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Outpatient medication use among patients with COVID-19 before admission to a tertiary care hospital in Bucaramanga

Uso extrahospitalario de medicamentos en pacientes con COVID-19 previo al ingreso a hospital de tercer nivel en Bucaramanga

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Abstract

Introduction: During the COVID-19 pandemic, the outpatient use of medications such as antibiotics and corticosteroids became widespread, despite the lack of supporting evidence. In our setting, no studies have reported on the use of these medications and their subsequent outcomes. **Objective**: To describe outpatient medication use in patients with COVID-19 and its association with ventilatory outcomes and mortality. **Methodology:** An observational, analytical, retrospective cohort study was conducted. A total of 984 patients aged 18 years and older with a positive COVID-19 test who were hospitalized between August 1, 2020, and August 31, 2021, at a tertiary care hospital in Bucaramanga were included. Pregnant women and patients with severe anemia (<7 g/dL) or severe frailty were excluded. Statistical analysis was performed using STATA 14, applying logistic regression models with subsequent adjustment for clinical variables. **Results:** A total of 60.1% of the population were male, with a median age of 59 years (IQR 47-69). At admission, 13.43% reported outpatient use of dexamethasone, 2.9% prednisolone, 3.46% ivermectin, and 7.32% azithromycin. Dexamethasone use was associated with an increased risk of mortality, severe pneumonia, and the need for mechanical ventilation (OR 1.80; 95% CI: 1.12-2.88). Azithromycin and prednisolone use were also associated with a higher probability of severe pneumonia, whereas ivermectin showed no effect on the outcomes. **Discussion:** Early corticosteroid use was associated with a higher frequency of severe pneumonia, whereas azithromycin showed contradictory results, possibly explained by selection bias. Ivermectin had no impact on clinical outcomes. **Conclusion**: Our findings suggest that self-medication was less frequent than previously reported in the literature and associated with the development of severe pneumonia in patients who self-medicated with dexamethasone; this supports current recommendations to avoid self-medication in COVID-19.

Keywords: COVID-19; Self-medication; Self-care; Self-administration; Azithromycin; Dexamethasone; Mechanical ventilation; Pneumonia.

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Introduction

During the COVID-19 pandemic, we faced not only the challenge of an unknown disease but also the widespread adoption of numerous therapeutic practices lacking scientific support. Among these, self-medication occupies an important place, particularly involving the use of corticosteroids, antibiotics, and antiparasitic agents in outpatient settings[1, 2].

Self-medication, defined as the use of medications without a prescription or medical supervision, is associated with well-known risks: drug interactions, symptom masking, delayed care, and antimicrobial resistance. In the context of COVID-19, these risks are heightened, as the early and inappropriate use of corticosteroids may suppress the immune response and promote infection progression, while antibiotics, such as azithromycin, in the absence of bacterial infection, provide no clinical benefit and contribute to antimicrobial resistance[2, 3].

International studies have reported substantial variability in self-medication during the pandemic. In India, nearly one-third of patients reported self-medicating with different drugs[4]. In Germany, three out of four outpatients used over-the-counter medications[5]. A global meta-analysis estimated the prevalence at 41.7%[6]. In Latin America, in addition to corticosteroids and antibiotics, the use of ivermectin and hydroxychloroquine became widespread, despite clinical trials demonstrating their lack of efficacy[7, 8].

To date, no specific studies exist in Colombia on medication use before hospitalization for COVID-19 and its association with subsequent outcomes in these patients. However, evaluating how outpatient medications can affect clinical outcomes in patients with COVID-19 is important, as identifying medication use and its association with better or worse outcomes could inform future therapeutic and management strategies. Accordingly, the objective of this study was to describe the types of medications used for self-medication during the pandemic and their association with clinical outcomes in a cohort of patients hospitalized for COVID-19 in Bucaramanga, Colombia.

Methodology

Study design: An observational, analytical, retrospective cohort study was conducted at a tertiary care university hospital in Bucaramanga, Colombia. The analysis period extended from August 1, 2020, to August 31, 2021, encompassing the three main pandemic peaks in Santander.

Participants: A total of 984 hospitalized patients were included between August 1, 2020, and August 31, 2021.

Inclusion criteria: Patients aged 18 years and older, with a positive rapid antigen test (RAT) or polymerase chain reaction (PCR) test for COVID-19, who were hospitalized between August 1, 2020, and August 31, 2021.

Exclusion criteria: Pregnant patients and those with severe anemia (hemoglobin <7 g/dL) or severe frailty were excluded.

Definitions

- Outpatient medication use: Medication use reported by the patient or a family member before hospitalization and corroborated through the medical record. Corticosteroids (dexamethasone, prednisolone), azithromycin, and ivermectin were included.
- Severe pneumonia: Defined according to the Infectious Disease Society of America (IDSA) guidelines for severe pneumonia[9]. It includes major criteria, such as need for invasive mechanical ventilation or septic shock requiring vasopressors, and/or three minor criteria; respiratory rate (RR) ≥ 30 rpm, $PaO_2/FiO_2 \leq 250$, multilobar infiltrates, confusion/disorientation, uremia (BUN ≥ 20 mg/dl), leukopenia (< 4000 cells/μl), thrombocytopenia (< 100,000/μl), hypothermia (< 36 °C), and CURB-65 score.
- Severe frailty: Determined by the treating team based on geriatric assessment, including the clinical frailty scale to assess frailty and predict survival and functional dependence measured by the Barthel Index, and advanced comorbidity, including terminal disease (diagnosis with expected survival < 6 months).

- Initial clinical severity: Classified based on admission parameters such as the need for supplemental oxygen, severe pneumonia criteria, and, when available, the CURB-65 score and News 2.

Data collection and quality control

Data were obtained from institutional electronic health records. The database was created in Microsoft Excel and subsequently verified in duplicate to minimize data entry errors. In addition, a random review of 10% of the records was conducted for quality control. The dataset was then exported to STATA version 14 for analysis.

Variables

The main exposure variables were outpatient use of dexamethasone, prednisolone, ivermectin, and azithromycin.

The clinical outcomes evaluated were:

Severe pneumonia.
Requirement for mechanical ventilation (MV).
Mortality within the first week of hospitalization.
Hospital discharge mortality.

Adjustment variables included age, sex, hypertension, diabetes mellitus, obesity, smoking status, and initial clinical severity.

Handling of missing data

In cases of incomplete information, records were excluded from the corresponding analyses. No statistical imputation was performed.

Sample size

No a priori sample size calculation was performed, given the complete availability of the population of interest, as identified through the statistics unit of the Hospital Universitario de Santander. A total of 1217 patients diagnosed with SARS-CoV-2 who were admitted between August 2020 and August 2021 were included. Of these, 984 patients met the inclusion criteria, and the entire available sample was analyzed to maximize statistical power and minimize selection bias.

Statistical analysis

Following approval by the ethics committees of the Universidad Industrial de Santander and the Hospital Universitario de Santander, data corresponding to the research objectives were obtained from the statistics unit of the university hospital. The data were recorded in anonymized form (numerical code sequence) in a Microsoft Excel spreadsheet and subsequently exported to the statistical software STATA (Stata Corp)14.

Continuous variables were assessed for normality using the Shapiro-Wilk test. Since they did not follow a normal distribution, they were described by median and interquartile range (IQR). Categorical variables were expressed as absolute frequencies and percentages.

Associations were assessed using bivariate analyses (chi-squared test) and multivariate logistic regression models. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, adjusting for age, comorbidities, and baseline severity. A p-value < 0.05 was considered statistically significant.

As a sensitivity analysis, the models were repeated excluding variables with more than 10% missing data, with no substantial changes in the results.

Ethical considerations

The protocol was reviewed and approved by the Research Ethics Committee of the Hospital Universitario de Santander and the Ethics Committee of the Universidad Industrial de Santander (Minutes No. 22, December 9, 2022). The study was classified as minimal-risk research in accordance with Resolution 8430 of 1993 of the Colombian Ministry of Health. All information was anonymized and coded, in compliance with Law 1581 of 2012 on personal data protection and the Declaration of Helsinki.

Results

A total of 1217 patients admitted between August 2020 and August 2021, a period encompassing the three main COVID-19 peaks, were identified and assessed for eligibility. Of these, 984 patients met the inclusion criteria (**Figure 1**).

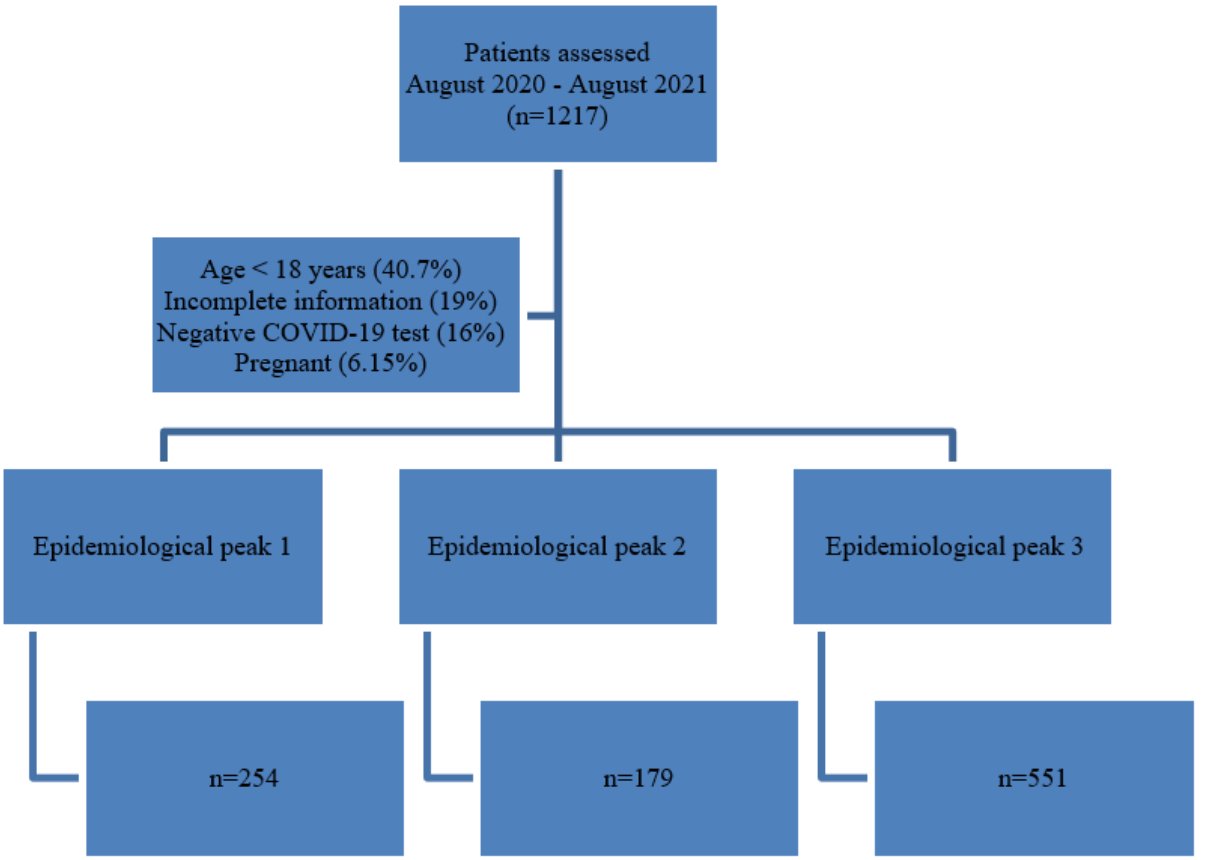

Figure 1. Flowchart of patient admission

Of the total population, 60.98% were male, with a median age of 59 years (IQR 47-69). Most of the population came from the metropolitan area, with 52.66% residing in Bucaramanga, followed by 8.23% from Floridablanca. A total of 29.27% had primary education, and the most commonly reported occupations were unemployed and homemaker.

Regarding medical history, 36.28% had hypertension, 34.74% has obesity, and 21.65% had type 2 diabetes mellitus. A history of smoking was reported by 22.73%, and 16.11% reported lifetime alcohol consumption. The remaining population characteristics are listed in **Table 1**.

Table 1. Sociodemographic characteristics and medical history of the population (n = 984)

Characteristics	% (n)
Sex	
Male	60.98 (600)
Female	39.02 (384)
Age, median (IQR)	59 (47-69)
Education level	
Primary	29.27% (288)
Secondary	21.24% (209)
Technical	4.17% (41)
University	5.59% (55)
No formal education	5.69% (56)
No information	34.04% (335)
Occupation	
Unemployed	19.72% (194)
Homemaker	19.31% (190)
Dealer	8.23% (81)
Farmer	3.96% (39)
Self-employed	3.46% (34)
Other occupations	28.46% (280)
No information	16.86% (166)
Residence	
Bucaramanga	52.66% (518)
Floridablanca	8.23% (81)
Girón	7.52% (74)
Piedecuesta	7.32% (72)
Other municipalities	23.88% (239)
No information	0.39% (4)
Medical history	
Obesity	34.74 (263)
High blood pressure	36.28 (357)
Type 2 diabetes mellitus	21. 65 (213)
Chronic kidney disease	10.16 (100)
Renal replacement therapy at admission	6.14 (52)
Smoking (current or former)	22.73 (223)
Lifetime alcohol consumption	16.11 (158)
Acute myocardial infarction	4.67 (46)
Chronic occlusive arterial disease	1.12 (11)
Dyslipidemia	7.52 (74)

At hospital admission, 13.43% of patients reported outpatient use of dexamethasone, 2.95% prednisolone, 3.46% ivermectin, and 7.32% azithromycin, as shown in **Table 2**.

Table 2. Medications and/or supplements used before hospital admission, and the percentage of use

Medications and/or supplements	% (n)
Dexamethasone	13.43 (132)
Prednisolone	2.95 (29)
Ivermectin	3.46 (34)
Azithromycin	7.32 (72)
Vitamin D	2.03 (20)

In the cohort, 15.7% of patients reported medication use before hospitalization. The most frequently used medications were dexamethasone, prednisolone, azithromycin, and ivermectin.

Corticosteroids (dexamethasone and prednisolone)

Outpatient use of dexamethasone was associated with a higher frequency of severe pneumonia (92.4% vs. 81.2%; p = 0.007). In multivariate analysis, this association remained significant (OR 1.80; 95% CI: 1.12–2.88; p = 0.014). A trend toward higher discharge mortality was also observed (53.0% vs. 43.8%; OR 1.32; 95% CI: 0.99–1.74; p = 0.053) (**Table 3**).

Table 3. Associations between medication use and clinical outcomes, including mortality (1-week and discharge mortality), and ventilatory outcomes (pneumonia and mechanical ventilation)

Medicine	Severe pneumonia (%)	MV (%)	1-week mortality (%)	Discharge mortality (%)	Adjusted OR Severe pneumonia (95% CI)	Adjusted OR Discharge mortality (95% CI)
Dexamethasone	92.4 vs. 81.2*	↑	18.0 vs. 13.2	53.0 vs. 43.8	1.80 (1.12–2.88) **	1.32 (0.99–1.74)
Prednisolone	100 vs. 82.2*	↑	20.0 vs. 13.4	51.0 vs. 44.6	1.52 (0.84–2.74)	1.18 (0.77–1.81)
Azithromycin	94.4 vs. 81.8*	↑	5.6 vs. 14.3*	44.0 vs. 45.6	1.68 (0.99–2.88)	0.95 (0.66–1.37)
Ivermectin	83.3 vs. 82.5	=	14.0 vs. 13.5	46.2 vs. 45.1	1.01 (0.62–1.63)	1.02 (0.74–1.42)

* p<0.05 in bivariate analysis. ** p < 0.05 in adjusted model. MV: Mechanical ventilation

Prednisolone use was associated with severe pneumonia in the bivariate analysis (100% vs. 82.2%; p = 0.043); however, the association was not sustained in the adjusted model (OR 1.52; 95% CI 0.84–2.74; p = 0.170) (**Table 3**).

Azithromycin

Patients who received azithromycin had a higher frequency of severe pneumonia (94.4% vs. 81.8%; p = 0.023). In the multivariate analysis, a trend toward an increased risk was observed (OR 1.68; 95% CI: 0.99–2.88; p = 0.056). However, azithromycin use was associated with lower 1-week early mortality (OR 0.28; 95% CI: 0.11–0.72; p = 0.008) (**Table 3**).

Ivermectin

Outpatient use of ivermectin was not significantly associated with severe pneumonia, mechanical ventilation, or in-hospital mortality (p > 0.05 in all analyses) (**Table 3**).

Discussion

In this cohort of 984 patients hospitalized with COVID-19, outpatient medication use was generally low, in contrast to findings in the literature. Medications such as corticosteroids were the most frequently used, followed by antibiotics such as azithromycin and antiparasitic agents like ivermectin in our population[7]. Furthermore, the use of dexamethasone, prednisolone, and azithromycin was associated with a higher frequency of severe pneumonia. In contrast, ivermectin was not associated with any clinically relevant outcome. Notably, azithromycin appeared to be related to lower 1-week mortality, although it had no impact on overall discharge mortality.

The findings regarding corticosteroids have a clear explanation. The RECOVERY trial demonstrated that dexamethasone is beneficial only in patients who require oxygen therapy or mechanical ventilation, that is, those with severe COVID-19. In patients without respiratory compromise, it may even be harmful[10]. In our setting, many patients likely received corticosteroids early, before hospital admission, which could explain the greater progression to severe pneumonia and the observed trend toward higher mortality. With prednisolone, a similar pattern was observed; the initial analysis suggested an increased risk, but after adjustment for comorbidities and severity, the association was no longer observed, indicating confounding by the patients' baseline clinical status.

In the case of azithromycin, the results were contradictory. Patients who used azithromycin more frequently developed severe pneumonia but had lower 1-week mortality. This does not align with large clinical trials, such as PRINCIPLE[11] and REMAP-CAP[12], which clearly demonstrated that azithromycin does not improve clinical outcomes or reduce mortality. The apparent "protective effect" most likely reflects selection bias: younger patients or those with milder disease may have received the antibiotic in the community and survived the initial phase more easily, without this implying any real therapeutic benefit.

Regarding ivermectin, our results are consistent with those reported in the most robust clinical trials, such as the TOGETHER trial, which ruled out any clinical benefit in COVID-19[13].

From a clinical perspective, these results highlight the importance of carefully evaluating outpatient treatments for COVID-19. Although some medications have been promoted as potentially useful, their use should be grounded in robust evidence. In particular, the use of azithromycin should be discouraged in this context, given its lack of efficacy and possible association with worse clinical outcomes. Furthermore, the use of corticosteroids such as dexamethasone should continue to be monitored to ensure their optimal use in patients for whom a benefit has been demonstrated.

One strength of this study is its inclusion of the entire cohort of patients hospitalized during a critical period of the pandemic, making the findings representative of real-world practice. However, its retrospective design entails unavoidable limitations, as we relied on patient or family reports regarding prior medication use and lacked details such as dosage or duration of self-medication. It is also possible that some findings were influenced by unmeasured variables, such as the exact time of symptom onset.

Taken together, these results show that the outpatient medication use for COVID-19 not only lacks proven benefit but may also be associated with worse outcomes when used without appropriate clinical criteria. This underscores the need to guide clinical practice based on robust evidence and to discourage the indiscriminate use of therapies that have already demonstrated a lack of efficacy.

Limitations

As a retrospective study, causal relationships between outpatient treatments and clinical outcomes cannot be established. Furthermore, the data were derived from information recorded by the healthcare staff who treated the patient, and there is potential information bias related to patient self-reporting. Some information was obtained from patients in poor general condition. The sample was limited to a single tertiary care hospital, which may not be representative of other settings. Moreover, initial classifications of cases requiring mechanical ventilation were not uniform and evolved during the course of the pandemic due to increased resource availability and greater understanding of the disease.

Conclusions

In our cohort of patients hospitalized with COVID-19, the outpatient use of dexamethasone, prednisolone, and azithromycin was associated with a higher frequency of severe pneumonia, whereas ivermectin showed no clinically relevant effect. These findings are consistent with international evidence and suggest that self-medication with these agents confers no benefit and may even worsen the course of the disease.

The apparent protective effect of azithromycin on early mortality should be interpreted with caution, as it likely reflects selection bias rather than a true therapeutic benefit. This underscores the importance of avoiding the extrapolation of observational associations as causal effects.

Taken together, our results reinforce the central message of international guidelines: COVID-19 treatment should be based on the best available evidence and delivered under medical supervision. Inappropriate outpatient medication use is not only ineffective but may also delay care or worsen patients' conditions.

Authors' contributions

SJGL: Study design, sample collection, data analysis and interpretation, and manuscript writing. DDCD: Sample collection, data analysis and interpretation, and manuscript writing. CLFP: Study design, critical revision of key intellectual content, and editing of the final manuscript. LRB: Study design, critical revision of important intellectual content, and final manuscript editing.

Ethical considerations

This study adheres to the ethical principles outlined in the Declaration of Helsinki, the Belmont Report, and the International Ethical Guidelines issued by the Council for International Organizations of Medical Sciences (CIOMS). It was classified as a "no-risk study" under section A of Article 11 of Resolution 8430 of 1993 of the Colombian Ministry of Health. Furthermore, each participant was assigned a coded and anonymized sequential number to ensure confidentiality, in accordance with Colombian Data Protection Law 1581 of 2012. Personal data was also protected.

Conflict of interest

The authors declare that they have no conflict of interest.

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The authors declare that no artificial intelligence, language models, machine learning technologies, or similar technologies were used to create or assist in the preparation or editing of the content of this document.

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