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Antibiotic Consumption Patterns in Urban Coari, Amazonas: High Azithromycin Use and COVID-19-Related Prescriptions

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Abstract: Background/Objectivses: Antibiotic consumption patterns in remote urban areas of the Amazon region are poorly understood. This study aimed to analyze antibiotic use in the adult population of Coari, a municipality in Amazonas, Brazil. **Methods**: A cross-sectional study was conducted between October and November 2021 in the urban area of Coari. 394 adults were interviewed using a structured questionnaire. Data on antibiotic use, sociodemographic factors, health service access, and self-reported illnesses were collected. Poisson regression was used to estimate prevalence ratios and identify factors associated with antibiotic use. **Results**: The prevalence of antibiotic use was 14.7% (n = 58). The most frequently used antibiotics were azithromycin (26.9%), cefalexin (20.9%), amoxicillin (19.4%), and ciprofloxacin (13.9%). Up to 34.5% of antibiotic use was conducted without a prescription, especially among adults aged 18 to 39 (59.1%). The main health problems that led to self-medication were COVID-19 (28.6%), urinary infection (14.3%), sore throat (37.5%), and intestinal infection (60.0%). Factors associated with antibiotic use included age 18 to 39 (adjusted PR = 3.73; CI = 1.37–10.09), having a family member hospitalized (adjusted PR = 2.61; CI = 1.39–4.89), having contracted COVID-19 (adjusted PR = 2.41; CI = 1.40–4.15), and frequency of visits by the community health agent to the home (adjusted PR = 0.35 CI = 0.15–0.81). **Conclusions**: The high use of broad-spectrum antibiotics (Watch), particularly azithromycin, for potentially inappropriate indications highlights the need to improve the management of antibiotic use in remote regions of Brazil. Community health agents, as key professionals between health services and the community, can play a key role in promoting the rational use of antibiotics and combating antimicrobial resistance in the Brazilian Amazon context.

Keywords: antibacterials; use of medicines; pharmacoepidemiology; human health; adult health

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1. Introduction

The discovery of antibiotics revolutionized the treatment of bacterial infections, extending human life expectancy by at least 23 years [1].

Despite these advances, there remains a global concern about the irrational use of antibiotics, often stemming from overprescription by healthcare providers or the availability of antibiotics without a prescription [2,3]. This irrational consumption can harm individual

and collective health. Individual risks include therapeutic failure due to an inappropriate selection or shorter duration than required [4], or increased risk of adverse reactions due to unnecessary use [5]. Among the collective problems is antimicrobial resistance (AMR) by bacteria, a well-known threat to global health [6,7].

Additionally, the overuse of antimicrobials increases the presence of antibiotics and resistance genes in the water, intensifying environmental stress [8]. In cities like Coari, where there is open sewage and limited access to health and drinking water [9], this scenario intensifies the spread of infections and the emergence of superbugs.

The World Health Organization (WHO) considers AMR one of the top ten risks to human health. It is estimated that it could be responsible for 10 million deaths annually by 2050 [1]. AMR was the object of a recent resolution by the United Nations General Assembly in September 2024 [10].

The inappropriate consumption of antibiotics is increasing in various regions of the world. One of its drivers is using antibiotics to treat viral infections that do not require or benefit from them [11], including medical prescriptions made because of parents' or patients' complacency or reassuring health professionals against a misdiagnosis [12,13].

In rural areas and places far from health system coverage, the inappropriate use of antibiotics is frequent due to the lack of diagnostic tools, laboratories, and qualified professionals [14]. Antibiotics such as azithromycin (29.2%), amoxicillin (11.4%), and amoxicillin-clavulanate (8.2%) are often prescribed inappropriately for acute bronchitis, upper respiratory infections and symptoms such as cough [15]. In Coari, dependence on laboratories in Manaus exacerbates delays in the diagnosis and treatment of infectious diseases.

Consuming antibiotics without a professional prescription, which is related to dispensing them without asking for a prescription, is especially concerning; despite the wide knowledge about its existence, it continues to be observed in LMICs (Ethiopia, Nigeria, Afghanistan) [5,16,17] but also in HICs (Saudi Arabia) [18].

A study conducted in Colombia found that 25% of patients diagnosed with viral infections were prescribed antibiotics. Among the associated factors, the study found that young adults aged between 18 and 45 and older adults aged between 45 and 65 were more likely to consume antibiotics inappropriately [19]. Recent studies in Brazil have shown that the prevalence of antibiotic consumption in the adult population of urban areas varied from 3.4% to 58.0% [20–23]. This variation does not seem to have an obvious reason. Still, it may be related to factors such as the health infrastructure of each region, epidemiological conditions of diseases, and different research methodologies.

Specifically in the Amazonas, the prevalence of inappropriate antibiotic consumption in urban adults increased from 19.2% in 2015 to 30.7% in 2019 [23]. This Brazilian region faces many healthcare challenges: it concentrates the worst rates of health service utilization in the country, even in urban areas [24], and the health infrastructure in municipalities distant from the capital, Manaus, may be insufficient to meet the population's demand, leading to self-medication [25]. Furthermore, the low supervision of the pharmaceutical network in the interior of Amazonas state contributes to the inappropriate consumption of antibiotics [4].

The combination of limited access to healthcare, high prevalence of infectious diseases, inadequate sanitation, and poor oversight of the sale of medicines in regions such as Coari [9,20] exacerbates the problem of indiscriminate use of antibiotics, contributing to the spread of AMR on a global scale.

The Amazon region, in particular, faces unique challenges related to AMR due to factors such as environmental degradation, deforestation, and limited access to healthcare. A recent study by Santos et al. highlighted the urgent need for targeted interventions to address the growing problem of AMR in the Amazon [26]. Thus, in remote locations where access to adequate healthcare can be a challenge, surveillance of antibiotic use by the adult population becomes fundamental not only for local but also for global AMR control efforts. Given that the Amazon River is one of the planet's major aquatic ecosystems (almost 7000 km long), with an incredible basin size (7,000,000 km²) and high discharge volume (209,000 m³/s), continuous surveillance of antibiotic use is necessary to guide policies and stewardship activities. Therefore, this study aimed to analyze antibiotic consumption in the adult population of the urban area of the municipality of Coari, Amazonas, Brazil.

2. Results

We collected information from 394 individuals, with a mean age of 45.3 years (SD ± 15.2), and it was found that 14.7% (n = 58) used antibiotics. Among these, 74.1% were female (53), 51.7% (30) were in the age group between 18 and 39 years, 82.8% (48) reported nine or more years of schooling, and 39.7% (23) had a family income of one to two minimum wages. There was an association between antibiotic use and age group (p = 0.022) and education level (p = 0.048), and their distribution is shown in Table 1. No statistical association was found with sex, marital status, or family income.

Table 1. Characteristics of participants according to their antibiotic use status. Coari, Amazonas, Brazil, 2021.

Variables	Antibiotic use		*p*-Value [a]
	Yes n = 58 (%)	No n = 336 (%)	
Age. years			0.022
18–39	30 (51.7)	130 (38.7)	
40–59	24 (41.4)	133 (39.6)	
≥60	4 (6.9)	73 (21.7)	
Education level			0.048
≥9 years	48 (82.8)	225 (67.0)	
Up to 8 years	8 (13.8)	78 (23.2)	
No education	2 (3.4)	33 (9.8)	
Frequency of CHA visits to the household			0.037
Monthly or less	54 (93.1)	276 (82.1)	
More than once in a month	4 (6.9)	60 (17.9)	
Preferred service in case of disease			0.007 *
Hospital	25 (43.1)	176 (52.4)	
Basic health unit	24 (41.4)	146 (43.5)	
Other **	9 (15.5)	14 (4.2)	
Illness in the last three months			0.003
Yes	53 (91.4)	246 (73.2)	
No	5 (8.6)	90 (26.8)	

Table 1. *Cont.*

Variables	Antibiotic use		*p*-Value [a]
	Yes n = 58 (%)	No n = 336 (%)	
Number of illness episodes in the Family in the last three months			0.014
1–4	45 (77.6)	214 (63.7)	
≥5	8 (13.8)	36 (10.7)	
None	5 (8.6)	86 (25.6)	
URTI with flu symptoms			0.007
Yes	29 (50.0)	107 (31.8)	
No	29 (50.0)	229 (68.2)	
COVID-19			<0.001 *
Yes	11 (19.0)	15 (4.5)	
No	47 (81.0)	321 (95.5)	
Case of hospital admission in the family in the last three months			0.002 *
Yes	5 (8.6)	3 (0.9)	
No	53 (91.4)	333 (99.1)	
Already took an expired medicine			0.055 *
Yes	7 (12.1)	16 (4.8)	
No	48 (82.8)	283 (84.2)	
Does not know	3 (5.2)	37 (11.0)	
Only takes prescribed antibiotic			0.015
Yes	38 (65.5)	128 (47.9)	
No	20 (34.5)	139 (52.1)	

[a] Pearson's Chi-square test; * Fisher's exact test; ** Tropical Medicine Institute, polyclinic, private service, pharmacy; URTI = Upper Respiratory Tract Infections.

Among the 58 antibiotic consumers, it was found that 45 (77.6%) had their household monitored by the Community Health Agent (CHA), and almost all (54; 93.1%) received home visits from the CHA once a month or less often. In total, 41 (70.7%) did not receive home visits from Primary Health Care (PHC) programmes, 56 (96.6%) first sought a health professional in case of illness, 25 (43.1%) preferred to seek the hospital in case of illness, and 55 (94.8%) sought health services once a month or less. There was an association with the frequency of CHA visits to the household ($p = 0.037$), and preference for health service in case of illness ($p = 0.007$) (Table 1).

Up to 70.7% of the participants taking antibiotics (n = 41) considered their health very good/good, and 87.9% (51) considered their family's health very good/good. A high proportion (53; 91.4%) fell ill in the last three months before the interview, and 77.6% (46) reported 1 to 4 diseases in the family. Concerning the described conditions, 50% (29) had upper respiratory tract infections (URTI) with flu-like symptoms; 19% reported having contracted COVID-19 in the last three months (11), and 5 (8.6%) had a case of hospital admission in the family.

Concerning access to the healthcare system, 52 (89.7%) managed to perform exams when requested by a professional, 19 (32.8%) tried to schedule an appointment when needed and failed, and 8 (13.8%) could not access medications prescribed by a professional in the last three months. There were no differences in these proportions and what was told by the 336 individuals that did not take any antibiotics.

2.1. Conditions Associated with the Use of Antibiotics

There was an association between antibiotic use and illness in the last three months before the interview ($p = 0.003$), number of diseases in the family ($p = 0.014$), URTI with flu-like symptoms ($p = 0.007$), COVID-19 ($p < 0.001$), and having a case of hospital admission in the family in the last three months ($p = 0.002$), as shown in Table 1.

Regarding antibiotic use and variables related to medication consumption, it was noted that, among the 58 participants who consumed antibiotics, 48 (82.8%) self-medicated with over-the-counter medication, and the same proportion kept medication at home; 46 (79.3%) declared that they usually read the medication package inserts. Concerning possible harms, 41 (70.7%) believed that over-the-counter medications could harm health. Almost all (55; 94.8%) usually checked the expiration date of medications, but 7 (12.1%) already took an expired medication.

Importantly, 26 (44.8%) used to store medications out of their original packaging, and 6 (10.3%) removed the tablets from the blister to store them elsewhere. It should be noted that these proportions were similar among the 336 participants who did not take any antibiotics in the last three months, thus showing what can be a pattern independent of the exposure to antibiotics.

More than half (34; 58.6%) declared using traditional remedies in the last three months before the interview. More than one-third (20; 34.5%) consumed antibiotics without a prescription, and this proportion was higher among antibiotic users than among non-exposed to antibiotics in the last three months (Pearson's Chi-square test, $p = 0.015$) (Table 1).

These 58 persons had consumed 67 antibiotics in the last three months before the interview. The most frequently consumed were azithromycin (18; 26.9%), cefalexin (14; 20.9%), amoxicillin (13; 19.4%), or ciprofloxacin (9; 13.4%) (Figure 1). Only 45 (67.2%) of these 67 antibiotics were prescribed; the remaining 22 (32.8%) were taken as self-medication. 80.8% of antibiotics were purchased in pharmacies.

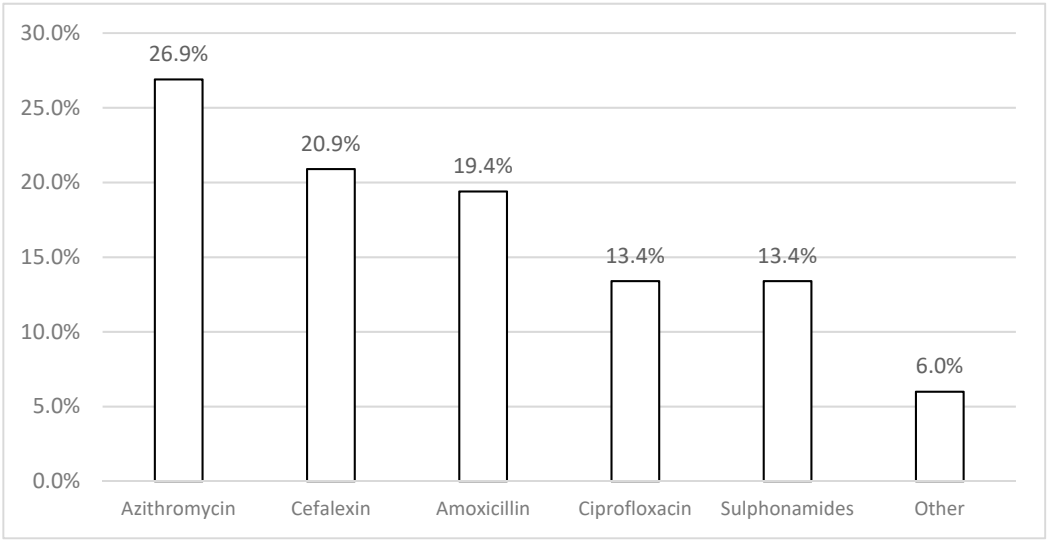


Figure 1. Distribution of the antibiotics used by the study participants. Percentage over the total (n = 58). Coari, Amazonas, Brazil, 2021.

The main reasons reported for antibiotic use were throat infections (mainly treated with amoxicillin and azithromycin) and urinary tract infections (mainly treated with ciprofloxacin and cefalexin) (see Table 2).

It is worth noting that five participants (8.6%) reported not having been ill in the last three months but consumed antibiotics. The antibiotics used were cefalexin for "skin inflammation" (1); cefalexin and ciprofloxacin for unknown reasons (1); cefalexin for "urinary symptoms" (1); cefalexin and ciprofloxacin for urinary complaints (1); and amoxicillin for urinary complaints (1).

Table 2. Distribution of antibiotic use according to health conditions described by the participants and the prescription status. Coari, Amazonas, Brazil, 2021.

Antibiotic Used		n	%	Self-Reported Health Condition	Prescribed Antibiotic	
					Yes (%)	No (%)
Azithromycin		7	38.8	Throat inflammation	7 (100)	-
		7	38.8	COVID-19	5 (71.4)	2 (28.6)
		1	5.6	Virus	1 (100)	-
		1	5.6	"Prevent" COVID-19	-	1 (100)
		2	11.2	Reason not identified	-	2 (100)
	Subtotal	18	26.9	-	13 (72.2)	5 (27.8)
Cefalexin		7	50.0	Urinary infection	5 (85.7)	2 (14.3)
		5	35.7	Reason not identified	1 (20.0)	4 (80.0)
		2	14.3	Skin infection	1 (50.0)	1 (50.0)
	Subtotal	14	20.9	-	7 (50.0)	7 (50.0)
Amoxicillin		8	72.7	Throat inflammation	5 (62.5)	3 (37.5)
		2	18.2	Throat discomfort	2 (100)	-
		1	9.1	Urinary infection	1 (100)	-
	Subtotal	11	16.4	-	8 (72.7)	3 (27.3)
Ciprofloxacin		8	88.9	Urinary infection	8 (100)	-
		1	11.1	Reason not identified	1(100)	-
	Subtotal	9	13.4	-	9 (100)	-
Sulfamethoxazole		5	62.5	Intestinal infection	2 (40.0)	3 (60.0)
		2	25.0	Diarrhea	2 (100)	-
		1	12.5	Urinary infection	-	1 (100)
	Subtotal	8	11.9	-	4 (50.0)	4 (50.0)
Other	Metronidazole	2	100.0	Intestinal infection	-	2 (100)
	Benzatin penicillin	2	100.0	Throat inflammation	1 (50.0)	1 (50.0)
	Tetracycline	2	100.0	Flu	2 (100)	-
	SFM + TMP	1	100.0	Stomach discomfort	1 (100)	-
	Subtotal	7	10.4	-	4 (57.1)	3 (42.9)
Total		67	100		45 (67.2)	22 (32.8)

SFM + TMP = sulfamethoxazole + trimethoprim.

One relevant finding is that Watch antibiotics were significantly more prescribed than taken as self-medication, compared to the Access ($p < 0.005$) (Table 3).

Table 3. Distribution of antibiotic use according to WHO-AWaRe classification and the prescription status. Coari, Amazonas, Brazil, 2021.

WHO AWaRe Category	Antibiotic	n	%	Prescribed Antibiotic *	
				Yes (%)	No (%)
Watch	Azithromycin	18	26.9	13 (72.2)	5 (27.8)
	Ciprofloxacin	9	13.4	9 (100)	-
	Subtotal Watch	27		22 (81.5)	5 (18.5)
Access	Cefalexin	14	20.9	7 (50.0)	7 (50.0)
	Amoxicillin	11	16.4	8 (72.7)	3 (27.3)
	Sulfamethoxazole	8	11.9	4 (50.0)	4 (50.0)
	Other Access	7	10.4	4 (57.1)	3 (42.9)
	Subtotal Access	40		23 (57.7)	17 (42.5)
Total		67	100	45 (67.2)	22 (32.8)

* The chi-square statistic with Yates correction is 8.5304. The *p*-value is 0.003493. Significant at $p < 0.05$.

2.2. Bivariate and Multivariate Analyses

In the bivariate analysis, the variables that showed the highest prevalence of antibiotic use were: age group of 18 to 39 years (crude PR = 3.60; CI = 1.31–9.88), URTI with flu-like symptoms (crude PR = 1.89; CI = 1.18–3.03), cases of COVID-19 (crude PR = 3.31; CI = 1.96–5.58), case of hospitalization in the family in the last three months (crude PR = 4.55; CI = 2.51–8.22), and consumption of expired medication (crude PR = 4.05; CI = 1.16–14.18).

The prevalence of antibiotic consumption was lower in people who usually seek the hospital in cases of illness (crude PR = 0.31; CI = 0.17–0.59), those who had no illness in the family in the last three months (crude PR = 0.30; CI = 0.10–0.89), and those who reported absence of illness in the last three months (crude PR = 0.29; CI = 0.12–0.72) (Table 4).

The multiple analysis showed that it was observed that belonging to the age group between 18 and 39 years (adjusted PR = 3.73; CI = 1.37–10.09), having a case of hospitalization in the family (adjusted PR = 2.61; CI = 1.39–4.89), and having contracted COVID-19 (adjusted PR = 2.41; CI = 1.40–4.15) increased the prevalence of antibiotic consumption. On the other hand, having reported the absence of illness in the last three months (adjusted PR = 0.31; CI = 0.12–0.77) and have received a home visit from CHA more than once a month (RP = 0.35; CI = 0.15–0.81) reduced the prevalence of antibiotic use (see Table 4).

Table 4. Variables associated with the use of antibiotics by adults. Coari, Amazonas, Brazil, 2021.

Variables	PR Crude *	CI 95% *	*p* *	RP Adjusted *	CI 95% *	*p* *
Age. years						
≥60	1.00					
18–39	3.60	1.31–9.88	0.013	3.73	1.37–10.9	0.010
40–59	2.94	1.66–13.21	0.039	3.28	1.19–9.04	0.021
Education level						
≥9 years	1.00					
Up to 8 years	0.52	0.26–1.07	0.078			
No education	0.32	0.08–1.27	0.108			

Table 4. *Cont.*

Variables	PR Crude *	CI 95% *	*p* *	RP Adjusted *	CI 95% *	*p* *
Frequency of CHA visits to the household						
Monthly or less	1.00					
More than once in a month	0.38	0.14–1.01	0.054	0.35	0.15–0.81	0.015
Preferred service in case of disease						
Other **	1.00					
Hospital	0.31	0.17–0.59	<0.001			
Basic health unit	0.36	0.19–0.67	0.002			
How often do you go to a healthcare facility						
Monthly or less	1.00					
More than once in a month	2.33	0.89–6.06	0.082			
Illness in the last three months						
Yes	1.00					
No	0.29	0.12–0.72	0.007	0.31	0.12–0.77	0.012
Number of illness episodes in the Family in the last three months						
≥5	1.00					
1–4	1.01	0.51–2.01	0.967			
None	0.30	0.10–0.89	0.030			
URTI with flu symptoms						
Yes	1.00					
No	1.89	1.18–3.03	0.008			
COVID-19						
No	1.00					
Yes	3.31	1.96–5.58	<0.001	2.41	1.40–4.15	0.001
Case of hospital admission in the family in the last three months						
No	1.00					
Yes	4.55	2.51–8.22	<0.001	2.61	1.39–4.89	0.003
Access to prescribed medication						
No	1.00					
Yes	0.59	0.30–1.14	0.117			
Check the expiry date of the medicine						
Yes	1.00					
No	0.47	0.15–1.43	0.184			
Already took an expired medicine						
Does not know	1.00					
No	1.93	0.63–5.92	0.248			
Yes	4.05	1.16–14.18	0.028			

* Crude prevalence ratio (PR crude); Adjusted prevalence ratio (RP adjusted); Confidence Interval (CI 95%); *p*-value (*p*). ** Tropical Medicine Institute, polyclinic, private service, pharmacy; CHA = Community Health Agent; URTI = Upper Respiratory Tract Infections.

2.3. Prescribed Antibiotics and Self-Medication

The 18–39 age group was the most prevalent among both self-medicated and prescribed antibiotic users. Amoxicillin was commonly used to treat throat-related complaints, while azithromycin was often used for COVID-19. Self-medication with antibiotics was

mainly for "throat inflammation" and had a shorter duration of use compared to prescribed antibiotics, which were used for a wider range of conditions, including urinary tract infections and diarrhea (Table 5).

Table 5. Characteristics of participants according to how they consume antibiotics—self-medication and prescribed. Coari, Amazonas, Brazil, 2021.

Age Range (Years)	Self-Medication with Antibiotics (n = 22/67) n (%)	Used Antibiotics	Reason of Use	Mean Use Time (Days) (±SD **)
18–39	13 (59.1)	Amoxicillin	Throat inflammation *	5 (±0)
		Azithromycin	COVID-19 *	7 (±0)
		Cefalexin	Skin infection	3 (±0)
		Sulfamethoxazole	Intestinal infection	7 (±0)
40–59	8 (36.4)	Azithromycin	COVID-19 "prevention" *	-
		Cefalexin	Urinary tract infection	5 (±0)
		Penicillin G Benzathine	Throat inflammation *	-
		Metronidazole	Intestinal infection *	10 (±0)
		Sulfamethoxazole	Intestinal infection *; Urinary tract infection	16 (±19.7)
≥60	1 (4.5)	Amoxicillin	Throat inflammation *	2 (±0)
Age range (years)	Prescribed antibiotics (n = 45/67) n (%)	Used antibiotics	Reason of use	Mean use time (days) (±SD **)
18–39	22 (48.9)	Amoxicillin	Throat inflammation *, sore throat *; urinary tract infection	10.8 (±6.6)
		Azithromycin	COVID-19 *, throat inflammation * virus *	6 (±1.4)
		Cefalexin	urinary tract infection	10 (±0)
		Ciprofloxacin	urinary tract infection	22.3 (±13.2)
		Penicillin G Benzathine	Throat inflammation *	-
40–59	20 (44.4)	Azithromycin	Throat inflammation * COVID-19 *	5.5 (±2.0)
		Cefalexin	urinary tract infection	6 (±1.7)
		Ciprofloxacin	urinary tract infection	-
		Sulfamethoxazole	Diarrhea	7 (±0)
		SFM + TMP	Stomach discomfort *	7 (±0)
≥60	3 (6.7)	Azithromycin	COVID-19 *	3 (±0)
		Tetracycline	Flu *	2 (±0)

* Non-bacterial conditions. ** SD = Standard Deviation.

3. Discussion

This study, conducted in the urban area of Coari, a city of 83 000 inhabitants in the Amazon basin in Brazil, showed that antibiotics were used by 14.7% of participants. The main reasons cited for antibiotic use included respiratory, urinary, and intestinal problems, some of which are likely viral infections, such as the flu, sore throat, or throat inflammation. The most commonly used antibiotics were macrolides (azithromycin), cephalosporins, peni-

cillins, and fluoroquinolones. While most macrolides and fluoroquinolones were prescribed, self-medication was more common with amoxicillin and sulphonamides. Antibiotic use was associated with younger age, presence of hospitalized relatives, COVID-19 infection and frequency of CHA home visits. Overall, the study pointed to a profile of participants with low economic level, more than nine years of education among adults, and ease of access to health services and antibiotics.

3.1. Availability of Antibiotics

The prevalence of antibiotic consumption in adults in this study was 14.7%, comparable to figures found in Eritrea, Africa (12.3%) [27], but lower than those found in other international studies conducted with adults in urban areas, where the frequency ranged from 20.4% in India [28], to 73.2% in Afghanistan [17]. It was also lower when compared to South America, where higher frequencies of use have been found (e.g., 24.8% [19] and 44.4% [29] in Colombia). In Brazil, the prevalence was lower than a study in the northeast region (58.0%) [21] and higher than a study in the midwest (6.8%) [30]. Compared to the Amazonian context, it should be highlighted that the prevalence in Coari was higher than in studies from Manaus, the capital of the Amazonas state, located almost 400 kilometres down the river; these studies found prevalences of 3.4% [22] and 8.0% [23].

Different factors can explain these differences, and access and infrastructure of the local health network may be particularly important. Coari is the sixth most populous municipality in Amazonas [31], with a healthcare network in the urban area that may facilitate access to health services and antibiotics. There is also an extensive private pharmaceutical network with little supervision in medication dispensing [4]. The low supervision in pharmacies may also contribute to the increased prevalence of antibiotic consumption, unlike Manaus, where supervision of antibiotic dispensing is more rigorous, which may be a limiting factor for the consumption of antibiotics without a medical prescription.

Seasonality can also be considered a factor that influences the prevalence of antibiotic consumption. Safaeian et al. report a higher frequency of antibiotic consumption during autumn and winter in Isfahan, Iran, seasons that occur between March and September in much of Brazil. The state of Amazonas has two seasons, a rainy one (December to May) and a dry one (June to November) [32]. During the dry season, the state of Amazonas experiences high concentrations of atmospheric pollutants from deforestation fires, often exceeding the WHO 24 h air quality limit. These fires significantly impact human health by increasing the incidence of respiratory diseases [33]. In this context, it is possible that the adverse effects of atmospheric pollutants on human health increase hospitalizations [34] and consequently the consumption of medications, including antibiotics. This can be considered another example of the effect of the climate crisis on human health. Our study was conducted in October and November, the dry season; therefore, the seasonal influence on the proportion of persons exposed to antibiotics cannot be ruled out.

The proportion of antibiotic consumption in this study was higher among females, although the difference was not statistically significant. In the municipality of Coari, according to estimates by the state social assistance secretariat, for the beginning of the 2020 decade, the urban population was mostly composed of men [35]. Then, a possible explanation for the higher proportion of women found in this study is that the approach to households was a face-to-face interview; as in other places, women are largely responsible for domestic activities in Coari. Furthermore, women have an increased susceptibility to urinary tract infections [36], and 27.5% of the 58 persons exposed to antibiotics declared to have taken these medicines to treat a urinary tract infection.

3.2. Prescription Status

More than one-third of the antibiotics used in this study (n = 22; 32.8%) were not prescribed. In 2011, the Brazilian Health Surveillance Agency (ANVISA) established that the sale of antibiotics requires a special medical prescription in two copies [37]. Despite the measures, the lack of effective oversight and inequalities in healthcare access in remote areas, such as Coari, encourage the irregular operation of pharmacies and promote self-medication with antibiotics [38].

The fact that 65.5% of the sample consumed prescribed antibiotics suggests that most adults in the urban area of Coari access the health system to obtain these medications. But this is not enough to ensure appropriate use; antibiotics should be prescribed following guidelines. Different studies have highlighted that the prescription of antibiotics does not always adhere to the existing guidelines or recommendations [12]. Our study provides an indirect measure of the lack of adherence to basic principles of antibiotic prescription, as azithromycin was the most frequently prescribed antibiotic for conditions that do not always warrant antibiotic use, such as "throat inflammation" and COVID-19. Unfortunately, the recommendation of using azithromycin for COVID-19 during the early days of the pandemic in 2020 and the persistence of that behaviour despite having shown the lack of evidence is well known [39–41]. Concerning other reasons of use, despite the fact that these are self-reported conditions, "throat inflammation", "sore throat", "virus", or "prevent COVID-19" strongly suggest an inappropriate antibiotic prescription; additionally, viruses are the main cause of upper respiratory tract infection, including rhinopharyngitis and pharyngitis [19]. It is important to note that most of the azithromycin prescriptions came from basic health units and the municipality's hospital. This information suggests that intervention efforts should be directed primarily at these health facilities. The reasons to explain this behaviour in Coari may be related to factors such as the complacency desire of the professionals to have a good relationship with patients and uncertainty about how to manage infectious diseases due to the lack of diagnostic resources [12,42]. All of this may reflect a gap in antibiotic prescription guidelines for health professionals in Coari. To reduce this practice, it is essential to develop specific guidelines that promote more careful prescribing. These findings highlight the need for municipal managers to implement clear protocols to guide health professionals, both in primary care units and in the municipal hospital, in the responsible prescription of antibiotics. By promoting more rational prescription, antimicrobial treatment guidelines ensure that antibiotics are recommended only for patients who really need them, especially those hospitalized with comorbidities and possible bacterial pneumonia [40].

Cases of urinary tract infections were common in our sample (n = 16). The most used antibiotics for this indication were cefalexin and ciprofloxacin. Unlike throat inflammation, urinary infections must be treated with antibiotics in most cases. The use of cefalexin or ciprofloxacin for urinary tract infection is recommended as a second-line therapy. At the same time, nitrofurantoin and fosfomycin remain reliable and recommended for empirical treatment of uncomplicated urinary infections [43]. However, none of the persons interviewed had taken these first-line medicines for urinary tract infections. Although the present study was not designed to assess the appropriateness of the management of urinary tract infections in the community, one recommendation is to design drug utilization studies to analyze the management of common infectious conditions in Coari specifically.

While most watch-list antibiotics were prescribed, 5/22 participants self-medicated with azithromycin. The rest primarily used cefalexin, amoxicillin, or sulfonamides. Despite being *Access* antibiotics, this does not mean that such a high level of self-medication does not require our attention, especially because the alleged reasons for use were to treat symptoms related to flu and common cold "intestinal infection" or diarrhea. This behaviour can be

attributed to multiple reasons, including misunderstanding the concept of "antibiotic" or convenience to avoid seeking health services.

3.3. Associated Factors

In agreement with international and national studies, adult antibiotic use was associated with younger age groups [23,44–46]. Interestingly, the frequency of antibiotic use among the elderly in our sample was low (6.9%); generally, the elderly are more vulnerable to infections, and therefore, higher antibiotic consumption is expected among them [19]. On the other hand, higher antibiotic consumption among young adults (51.7%) may reflect the fact that this economically active age group seek quick relief from symptoms to avoid the risk of forced medical leave, resorting to self-medication with antibiotics, so as not to compromise their domestic or professional activities [27].

This study found a curious association between antibiotic consumption and participants with relatives from the same household who were hospitalized in the last three months. A possible reason for this may be the psychological impact inherited from the pandemic, such as fear and panic. These feelings may have influenced individuals with hospitalized relatives to seek health services or self-medicate, believing that antibiotics could prevent infections or treat initial symptoms of respiratory infection or other infectious problems [42,45]. These psychological issues may also have affected the doctor-patient relationship, increasing the likelihood of patients asking doctors for antibiotics due to fear of developing severe forms of COVID-19, with consequent hospitalization [45].

Given the Amazonian context, it is worth highlighting the frequency of CHA visits to households. The inverse relationship between the frequency of CHA visits and antibiotic use is a relevant aspect. This result indicates that CHAs, as key primary healthcare professionals in Coari, play a strategic role in promoting the rational use of antibiotics. More frequent visits can intensify health education, facilitate early identification of conditions that do not require antibiotics and increase access to appropriate health services. When properly trained [47], CHAs have the potential to reduce both the need for and inappropriate use of these drugs, promoting more responsible and effective management.

Given all this, the inappropriate use of antibiotics, whether through self-medication or prescriptions for suspected viral infections, identified in this study, is a cause for concern, as it could accelerate the development of AMR in the region. The presence of resistant bacteria in Coari compromises the treatment of common and serious infections, increasing the municipality's dependence on the capital, Manaus, for critical care. In addition, the inadequate disposal of antibiotics and the lack of sewage treatment contribute to the contamination of water resources in the Amazon basin, promoting the selection and spread of resistant bacteria. Given the ecological relevance of the Amazon and the close link between human and environmental health, the spread of AMR represents a major threat to public health, both regionally and globally. It is essential to implement enforcement, health education and AMR monitoring measures to mitigate the impacts of inappropriate antibiotic use in Coari. This concern has been addressed in national recommendations. Law 14.912, of 3 July 2024, which amends the Brazilian Organic Health Law, requires managers to promote permanent awareness campaigns about the risks of self-medication, with a focus on the inappropriate use of antibiotics and special control drugs [48].

3.4. Limitations

This study has different limitations that must be described to avoid misleading interpretations of the results. This study was designed to collect information about health issues directly from the general population through a face-to-face interview. First, the collection of information about medications was over the last 3 months and there is possible memory

bias; this bias may have made it difficult for participants, especially the less educated, to distinguish antimicrobials from other medications. Second, data collection was carried out in person at households, which may have influenced respondents' answers due to fear, shame, or reluctance to inform which medications were taken, what they were used for, who indicated them, and where they were obtained. Third, the participants were not healthcare professionals or community health professionals; therefore, the declared reasons for use can be imprecise, depending on their schooling and background.

Despite these limitations, the results obtained can generate hypotheses to help in the formulation of future studies, focused mainly on antibiotic prescription practises in public health establishments in the urban area of Coari, as well as on the dispensing of these medications at points of sale.

4. Materials and Methods

4.1. Study Design and Setting

This cross-sectional analysis of antibiotic consumption was part of a larger cohort study titled "Climatic events and health conditions of adults in the Amazon region: a population-based study". The research was conducted in the urban area of Coari, a municipality located in the central region of Amazonas State, Brazil. Coari is 363 km from Manaus, with an estimated population of 70.616 as of the 2022 demographic census (see Figure 2).

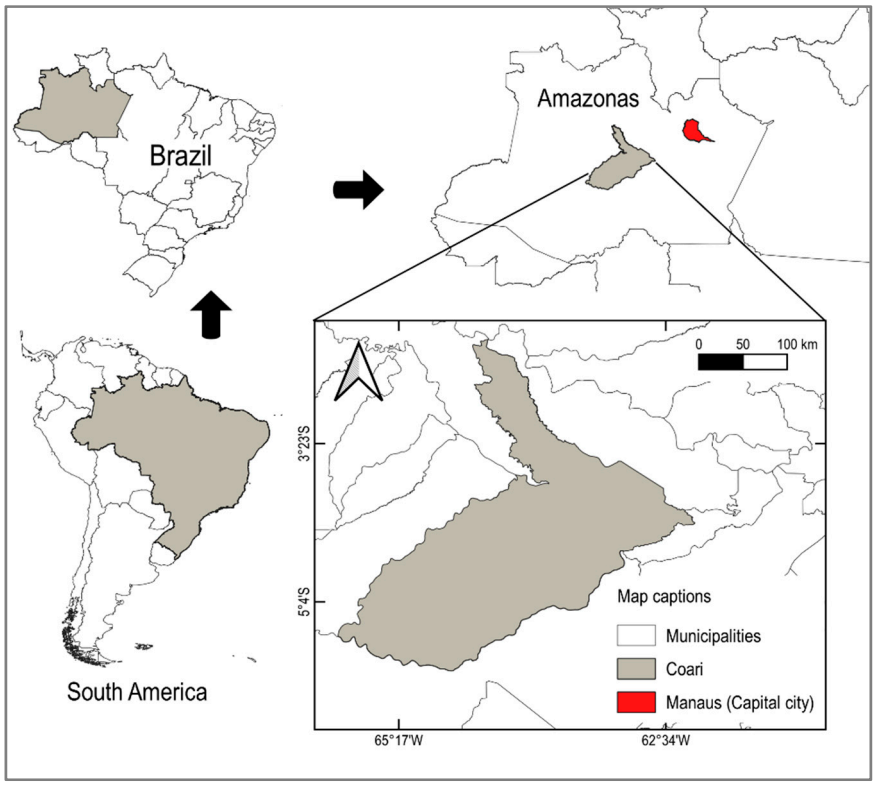


Figure 2. Location of the state of Amazonas and the city of Coari, Amazonas, Brazil 2024. Source: *Instituto Brasileiro de Geografia e Estatística*. Tool: qgis.org version 3.34.7. Bold arrows: Brazil in South America and the state of Amazonas in Brazil. White arrow: north arrow.

4.2. Sample Size and Selection

The sample was probabilistic and stratified by streets and households. The adult population of the 15 neighbourhoods in the municipality's urban area was considered to obtain the sample unit. The population data were based on the 2010 demographic census. The number of adult residents in the municipality's urban area was 13.476 (N).

The formula for determining the sample size (n) was based on the estimate of the population proportion [Source: Levine, Berenson and Stephan]

$$n = \frac{N \cdot \hat{p} \cdot \hat{q} \cdot (Z_{\alpha/2})^2}{\hat{p} \cdot \hat{q} \cdot (Z_{\alpha/2})^2 + (N-1) \cdot E^2} \quad (1)$$

where

n ˆ = number of individuals in the sample;

N = total population of the study;

p = population proportion of individuals belonging to the category of interest in the study;

q = population proportion that does not belong to the category of interest in the study ($q = 1 - p$);

$Z_{\alpha/2}$ = critical value corresponding to the desired degree of confidence;

E = margin of error or maximum estimate error. It identifies the maximum difference between the sample and true population proportions (p).

As the values of p and q, proportional, were not known, they were replaced by 0.5, as proposed by Levine, Berenson, and Stephan (1998) [49]. A 95% confidence level and 5% standard error were used, corresponding to the critical value of 1.96 associated with the confidence level in the sample.

Thus, considering that the adult population residing in the neighbourhoods of the urban area of the municipality, including residents of floating houses adjacent to the neighbourhoods, totalled 13.476 adults (N), and was considered a finite population, the recommended "n" for this study was 394 adults, with the appropriate statistical inferences and obeying the margin of error of 5% and confidence level of 95% and considering a non-response rate of 10%.

4.3. Data Collection Process

Data collection occurred during the ebbing of the Amazon River between October and November 2021. The process was operationalised in two stages: (1) selection of all 15 neighbourhoods in the city urban area, and (2) random selection of streets and households in each selected neighbourhood. Initially, all the streets in each neighbourhood were listed sequentially, in ascending order. Then, using a random number generator, the streets in each neighbourhood were randomly drawn. The complete list of streets in the 15 neighbourhoods was provided by the municipal infrastructure department. After this, the houses in each street were selected alternately, including the first, excluding the second and so on. In cases of absence, the interviews were rescheduled for a suitable date and time.

Data collection was conducted using a structured form comprising sections on sociodemographic information, access to health services, self-reported illnesses, and medication consumption. After signing the Informed Consent Form, interviews were conducted in households with family heads, maintaining a social distancing of 1.5 m in compliance with health regulations during the COVID-19 pandemic.

4.4. Eligibility Criteria

Inclusion criteria: Age ≥18 years, responsible for family income, resident of Coari's urban area.

Exclusion criteria: Physical or mental difficulties preventing interview response or absence after two contact attempts.

4.5. Variables

The dependent variable was antibiotic consumption, defined as the use of at least one antibiotic, with or without prescription, in the last three months before the interview. The study subjects were encouraged to show the packaging or prescription of the antibiotics. Independent variables included sociodemographic factors (age, gender, education, income), health service access (frequency of community health agent visits, preferred health service), self-reported illnesses (presence of diseases, COVID-19 diagnosis), and medication use habits (self-medication, storage practises).

4.6. Antibiotic Classification

Antibiotics were classified using two systems:

The Anatomical Therapeutic Chemical Classification System (ATC), which allows for the standardization of drug groupings and comparisons across different healthcare settings.

The WHO *AWaRe* (Access, Watch, Reserve) classification, which was introduced in 2017 to address concerns about irrational use and increasing antibiotic resistance. This system categorizes antibiotics into three groups based on their clinical importance and resistance potential: Access, Watch, and Reserve [50].

4.7. Data Analysis

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 20.0 for Windows. Quantitative variables were described using central tendency and dispersion measures, while categorical variables were described using absolute and relative frequency calculations.

To identify possible associated factors, Poisson regression analysis with robust variance was employed to estimate crude (RPbr) and adjusted (RPaj) Prevalence Ratios and their respective 95% Confidence Intervals (CI95%). This regression model was chosen because it provides direct and reliable estimates of the prevalence ratio, which allows for more precise epidemiological analysis [51].

Pearson's chi-square test was used to select factors and establish their respective order of entry into the multivariate model, first inserting those with the lowest value up to the maximum threshold of $p < 0.20$. When the assumptions of this test did not allow its application, Fisher's exact test was applied.

A Backward elimination variable selection procedure was used to remove variables with the least effect on the outcome. In the final model, variables that presented $p \leq 0.05$ were retained. This variable selection method was chosen because of its ability to simplify regression models, resulting in more interpretable and efficient models.

The chi-square test or Fisher's exact test (when chi-square assumptions were not met) was used to select factors and establish their order of entry into the multivariate model, with a threshold of $p < 0.20$.

4.8. Ethical Considerations

The study was approved on 24 April 2021 by the Human Research Ethics Committee of the Federal University of Amazonas (Approval number: 4.668.564, CAAE: 43767420.9.0000.5020). This approval ensures compliance with the guidelines for research involving human subjects, as per Resolution No. 466 of the National Health Council. The Informed Consent Form was signed in duplicate, with one copy for the researcher and another for the participant.

4.9. Research Team and Training

The research team comprised the main researcher, physiotherapists, nurses, and volunteer students from undergraduate courses at the Institute of Health and Biotechnology of the Federal University of Amazonas. Team training was conducted in the institute's laboratories to ensure standardized data collection procedures.

5. Conclusions

The use of antibiotics in the urban area of Coari is prevalent, and one-third of the declared use was without a prescription. Among the antibiotics obtained after a medical prescription, the most relevant finding was the use of the Watch macrolide azithromycin for common upper respiratory tract conditions such as rhinopharyngitis and for the management or prevention of COVID-19.

Based on this study's findings, greater control over antibiotic use is needed. This includes revising and updating guidelines in public health facilities and increasing their adherence. Monitoring dispensation is probably a global need, but the challenge can be greater in places that are not capital cities and in areas with poor healthcare facilities and a reduced number of healthcare professionals, such as Coari, in the heart of the Amazon basin.

Finally, this study points out the need to improve the population's basic healthcare education and strengthen the network of community health agents, as these professionals become the first aid in areas such as the studied.

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Institutional Review Board Statement: The study was conducted in accordance with the guidelines of the Declaration of Helsinki and the protocol was approved by the Research Ethics Committee of the Federal University of Amazonas (protocol code 43767420.9.0000.5020) on 24 April 2021.

Informed Consent Statement: Informed consent was obtained from all the subjects involved in the study.

Data Availability Statement: Third-party data. Restrictions apply to the availability of these data. The data were obtained from third parties and is available with the permission of Prof. Dr. Edivã Bernardo da Silva [edivasilva@ufam.edu.br].

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