# Profile of drug consumption during the COVID-19 pandemic in a pharmacy in the city of Teresina-PI

Perfil do consumo de medicamentos durante a pandemia da COVID-19 em uma farmácia na cidade de Teresina-PI

Perfil de consumo de medicamentos durante la pandemia de COVID-19 en una farmacia de la ciudad de Teresina-PI

Analina Beserra Martins[1], Márcia dos Santos Rizzo[1],José de Sousa Lima Neto[1], Hilris Rocha e Silva[1], Marcília Pinheiro da Costa[1].

**ABSTRACT**

**Objective:** To evaluate the consumption of vitamin, flu, antibiotic, anti-inflammatory and antiparasitic medications before and during the COVID-19 pandemic in a community pharmacy in Teresina, in the state of Piauí, Brazil. **Methods:** This retrospective observational case study evaluated the consumption of five classes of medications, including vitamins, flu, antibiotics, anti-inflammatory and antiparasitic drugs, in the period before and in the pandemic. Data analyses were performed using the SPSS program, and p<0.05 was significant. **Results:** During the pandemic period, vitamin (36%), flu (34%), and antiparasitic (22%) drugs werethe most consumed during the study period. The chi-square test of independence showed an association between medication consumption (influenza, ivermectin, antiparasitic, multivitamins, and vitamin C) and the COVID-19 pandemic. When comparing the period before and during the pandemic, it was observed that onlythe drug ivermectin used as off-label had an increase in consumption of 917.65%. **Conclusion:** The study corroborated the national and international results that observed a significant increase in the consumption of some medications, especially ivermectin and multivitamins. Then, our results reinforce the importance of the correct use of drugs, the risks of self-medication and the monitoring of patients using drugs in an off-label regimen.

**Keywords:** Pharmaceutical attention, Off-label use, Self-medication, Coronaviruses, SARS-CoV-2.

**RESUMO**

**Objetivo:** Avaliar o consumo de medicamentos vitamínicos, gripais, antibióticos, anti-inflamatórios e antiparasitários antes e durante a pandemia de COVID-19 em uma farmácia comunitária de Teresina, Piauí, Brasil. **Métodos:** Este estudo de caso observacional retrospectivo avaliou o consumo de cinco classes de medicamentos, incluindo vitaminas, gripe, antibióticos, anti-inflamatórios e antiparasitários, no período anterior e durante a pandemia. A análise dos dados foi realizada no programa SPSS (p<0,05). **Resultados:** Durante o período de pandemia, os medicamentos vitamínicos (36%), gripe (34%) e antiparasitários (22%) foram os mais consumidos no período do estudo. O teste qui-quadrado de independência mostrou associaçãoentre o consumo de medicamentos (influenza, ivermectina, antiparasitário, multivitamínicos e vitamina C) e apandemia de COVID-19. Ao comparar o período antes e durante a pandemia, observou-se que apenas o medicamento ivermectina utilizado como off-label teve um aumento no consumo de 917,65%. **Conclusão:** O estudo corroborou os resultados nacionais e internacionais que observaram um aumento significativo no consumo de alguns medicamentos, principalmente ivermectina e polivitamínicos. Nossos resultados reforçama importância do uso correto dos medicamentos, os riscos da automedicação e o acompanhamento de pacientes que utilizam medicamentos em regime off-label.

**Palavras-chave:** Atenção farmacêutica, Uso *off-label,* Automedicação, Coronavírus, SARS-CoV-2.

[1] Universidade Federal do Piauí (UFPI), Teresina - PI.

**SUBMETIDO EM: 7/2022 | ACEITO EM: 8/2022 | PUBLICADO EM: 9/2022**

**RESUMEN**

**Objetivo:** Evaluar el consumo de medicamentos vitamínicos, antigripales, antibióticos, antiinflamatorios y antiparasitarios antes y durante la pandemia de COVID-19 en una farmacia comunitaria de Teresina, en el estado de Piauí, Brasil. **Métodos:** este estudio de caso observacional retrospectivo evaluó el consumo de cinco clases de medicamentos, incluidas vitaminas, antigripales, antibióticos, antiinflamatorios y antiparasitarios, en el período anterior y durante la pandemia. **Resultados:** Durante el período de pandemia, los medicamentos vitamínicos (36%), antigripales (34%) y antiparasitarios (22%) fueron los más consumidos durante el período de estudio. La prueba de independencia chi-cuadrado mostró una asociación entre el consumo de medicamentos (influenza, ivermectina, antiparasitarios, multivitamínicos y vitamina C) y la pandemia de COVID-19. Al comparar el período antes y durante la pandemia, se observó que solo el fármaco ivermectina utilizado como off-label tuvo un incremento en el consumo del 917,65%. **Conclusión:** El estudio corroboró los resultados nacionales e internacionales que observaron un aumento significativo en el consumo de algunos medicamentos, especialmente ivermectina y multivitamínicos. Nuestros resultados refuerzan la importancia del uso correcto de los medicamentos, los riesgos de la automedicación y el seguimiento de los pacientes que usan medicamentos en un régimen fuera de etiqueta.

**Palabras clave:** Atención farmacéutica, Uso off-label, Automedicación, Coronavirus, SARS-CoV-2.

## INTRODUCTION

The COVID-19 pandemic has had a disastrous effect on world demography (WORLD HEALTH ORGANIZATION, 2021). The epidemic, which began in December 2019 in Wuhan, China, is caused by the new SARS-CoV-2 coronavirus, whose form of transmission by air, between an infected person to a susceptible, occurs through droplets of flügge containing the infectious agent (WORLD HEALTH ORGANIZATION, 2020). COVID-19 has a wide spectrum of clinical manifestations with mild signs and symptoms similar toflu and colds, and even progressing to critical clinical conditions such as respiratory failure, septic shock, andacute respiratory distress syndrome, rapidly progressing to death (NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE, 2020).

At the beginning of the pandemic the therapeutic protocol was limited due to the lack of knowledgeabout the virus, its pathogenic mechanism and the disease evolution. Therefore, in the absence of an effectiveand specific pharmacological treatment, we opted for the compassionate use of medications and off-label use,considering the known advantages of safety profile, dosage and adverse effects recommended in the packageinserts. Several drugs began to be investigated as potential agents to eliminate the virus or limit the severity of the disease, aiming to increase survival rates (ERKU D, et al., 2021). Drugs such as remdesivir developedfor the treatment of ebola (LAMB Y, 2020) chloroquine and hydroxychloroquine (antimalarials), which have been shown to inhibit the replication of SARS-CoV-2 in in vitro cell models (WANG M, et al., 2020), and azithromycin (broad-spectrum antibiotic), which blocks the replication of the Zika virus and influenza virus in human cells in vitro were also investigated (HUU D, et al., 2019).

In Brazil, remdesivir was the first drug indicated in the package insert to treat patients infected with COVID-19. At the end of May 2020, this drug had been approved in several countries, including the UnitedStates, European Union, and Canada (LAMB Y, 2020). The possibility of treatment for the disease opens a new perspective for solving this serious public health problem, which has already caused, until August 2021, more than 4.3 million deaths worldwide and more than 570,000 deaths in Brazil (WORLD HEALTH ORGANIZATION, 2021).

During the pandemic, a change in drug consumption patterns in Brazil was observed. The focuswas the consumption of drugs without conclusive scientific evidence in the first half of 2020 and administeredas off-label medication. As soon as the preliminary results of some of these studies were published, there wasan increase in prescriptions and self-medication with drugs such as hydroxychloroquine or chloroquine, associated with azithromycin, ivermectin and nitazoxanide, in addition to zinc supplements and vitamins C and D (MELO JRR, et al., 2020).

According to Quincho-Lopez A, et al. (2021), the fear of infection, low access to health services, and misinformation led people to self-medicate during the COVID-19 pandemic. The main problems caused by self-medication include unnecessary expenses, adverse drug reactions, drug toxicity, incorrect choice of medication, delay in primary health care, masking of symptoms, and possible drug interactions (QUINCHO-LOPEZ A, et al., 2021, BARACALDO-SANTAMARÍA D, et al., 2022). As reported by Baracaldo-Santamaría D, et al. (2022), there is evidence indicating that the COVID-19 pandemic has increased cases of adverse drug reactions (ADRs) related to self-medication.

Geller A, et al. (2021) observed that, in the United States, after the national emergency declaration, the distribution of seven drugs proposed for the treatment of COVID-19 increased significantly above pre-pandemic baselines. The increase in the dispensing of ivermectin, dexamethasone and zinc coincided with the increase in cases of COVID-19 in July 2020, despite these treatments not being recommended by the treatment guidelines in that country (GELLER A, et al., 2021). Brazil followed the samepattern of behavior. For example, ivermectin, an easily accessible and available drug, began to be used immediately in treating SARS-CoV-2 after releasing preliminary data from the in vitro studies conducted by Caly L, et al. (2020). Its low price and easy access caused a drastic increase in its use, reflecting an increasein consumption of 829% in 2020 (BRASIL, 2020).

According to the National Controlled Products Management System (NCPMS) database, between March 2020 and March 2021, more than 6.6 million cases of hydroxychloroquine sulfate, azithromycin, ivermectin, and nitazoxanide were sold in national private community pharmacies. Hydroxychloroquine was the most sold drug during the pandemic, followed by azithromycin (BRASIL, 2020).

The increase in sales of these drugs brought severe problems such as self-medication and adverse reactions (MELO PVM, et al., 2020). Thus, this study aimed to compare the drug consumption proposed as “treatment or prevention” of COVID-19, before and during the pandemic, in a pharmacy in Teresina, Piauí, Brazil.

## METHODS

The present work was a retrospective observational case study carried out in an independent community pharmacy in Teresina, Piauí, Brazil. The work was carried out in agreement with the pharmaceutical establishment. The convenience sample used in the study included five classes of medication, including vitamins, colds, antibiotics, anti-inflammatory and antiparasitic drugs. In this study, the drugs that had greater commercial relevance before and during the first year of the COVID-19 pandemic and were marketed in the pharmacy were considered. Data referring to the number of boxes of eachdrug sold were used. In this study, drug prescriptions were not used. The work used available sales data, and it was impossible to identify the buyers; then, the work was carried out following chapter IX, article 26 of RESOLUTION No. 674, MAY 6, 2022.

For sales volume comparison purposes two distinct periods were considered. The period preceding the COVID-19 pandemic, from April 2019 to March 2020, and the first year of the pandemic, from April 2020 to March 2021, were included in the study.

Each group of drugs was considered each month and at two different times before the COVID-19 pandemic in Brazil and during the pandemic. Data were extracted from monthly pharmacy reports to Excel® spreadsheets and then analyzed. The graphics were plotted using the *OriginPro® Software*. The chi-square association test was used to verify whether the studied variables (units of medicines sold and period before and during the pandemic) were associated or not (GOTELLI NJ and ELLISON AM, 2011; FÁVERO LP and BELFIORE P, 2017). The Statistical Package for Social Sciences (IBM SPSS Statistics) program was used for data analysis, and a significance level of $p < 0.05$ was considered.

## RESULTS AND DISCUSSION

This retrospective study made it possible to compare the sales volumes of drugs in the vitamin, flu, antibiotic, anti-inflammatory, and antiparasitic classes before and during the COVID-19 pandemic. The presentations and dosages of the drugs evaluated in this study are presented in **Chart 1**.

**Chart 1** - Pharmaceutical presentations of the drugs considered in the survey data collection.

| Class of medications | Active principle | Types of medication |
|---|---|---|
| Vitamins | Vitamin C | Coated tablet 500mg<br>Ascorbic acid effervescent tablet 1g<br>Ascorbic acid and zinc efervescente tablet(1g + 10mg) |
| | | Ascorbic acid and arginine aspartateeffervescent tablet (1g + 1g)<br>Ascorbic acid, zinc and vitamin D tablet(1g + 10mg + 400UI)<br>Ascorbic acid oral suspention in drops 200mg/mL |
| | Vitamin D | Softgel capsule 1000 UI<br>Softgel capsule 2000 UI<br>Softgel capsule 7000 UI<br>Softgel capsule 50000 UI<br>Solução oral 200 UI |
| | Vitamin E | Softgel capsule 400mg |
| | Multivitamins | Multivitamins oral suspention<br>Vitamin B complex, ascorbic acid andcyproheptadine hydrochloride oral suspention<br>Capsules<br>Coated tablet<br>Effervescent tablet<br>Oral suspention in drops |
| Anti-flu | Analgesic (acetaminophen, dipyrone, acetylsalicylic acid) + anti allergic drugs | Dipyrone monohydrate, ascorbic acid and chlorpheniramine maleate coated tablet (100mg + 50mg + 1mg)<br>Dipyrone, chlorpheniramine and caffeine coated tablet (250mg + 2mg + 30 mg)<br>Acetaminophen, chlorpheniramine maleateand phenylephrine hydrochloride tablet(400mg + 4mg + 4mg)<br>Acetylsalicylic acid, dexchlorphe-niraminemaleate, phenylephrine hydrochloride and caffeine tablet (400mg + 1mg + 10mg + 30mg)<br>Acetaminophen and felinephrine tablet(400mg + 20mg)<br>Acetaminophen and phenylephrine tablet(400mg + 20mg)<br>Acetaminophen and carbinoxaminemaleate tablet (400mg + 4mg)<br>Dipyrone and chlorpheniramine coatedtablet (250mg + 2mg)<br>Dipyrone and caffeine coated tablet(250mg + 30mg)<br>Acetaminophen, phenylephrine hydrochloride and carbinoxamine maleateoral suspention (40mg + 1mg + 0,4mg)<br>Acetaminophen, chlorpheniramine maleateand phenylephrine hydrochloride oral suspention (100mg + 2mg + 2mg)<br>Acetaminophen, chlorpheniramine maleateand phenylephrine hydrochloride oral suspention (40mg + 0,6mg + 0,6mg)<br>Acetaminophen, phenylephrine hydrochloride and carbinoxamine maleateoral suspention (13,3mg + 0,33mg + 0,13mg) |
| Antibiotics | Azithromycin | Tablet 500 mg |
| Anti-inflammatories | Prednisone<br>Dexamethasone | Tablet 5mg or 20 mg<br>Tablet 4 mg |
| Antiparasitic | Ivermectin | Tablet 6 mg |

**Source:** Martins AB, et al., 2022.

In order to verify whether there is an association between the period before and during the pandemic in drug consumption, the chi-square test of independence was performed, according to the data presented in **Table 1**. Through the analysis of the count of medicines consumption (observed frequency) and the expected count (expected frequency), it is possible to verify the existence of a significant deviation between these frequencies, indicating a possible significant difference between the consumption of medicines due to the Coronavirus pandemic. Adjusted residual indicates when the difference between frequencies was significant for each drug analyzed, assuming values lower than -1.96 and higher than +1.96 ($\chi 2$ tabulated value for $\alpha = 0.05$, with 9 degrees of freedom).

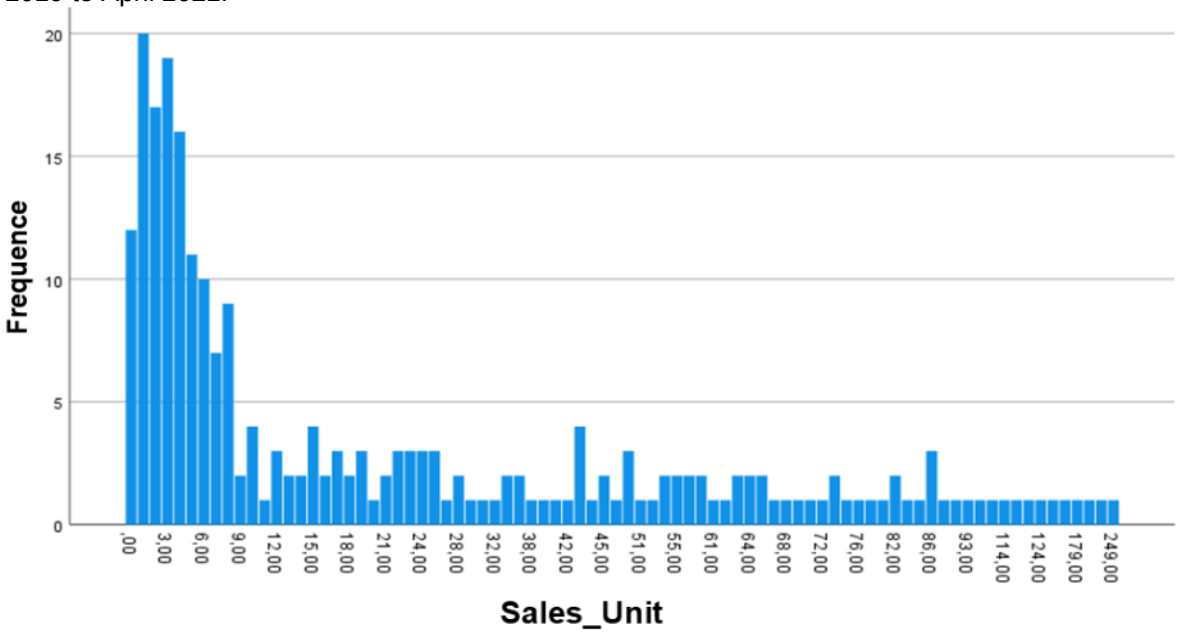
**Table 1 -** Observed and expected frequencies and value of standardized or adjusted residues in drugconsumption before and during the COVID-19 pandemic.

| Drug | Time course | | | | | | Total count | |
|---|---|---|---|---|---|---|---|---|
| | Before the pandemic | | | During the pandemic | | | | |
| | Observed frequency | Expected frequency | Adjusted residual | Observed frequency | Expected frequency | Adjusted residual | Observed frequency | Expected frequency |
| Anti-flu | 1129 | 913.1 | 11.4 | 1045 | 1260.9 | -11.43 | 2174 | 2174 |
| Azithromycin | 68 | 62.2 | 1.0 | 80 | 85.8 | -1.0 | 148 | 148 |
| Dexamethasone | 37 | 35.7 | 0.3 | 48 | 49.3 | -0.3 | 85 | 85 |
| Ivermectin | 68 | 319.2 | -19.6 | 692 | 440.8 | 19.6 | 760 | 760 |
| Other antiparasitic | 762 | 639.7 | 7.2 | 761 | 883.3 | -7.2 | 1523 | 1523 |
| Multivitamins | 225 | 336.8 | -8.5 | 577 | 465.2 | 8.5 | 802 | 802 |
| Prednisone | 63 | 70.6 | -1.2 | 105 | 97.4 | 1.2 | 168 | 168 |
| Vitamin C | 409 | 372.1 | 2.7 | 477 | 513.9 | -2.7 | 886 | 886 |
| Vitamin D | 29 | 37.8 | -1.9 | 61 | 52.2 | 1.9 | 90 | 90 |
| Vitamin E | 6 | 8.8 | -1.2 | 15 | 12.2 | 1.2 | 21 | 21 |
| **Total** | 2796 | 2796 | | 3861 | 3861 | | 6657 | 6657 |

**Source:** Martins AB, et al., 2022.

It was also observed the sales count data of the drugs listed in Table 1, in the histogram (**Figure 1**), and it was possible to verify a Poisson distribution, being necessary to observe whether the data were related randomly or not (interdependent). The statistical test to verify these associations between the variablesperiod and medication consumption is the independent chi-square test.

**Figure 1 -** Histogram of the frequency distribution of counting drug sales during the period from April 2019 to April 2021.



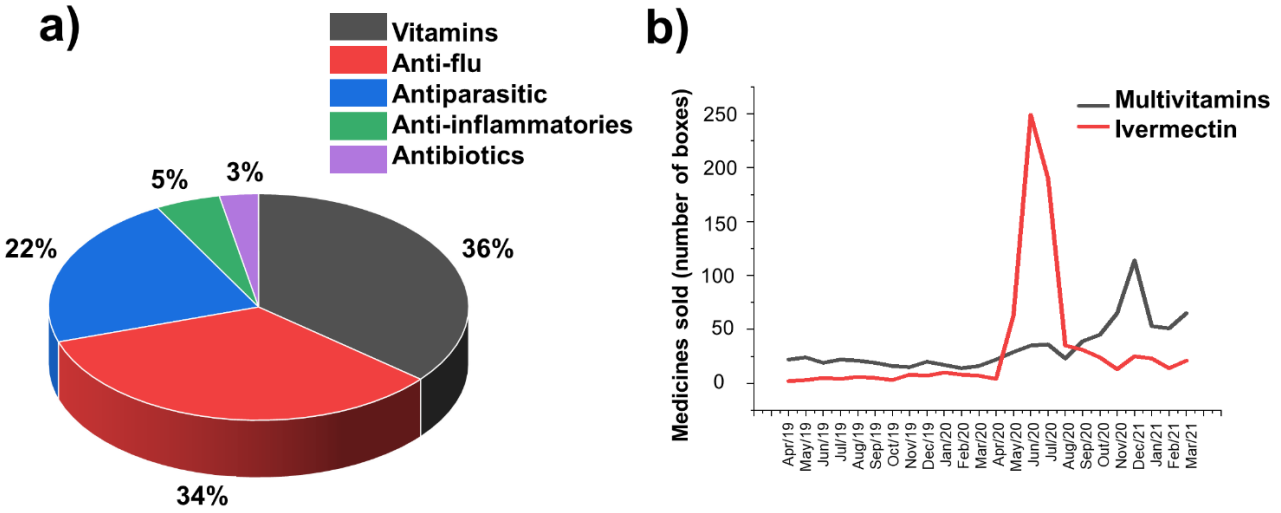

**Source:** Martins AB, et al., 2022.

These distributions have a probability density function with a chi-squared distribution, which justifies the application of the statistical test to check, during the months of study, whether there is an association of dependence in the consumption of specific medications between the beginning and the course of the COVID-19 pandemic. The Null Hypothesis (H0) of this statement is that the COVID-19 pandemic did not influence the consumption of these medications; that is, the consumption of medications was statistically equal or was randomly associated regardless of the period analyzed. The Alternative Hypothesis (H1) defines that there was an influence of the COVID-19 pandemic on the consumption of medicines and, therefore, they are statistically different, for a significance of ($\alpha = 0.05$, with 9 degrees of freedom (gl, and $\chi 2$ critical) = 19.337).

Pearson's chi-square is the chi-square or association value with a value greater than the critical $\chi 2$ and, in addition, the test's significance value (p) was less than 0.05 ($p<0.001$), both for 9 degrees of freedom,indicating that there is a non-random association between periods and drugs consumed, so the alternative hypothesis (H→1) was accepted. The standardized adjusted residual values (**Table 1**) for $p = 0.05$ should be between -1.96 and 1.96. The chi-square test indicated an association between the variables. Some of these adjusted residuals presented values outside this range of - 1.96 and 1.96. This indicates which categories of variables were associated.

Crossed data between observed and expected (**Table 1**) showed that the most significant differences between the observed and expected frequencies of each categorical variable are found in the following associations: anti-flu, ivermectin, other antiparasitic, multivitamins, and vitamin C, all these variables versus the time. The top-selling drugs during the COVID-19 pandemic can be seen in **Figure 2a**.

**Figure 2 - a)** Top-selling drugs during the COVID-19 pandemic; **b)** Antiparasitic sales volume before and duringthe COVID-19 pandemic.




**Source:** Martins AB, et al., 2022.

Regarding vitamin C and the period observed in our study, the expected value for this association differs from the observed value (**Table 1**). This analysis showed a positive relationship of 2.6956 before the onset of the pandemic. Thus, the amount of vitamin C consumed was higher before the pandemic in the studied pharmacy.

Concerning multivitamins and the period observed in our study, the expected value for this association differs from the observed value (**Table 1**). The analysis showed a positive relationship of 8.5325 during the pandemic and thus consumption of this drug increased significantly during the pandemic.

The concern with self-care intensified during the pandemic period, triggering the adoption of new health habits, given that COVID-19 affects immunosuppressed people, people with chronic diseases, and theelderly more intensely (JOVIC T, et al., 2020). This data can justify the growth in the consumption of medicines in the vitamin class.

The most consumed vitamins during the COVID-19 pandemic period were vitamins C and D, in addition to multivitamins. The maximum peak of vitamin C use occurred in March 2020, with smaller peaks occurring in July, November and December 2020. In the chosen community pharmacy, the results for vitaminD were not relevant concerning the others. However, multivitamins, which also have vitamins C and D in theircomposition, increased demand from March 2020, with a maximum peak in December 2020 and demand of 114 boxes. The growth trend of the three categories of vitamins from February 2021 can also be seen.

Despite the little relevance to vitamin C and multivitamins, when evaluated in isolation, it was possible to see, in our study, that in the first year of the pandemic course, vitamin D consumption had an overall increase of 110.34% over the year above (**Table 1**). The study carried out by the IMS Health/Quintiles (IQVIA) consultancy for the Conselho Federal de Farmácia found a significant increase of 35.56% in vitamin D sales during the pandemic compared to 2019, throughout the Brazilian territory (CONSELHO FEDERAL DE FARMÁCIA, 2020).

From December 2019, there was a sharp growth in the consumption of anti-flu drugs that culminated in a peak in March 2020. The same was not observed in the pandemic period. Regarding flu drugsand the period, the expected value for this association differs from the observed value. Thus, a positive relationship of 11.4324 was determined for the adjusted residual value before the pandemic. The drugs sold were higher before the pandemic and the consumption of this class of drugs was not affected by the pandemic. Then, during the pandemic, its consumption was reduced (**Table 1**).

Regarding ivermectin and the period observed in our study, the count value was very discrepant before and during the pandemic (**Table 1**). It was possible to observe a positive relationship of 19.6159 duringthe pandemic period. Thus, the pandemic significantly increased the consumption of ivermectin (**Figure 2b**). In our study, there was an increase of 395.24% in sales of ivermectin from April to May 2020 and a growth of 917.65% when comparing the pre-pandemic period and the first year of the pandemic.

The release of preliminary data from the study by Caly L, et al. (2020) on the antiviral activity of ivermectin in vitro on social media added to the fear of infection, encouraged health managers, medical professionals and even the population itself to buy medicines in an attempt to fight the coronavirus. Ivermectin and other medications are now included in the protocols for COVID-19 patients in Brazil (MELO PVM, et al., 2020; BARJUD MB, 2020a; BARJUD MB, 2020b), including the protocol for the care of COVID-19 in primary and hospital care asan alternative treatment for patients with contraindications to the use of hydroxychloroquine and azithromycin (FREITAS TIS, 2020).

In the United States, Geller A, et al. (2021) determined whether the frequency of outpatient retail dispensing of 17 potential treatments for COVID-19 had increased since March 13, 2020, when a national emergency was declared in the country. Among those drugs, ivermectin peaked in prescriptions in the week ending July 24 and rose again through December 18. After declaring a national emergency, the number of prescriptions dispensed increased by 583.4% until December 18, 2020 (GELLER A, et al., 2021).

In Brazil, in a survey carried out by the IQVIA consultancy, it was found that the volume of ivermectinsales in June 2020 was more significant than the total sales of this drug in the entire year of 2019. Similar behavior was observed in the present study, in which the number of ivermectin cases sold in June 2020 exceeded the total sold in 2019 by 366%. Furthermore, the prescriptions for this drug increased 1921% compared to the same period in 2019 (CONSELHO FEDERAL DE FARMÁCIA, 2020). All months considered after the start of the pandemic, the consumption of this drug was higher, except for March and April 2020, which is justifiable. After the release of the results of Caly L, et al. (2020) in April 2020, physicians worldwide began to prescribe or recommend ivermectin for the prevention and treatmentof the disease. As a result, in May 2020, there was an increase of 1575% compared to the previous month and a maximum peak that reached the total consumption of 249 boxes of ivermectin, a behavior that was maintained in July 2020. In August, there was a decrease of 543%; even so the consumption of this drug remained relevant throughout 2020 and the beginning of 2021.

We also compared the results obtained with the consumption profile of other antiparasitic drugs marketed in that pharmacy and found no significant difference between the two periods, as shown in **Table 1**. Regarding

other antiparasitic drugs and the period observed in this study, the expected value for this association differs from the observed value (**Table 1**). A positive relationship of 7.2317 was found before the pandemic. Thus, the consumption of this drug was affected by the pandemic, causing a significant decrease in its consumption during the pandemic.

Another class of drugs widely prescribed during the pandemic was antibiotics. Touret F, et al. (2020) observed that azithromycin efficiently inhibited the in vitro replication of SARS-CoV-2 and that its association with hydroxychloroquine completely blocked viral replication. These findings supported the off-label use of azithromycin, although no current clinical evidence supports the drug's efficacy and safety against any coronavirus in humans, including SARS-CoV-2 (KALIL AC, 2020).

Studies carried out by Gautret P, et al. (2020) recommended that patients with COVID-19 be treatedwith hydroxychloroquine and azithromycin to cure their infection and limit transmission of the virus to others. INFORMATIVE NOTE Nº 17/2020- SE/GAB/SE/MS in June 2020 included in its guidelines for the management and early treatment of patients affected by COVID-19 the associations of hydroxychloroquine +azithromycin or chloroquine + azithromycin for patients with mild and moderate conditions, or if they were in stages 1 (1st to 5th day of infection) or 2 (6th to 14th day) of the disease (MINISTÉRIO DA SAÚDE, 2020).

Preliminary studies by Gautret P, et al. (2020) also suggested a synergy effect in the combination of hydroxychloroquine and azithromycin. Azithromycin is active in vitro against Zika and Ebola viruses (HANNA R, et al., 2016; BOSSEBOEUF E, et al., 2018) 24,25 and prevents severe respiratory tract infections when administered to patients suffering from viral infection (BACHARIER LB, et al., 2015).

In our study, azithromycin sales volume peaked in June 2020 with the sale of 36 boxes, 720% higherthan the same period last year. The demand for ivermectin versus azithromycin was also evaluated, an association now adopted asa treatment protocol for SARS-CoV-2 infection. Although the sales volume of azithromycin was much lower than that of ivermectin, its sales behavior was similar, and the maximum peak occurred in June 2020. In the first place, this difference is due to the need for antibiotic prescription and its retention, which did not impede ivermectin since, despite being a red stripe drug, it is freely sold in pharmacies and drugstores.

Some anti-inflammatory drugs were also evaluated for their consumption. When comparing the consumption of dexamethasone before and during the pandemic, an increase of 333% can be seen in June 2020, compared to the previous month. Looking at the same period of the previous year, there was an increase of 500%.

In June 2020, researchers at the University of Oxford, through the Recovery study, announced the first scientific evidence that dexamethasone would reduce mortality in 1/3 of patients on mechanical ventilationand 1/5 of patients on oxygen therapy (RUBIO JLC, et al., 2021). This study provided strong evidence in favorof treating patients with COVID-19 under mechanical ventilation with 6 mg of dexamethasone once daily for ten days (PETER H, et al., 2021). It was concluded that this drug could be used to modulate inflammation- mediated lung injury that can occur during SARS-CoV-2 infection (ZANGRILLO A, et al., 2021).

The reflection of the publication of this study in June 2020 can be seen in the increased search for the drug in drugstores, despite the lack of indication of dexamethasone as a prophylactic or for the treatment of mild cases (PASIN L, et al., 2021). There was a sharp spike in sales in June 2020 for both dexamethasone4 mg and prednisone 20 mg. It is interesting to note that, from May 2020, the peaks of the two drugs occurredin the same months, in September 2020 and January 2021.

World Health Organization (WHO) guidelines for the treatment of COVID-19 have recommended dexamethasone or other corticosteroids such as hydrocortisone and methyl-prednisolone for critically ill patients (WORLD HEALTH ORGANIZATION, 2016). Dexamethasone and prednisolone are among the drugs most commonly on nationalessential drug lists; listed by 95% of countries (ROCHWERG B, et al., 2020), with prednisolone being the mostprescribed corticosteroid in Brazil, due to its high efficacy in respiratory infections and, mainly, because it hasa lower adverse effect on patients when compared to other corticosteroids such as dexamethasone.

Therefore, it was important to note in our study that the chi-square test of independence showed an association between drug consumption (influenza, ivermectin, antiparasitic, multivitamin, and vitamin C) and the COVID-19 pandemic [χ2 (9) = 547.048; p<0.001] (**Table 2**).

**Table 2 -** Results obtained from the χ2 Test between categorical variables, types of medications and time period (before the start of the COVID-19 pandemic, from April 2019 to March 2020, and during its course, from April 2020 to March 2021).

| Parameters | Value | df | Asymptotic Significance (Bilateral) |
|---|---|---|---|
| Likelihood ratio | 547.048[a] | 9 | <.001 |
| | 621.446 | 9 | <.001 |
| N of valid cases | 6657 | | |

**Legenda:** a= 0 cells (0.0%) expected a count less than a 5. The minimum expected count is 8.82. (prerequisites of χ2 met); df= degrees of freedom.
**Source:** Martins AB, et al., 2022.

The results presented also demonstrate the Brazilian population's use of medication indiscriminately.It was found that self-medication is a common habit for 77% of Brazilians who used medication in the last six months prior to the study carried out in 2019. Nearly 47% of the people self-medicate at least once a month, 25% do it every day or at least once a week (CONSELHO FEDERAL DE FARMÁCIA, 2020).

The COVID-19 pandemic brought with it an epidemic of irrational drug use. In recent months after the record of the first case of the disease in Brazil, sales of some drugs disclosed for the prevention or controlof the disease have increased dramatically, such as ivermectin (857%), hydroxychloroquine (126%), and dexamethasone (18%). We can assume that at least part of this excess consumption occurred due to self- medication since, in Brazil, 79% of people over 16 years of age admit to taking the medication without a medical prescription. Although responsible self-medication can be beneficial in a situation such as a pandemic, allowing patients to become responsible and gain confidence in managing their health, this wrongly performed practicebased on unreliable sources of information poses serious health risks (CONSELHO FEDERAL DE FARMÁCIA, 2020).

Adverse drug reactions (ADRs) are considered a severe public health problem and contribute to increased morbidity, mortality and costs for patients and health systems. ADRs can prolong the length of the patient's hospital stay, further aggravating the search for beds for newly infected patients (MELO PVM, et al.,2020).

Melo PVM, et al. (2021) carried out a cross-sectional study to assess the presence of adverse drugreactions (ADRs) resulting from treatments for COVID-19 in hospitalized patients collected in the pharmacovigilance system in Brazil. The drugs most implicated in adverse reactions were hydroxychloroquine (59.5%), azithromycin (9.8%), and chloroquine (5.2%). 38.8% of cardiac reactions were reported, 14.4% in the gastrointestinal system, 12.2% in the skin tissue, and 8.9% in the liver. Chloroquine and hydroxychloroquine were the only drugs associated with severe ADR. In addition, the authors identified that men and elderly people over 65 years of age were more likely to have severe ADR than others (MELO PVM, et al., 2020).

## CONCLUSION

Given the above, we verified that our analysis of the drug consumption pattern during the pandemic corroborated national and international results of a significant increase in drug consumption such as azithromycin and ivermectin, dexamethasone and vitamins. In addition, we note the urgency of implementing strategies on the proper use of medicines, aiming to reduce their indiscriminate use, as shown by our results and, thus, protect the population from adverse effects and damage to their health. Even more, our results reinforce the importance of monitoring patients using drugs in an off-label regimen, in addition to providing subsidies for better practices in pharmacovigilance.

## ACKNOWLEDGMENT

We thank the pharmacy that provided the drug sales data and the Graduate Program in Pharmaceutical Sciences at UFPI for their collaboration and trust in developing this research.

## REFERENCES


1. BACHARIER LB, et al. Early administration of azithromycin and prevention of severe lower respiratory tract illnesses in preschool children with a history of such illnesses: A randomized clinical trial. JAMA, 2015; 314(19): 2034–44.
2. BARACALDO-SANTAMARÍA D, et al. Drug safety of frequently used drugs and substances for self-medication in COVID-19. Therapeutic Advances in Drug Safety, 2022; 13: 1-14.
3. BARJUD MB. Protocolo para tratamento da Covid-19 no pronto atendimento, Teresina- Piauí. 4ª atualização, 30 de abril de 2020a. Disponível em: https://www.gp1.com.br/media/uploads/2020/05/14/processo.pdf. Acessado em: 23 de agosto de 2022.
4. BARJUD MB. Recomendações para tratamento de pacientes Covid-19: Baseado nos protocolos estabelecidos pelos seguintes Hospitais: Grupo HM Hospitais, H. La Paz, H. Ramón y Cajal, Fundación Jiménez Díez, H. 12 de Octubre (Espanha); e no protocolo de tratamento precoce Covid-Piauí. 5ª atualização, 2020b.
5. BRASIL. MS. CONSELHO NACIONAL DE SAÚDE. RESOLUÇÃO Nº 674, DE 06 DE MAIO DE 2022. Dispõe sobre a tipificação da pesquisa e a tramitação dos protocolos de pesquisa no Sistema CEP/Conep. Disponível em: https://conselho.saude.gov.br/images/Resolucao_674_2022.pdf. Acessado em: 23 de agosto de 2022.
6. BOSSEBOEUF E, et al. Azithromycin inhibits the replication of Zika virus. Journal of Antivirals & Antiretrovirals, 2018; 10(1): 6–11.
7. BRASIL. Venda de medicamentos controlados e antimicrobianos, 2020. Disponível em: https://dados.gov.br/dataset/venda-de-medicamentos-controlados-e-antimicrobianos-medicamentos- manipulados. Acessado em: 23 de agosto de 2022.
8. CALY L, et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. AntiviralResearch, 2020; 178: 104787.
9. CONSELHO FEDERAL DE FARMÁCIA (CFF). Plano de resposta para as farmácias privadas e públicas da atenção primária. Brasília. 2020; 21p.
10. ERKU D, et al. When fear and misinformation go virual: Pharmacists' role in deterring medication misinformation during the 'infodemic' surrounding COVID-19. Research in Social and Administrative Pharmacy, 2021; 17(1): 1954-1963.
11. FÁVERO LP, BELFIORE P. Manual de Análise de Dados - Estatística e Modelagem Multivariada com Excel®, SPSS®. Editora Gen LTC: São Paulo, 2017, 1216.
12. FREITAS TIS (org). Protocolo para atendimento da COVID-19 na atenção primária e hospitalar. Carmopólis de Minas-Piauí: EDUFPI, 2020. Disponível em: https://www.ufpi.br/arquivos_download/arquivos/PROTOCOLO_PARA_ATENDIMENTO_DA_COVID_Diagramado_paginado_justificadoNovo_PDF20200706211125.pdf. Acessado em: 23 de agosto de 2022.
13. GAUTRET P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open- label non-randomized clinical trial. International Journal of Antimicrobial Agents, 2020; 56: 105949.
14. GELLER A, et al. Assessment of Outpatient Dispensing of Products Proposed for Treatment or Prevention ofCOVID-19 by US Retail Pharmacies During the Pandemic. JAMA Internal Medicine, 2021; 181(6): 869-872.
15. GOTELLI NJ, ELLISON AM. Princípios de Estatística em Ecologia. Artmed Editora. Porto Alegre, 2011. 528.
16. HANNA R, et al. Zika virus cell tropism in the developing human brain and inhibition by azithromycin. Proceedings of the National Academy of Sciences of the United States of America, 2016; 13: 113(50).
17. HUU D, et al. Azithromycin, a 15-membered macrolide antibiotic, inhibits influenza A(H1N1) pdm09 virusinfection by interfering with virus internalization process. The Journal of Antibiotics, 2019; 72: 759–768.
18. JOVIC T, et al. Could Vitamins Help in the Fight Against COVID-19? Nutrients, 2020; 12: 2550.
19. KALIL AC. Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics. JAMA, 2020; 323(19): 1897–1898.
20. LAMB Y. Remdesivir: First Approval. Drugs 2020; 80: 1355–1363.
21. MELO PVM, et al. Enfrentamento da COVID-19 na atenção primária. Amapá, 2020. Disponível em: https://apublica.org/wp-content/uploads/2020/10/enfrentamento-da-covid-19-na-atencao- primaria.pdf. Acessado em: 23 de agosto de 2022.
22. MELO JRR, et al. Automedicação e uso indiscriminado de medicamentos durante a pandemia da COVID-19. Cadernos de Saúde Pública, 2021; 37(4): e00053221.
23. MINISTÉRIO DA SAÚDE. Plano nacional de operacionalização da vacinação contra a COVID-19. Brasília, 10de dezembro de 2020. Disponível em: https://www.gov.br/saude/pt- br/media/pdf/2020/dezembro/12/2020_12_11_plano-de-vacinacao-covid19-_revisado.pdf. Acessado em: 23 de agosto de 2022.
24. NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE). COVID-19 rapid guideline: critical care in adults; 2020. Disponível em: https://www.nice.org.uk/guidance/ng159. Acessado em: 23 de agosto de 2022.
25. PASIN L, et al. Corticosteroids for Patients with Coronavirus Disease 2019 (COVID-19) With Different DiseaseSeverity: A Meta-Analysis of Randomized Clinical Trials. Journal of Cardio and Vascular Anesthesia, 2021; 35(2): 578-584.

26. PETER H, et al. Dexamethasone in Hospitalized Patients with Covid-19. New England Journal of Medicine, 2021; 384(8): 693-704.
27. QUINCHO-LOPEZ A, et al. Self-medication practices to prevent or manage COVID-19: A systematic review. PLoS One, 2021; 16(11): e0259317.
28. ROCHWERG B, et al. A living WHO guideline on drugs for covid-19. BMJ 2020; 370: m3379.
29. RUBIO JLC, et al. Precaución con el uso de dexametasona en pacientes con COVID-19 en sus fases iniciales. Revista Clínica Española, 2021.
30. WANG M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-dCoV) in vitro. Cell Research, 2020; 30: 269-271.
31. WORLD HEALTH ORGANIZATION (WHO). Therapeutics and COVID-19: living guideline, 31 de março de 2021. Disponível em: https://www.who.int/publications/i/item/WHO-2019-nCoV- therapeutics-2021. Acessado em: 23 de agosto de 2022.
32. WORLD HEALTH ORGANIZATION (WHO). WHO Coronavirus dashboard, 2021. Disponível em: https://covid19.who.int/. Acessado em: 23 de agosto de 2022.
33. WORLD HEALTH ORGANIZATION (WHO). Novel Coronavirus (2019-nCoV), Situation Report – 1, 21January 2020. Disponível em: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf?sfvrsn=20a99c10_4. Acessado em: 23 de agosto de 2022.
34. TOURET F, et al. In vitro screening of a FDA approved chemical library reveals potential inhibitors of SARS-CoV-2 replication. Scientific Reports, 2020; 10(1): 13093.
35. ZANGRILLO A, et al. Dexametasona en COVID-19: ¿un medicamento para todos? Medicina Intensiva, 2021.