevalence at 17.3% [12]. and in another study in Santo Antônio de Jesus/BA. it appeared as the most chosen analgesic at 21.3% [13]. Convenience sample studies report lower prevalence. such as those observed in João Pessoa/PB at 4.93% [33]. Natal/RN at 13.1% [34]. Piracicaba/SP at 6.3% [35]. and Campinas/SP in 5.5% of pregnant women [21].

International studies indicate higher prevalence than in Brazil. likely due to the prohibition and/or contraindication of dipyrone in their countries. In three studies in Denmark. with cohort and cross-sectional designs. the following prevalence were reported: in a cohort study with 63.652 pregnant women. paracetamol use during pregnancy was 56.3% [36]; another cohort with 64.322 participants where 56% reported paracetamol use during pregnancy [37]; in a cross-sectional study with 10.209 pregnant women. prevalence of 35.2% and 6.5% before and at the beginning of pregnancy. respectively [38]. In New Zealand. a cohort study with 871 pregnant women reported a prevalence of paracetamol exposure during pregnancy at 49.8% [39]. and in Chicago. USA. a cohort study with 345 women observed that 70% declared paracetamol use at least once during pregnancy [40].

Alternative Risks associated with the use of paracetamol. as mentioned in the literature and warranting further exploration. include an association with respiratory problems such as asthma. wheezing. and chest tightness in children under one year. These effects are believed to be a result of paracetamol use after the twentieth week of gestation. Additionally. some studies suggest an increased risk of childhood autism. attention deficit disorders. and the occurrence of the congenital malformation gastroschisis [36,38,40–42].

Nimesulide. reported by 16.1% of pregnant women. is not a preferred anti-inflammatory for use during pregnancy. as the risks to the fetus due to its use are not well elucidated in humans and have been deemed inappropriate in animal trials [31,43]. Some studies describe the risk of this medication being associated with fetal cardiac abnormalities. but these studies have methodological limitations. and their conclusions should be approached with due care and caution [44,45].

The use of diclofenac was reported by 5.2%. This medication is not among the first-choice anti-inflammatories. although it is classified as low risk for the gestational period [43]. This finding aligns with low prevalences reported in

studies conducted in other locations [17,18,46]. Risks associated with its use include low birth weight when used in the second trimester and a significant association with maternal vaginal bleeding when used in the third trimester (OR 1.8; 95% CI 1.1-3.0) [18]. In other studies. diclofenac has been strongly associated with episodes of spontaneous abortion [17,46].

When analyzing the use of anti-inflammatories collectively. this study indicated a higher odds ratio among pregnant women who consumed alcohol. On the other hand. the likelihood of exposure to anti-inflammatories was lower in pregnant women with a college education compared to those with only a basic education. as well as among primiparous women. those with six to eight prenatal consultations. and pregnant women experiencing moderate to severe food insecurity. Higher educational attainment appears to lead to a better understanding of the inherent risks of medication use. while being a first-time mother reflects self-care and maternal inexperience. Adequate prenatal care is consistently identified in various studies as a protective factor against the use of risky medications. Alcohol consumption. besides indicating a lack of care during pregnancy. also necessitates addressing the adverse effects resulting from alcohol use [11,47–49].

Given the cross-sectional design and the use of interviews as a data collection technique. albeit with the utilization of institutional records from the maternity card and medical records. it is essential to describe limitations. There is a possibility of memory bias. confusion with medication names. and the reluctance of pregnant women to report use. knowing the potential implications for the neonate. These limitations were duly considered during the research implementation. with all measures taken to overcome them.

Despite knowing the gestational complications that require the use of medications in this therapeutic class and recognizing the influence of the service with excellent prenatal coverage. it is concluded that the prevalence of using these medications was high. In this regard. measures can and should be taken to restrict this practice.

Despite studies emphasizing the benefits that outweigh the risks. these risks should not be disregarded. It is possible to introduce alternative therapies such as physiotherapy. acupuncture. and physical activities. among others. capable of alleviating pain and inflammation. thus limiting drug therapy only to cases where it is essential. The findings of this study are critical for informing clinical practices and public policies aimed at reducing the inappropriate use of anti-inflammatory drugs during pregnancy. Given the high prevalence of NSAID use in vulnerable populations. healthcare providers must focus on educating pregnant women about safer alternatives like physiotherapy and acupuncture. Public health campaigns should also raise awareness of the risks associated with NSAID use. particularly in women with lower education levels and limited access to prenatal care. Stricter regulations on over-the-counter drug sales may further mitigate this risk. especially in underserved regions. By addressing these factors. health professionals and policymakers can promote safer pregnancy practices. reducing medication misuse and improving maternal and fetal outcomes

4.1 What does this Article add to the Field?

This article contributes to the existing literature by providing insights into the prevalence and patterns of using anti-inflammatory. analgesic. and antipyretic medications during pregnancy in Rio Branco/AC. Brazil. The study not only presents the prevalence of medication use but also delves into specific drugs such as dipyrone. paracetamol. nimesulide. and diclofenac.

The findings shed light on the high prevalence of medication use during pregnancy in the studied population. with a particular emphasis on the widespread use of dipyrone and paracetamol. Moreover. the study identifies associated factors. including demographic. socioeconomic. reproductive. and lifestyle factors. providing a comprehensive understanding of the context in which these medications are utilized.

Comparisons with existing literature highlight the unique aspects of medication use in this specific region. as prevalence may differ across populations and geographies. The article also discusses the controversies surrounding certain medications. such as dipyrone. providing a nuanced perspective on the risks and benefits associated with their use during pregnancy.

Furthermore. the study emphasizes the need for alternative therapeutic approaches. suggesting that interventions like physiotherapy. acupuncture. and physical activities could be considered to reduce reliance on medication.

particularly in cases where the risks of drug use need careful evaluation.

In summary. this article adds valuable information to the literature by offering a detailed analysis of medication use during pregnancy in a specific Brazilian region. contributing to a broader understanding of prescription patterns. associated factors. and potential avenues for promoting safer therapeutic practices during gestation.

Although our manuscript has a robust conjunct of data. we need to consider limitations. Firstly. its cross-sectional design restricts establishing causal relationships. Secondly. reliance on self-reported data introduces potential recall and social desirability biases. Thirdly. the findings' generalizability is constrained to the Rio Branco/AC population. Lastly. incomplete medication assessment and the absence of longitudinal data limit the study's depth and understanding of medication use during pregnancy.

5. CONCLUSIONS

In conclusion. this study sheds light on the prevalent use of anti-inflammatory. analgesic. and antipyretic medications during pregnancy in Rio Branco/AC. The high prevalence. especially considering potential associated risks. underscores the need for cautious evaluation and alternative approaches. The findings emphasize the importance of informed decision-making. personalized care. and promoting non-pharmacological interventions. Despite the study's contributions. addressing this complex issue requires a comprehensive. multidisciplinary approach. integrating healthcare. education. and public awareness initiatives to optimize maternal and fetal well-being during pregnancy.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

The authors hereby declare that generative AI technology. CHAT GPT 4.0. was used for editing the English language of the manuscript. The request was solely to correct spelling. punctuation. and grammar. without altering. adding. omitting information or data. or changing the meaning of the text.

CONSENT

As per international standards or university standards. respondents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

This study adhered to ethical principles in line with Resolution No. 466/12 of the National Health Council. Authorization was obtained from the institutions where data collection took place. The main project was approved by the Research Ethics Committee of the Federal University of Acre. and this subproject was approved by the Research Ethics Committee of the National School of Public Health.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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