



## Original Article

# Physician adherence to guideline recommendations for mild COVID-19 in Peru: A cross-sectional study

## Adherencia médica a las recomendaciones de las guías para COVID-19 leve en Perú: Un estudio transversal

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### ABSTRACT

**Objective:** To examine the factors associated with Peruvian physicians' adherence to guidelines for managing mild COVID-19 cases. **Methods:** An analytical cross-sectional study was conducted, surveying certified Peruvian physicians from different regions. A simulated clinical case was used to evaluate their knowledge of the pharmacological management of mild COVID-19 and the potential adverse effects of prescribed medications. Adherence to guidelines was defined as prescribing only acetaminophen and/or non-steroidal anti-inflammatory drugs (NSAIDs) for the proposed mild COVID-19 case, in accordance with international recommendations. Factors associated with adherence were analyzed using prevalence ratios, calculated through Poisson regression with robust variance. **Results:** A total of 339 physicians participated, 85.0% of whom adhered to the recommended guideline. The most frequently prescribed drugs were acetaminophen (96.2%), non-steroidal anti-inflammatory drugs (11.5%), and ivermectin (6.8%). Physicians who graduated from private universities exhibited greater adherence to the guidelines (PR: 1.14; 95% CI 1.05-1.23), while those affiliated with the Ministry of Health (MINS) demonstrated lower adherence (PR: 0.87; 95% CI: 0.79-0.84). **Conclusion:** Most physicians adhered to the guidelines for managing mild COVID-19. Higher adherence was associated with graduating from private universities and working outside MINS affiliated institutions.

**Keywords:** COVID-19; Physicians; Drug Prescriptions; Drug-Related Side Effects and Adverse Reactions (Source: DeCS-BIREME).

### RESUMEN

**Objetivo:** Examinar los factores asociados con la adherencia de los médicos peruanos a las guías de manejo de casos leves de COVID-19. **Materiales y métodos:** Se realizó un estudio analítico transversal, encuestando a médicos peruanos certificados de diferentes regiones del Perú. Se utilizó un caso clínico simulado para evaluar sus conocimientos sobre el manejo farmacológico de COVID-19 leve y los posibles efectos adversos de los medicamentos prescritos. El cumplimiento de las directrices se definió como la prescripción únicamente de acetaminofén y/o antiinflamatorios no esteroideos (AINES) para el caso propuesto de COVID-19 leve, de acuerdo con las recomendaciones internacionales. Los factores asociados con la adherencia se analizaron mediante razones de prevalencia, calculadas mediante regresión de Poisson con varianza robusta. **Resultados:** Participaron un total de 339 médicos, de los cuales el 85,0% cumplió las recomendaciones de las directrices. Los fármacos prescritos con mayor frecuencia fueron el acetaminofén (96,2%), los antiinflamatorios no esteroideos (11,5%) y la ivermectina

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### CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare for this study.

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K.W: Protocol development, formal analysis, investigation, and original draft preparation.  
K.T: Protocol development, investigation, data curation, review and editing.  
W.A.T.B: Conceptualization, formal analysis, original draft preparation, review and editing.  
G.T.S: Original draft preparation, investigation, review and editing.  
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### PEER REVIEW

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(6,8%). Los médicos egresados de universidades privadas presentaron mayor adherencia a las guías (RP: 1,14; IC 95%: 1,05-1,23), mientras que los afiliados al Ministerio de Salud (MINSA) demostraron menor adherencia (RP: 0,87; IC 95%: 0,79-0,84).

**Conclusión:** La mayoría de los médicos cumplieron con las pautas para el manejo de la COVID-19 leve. Una mayor adherencia se asoció con graduarse de universidades privadas y trabajar fuera de instituciones afiliadas al MINSA.

**Palabras Clave:** COVID-19; Médicos; Prescripción de Medicamentos; Efectos Colaterales y Reacciones Adversas Relacionados con Medicamentos (Fuente: DeCS-BIREME).

## INTRODUCTION

The COVID-19 pandemic has resulted in over 775 million cases and more than 7 million deaths worldwide by May 2024<sup>(1)</sup>. Peru, in particular, has recorded the highest number of deaths per million inhabitants according to the World Health Organization (WHO)<sup>(2)</sup>. The country faced significant challenges in responding to the pandemic, including a weak healthcare infrastructure, a shortage of medical personnel, and widespread non-compliance with preventive measures<sup>(3,4)</sup>.

While COVID-19 can lead to severe outcomes such as hospitalization and death, the majority of cases presented with mild symptoms<sup>(5)</sup>. However, incorrect use of medications in these early stages can worsen the patient's condition<sup>(6)</sup>. To address this, the Peruvian Ministry of Health (MINSA) issued technical guidelines in 2020 for managing mild COVID-19 cases, initially recommending acetaminophen and hydroxychloroquine, and leaving the use of ivermectin to physician discretion<sup>(7,8)</sup>. By May 2021, however, the Peruvian Social Health Insurance (ESSALUD) discouraged the use of hydroxychloroquine, ivermectin, and other medications for mild cases due to a lack of scientific evidence<sup>(9)</sup>.

Despite these guidelines, confusion persisted among healthcare workers, particularly when MINSA's updated 2021 guidelines did not clearly address the use of ivermectin<sup>(10)</sup>. As a result, many physicians continued prescribing unproven treatments, driven by early studies that suggested potential benefits. Later research, however, showed that medications like ivermectin and hydroxychloroquine were not only ineffective but also associated with higher mortality rates<sup>(11,6)</sup>. In light of this, the objective of our study was to examine the factors associated with Peruvian physicians' adherence to guidelines for managing mild COVID-19 cases during the pandemic.

## MATERIALS AND METHODS

### Study design

We conducted an analytical cross-sectional study by surveying certified physicians in Peru. The survey was distributed online from June 21 to July 5, 2021, during the second wave of COVID-19 in Peru, when the P.1 variant (also known as the Brazilian variant) was predominant<sup>(12)</sup>.

### Study population

Our target population included 86 252 physicians certified by

the College of Physicians of Peru (CMP). The sample size was calculated using the RAOSOFT online calculator, with a 95% confidence level and a 5% margin of error. Without prior data on expected adherence rates, we assumed a 50% adherence rate to maximize the sample size, which resulted in a target of 385 physicians. We used snowball sampling to recruit participants, excluding those who responded after the survey deadline or failed to provide essential data.

### Data collection tool

The survey was designed by the research team and consisted of 33 multiple-choice questions divided into three sections: informed consent, a hypothetical clinical case, and sociodemographic information (Supplementary material). The hypothetical case involved a patient with mild COVID-19, classified according to severity guidelines from the WHO, National Institutes of Health (NIH), and ESSALUD<sup>(9,13,14)</sup>. Physicians were asked to classify the case (asymptomatic, mild, moderate, severe, or critical), choose appropriate medications, and list potential side effects. To avoid confusion regarding oxygen saturation due to altitude, the hypothetical case was set at 100 meters above sea level.

The simulated clinical case was validated through several stages: Initially, it was reviewed by three internal medicine specialists with COVID-19 experience. After incorporating their suggestions, a second review was conducted by five additional experts to ensure clarity. The survey was then piloted with five physicians for final validation<sup>(15)</sup>. The survey was administered using Kobotoolbox, an online platform, and was distributed via medical groups on Facebook and WhatsApp, as well as through direct contact by medical students across different regions.

### Variables

Adherence to guidelines was defined as the prescription of only acetaminophen and/or NSAIDs for the hypothetical mild COVID-19 case, following recommendations from the WHO, NIH, and ESSALUD<sup>(9,13,14)</sup>. Additionally, physicians who prescribed paracetamol and/or NSAIDs along with another therapy were considered to have made an incorrect medical prescription.

Independent variables included sociodemographic factors such as gender (male, female), age ( $\leq 29$  years, 30-59 years,  $\geq 60$  years), undergraduate university (public, private), academic degree (general practitioner, resident physician, medical specialist), city of residence (province, Lima), medical institution affiliation (MINSA, ESSALUD, clinic, Private practice, Armed Forces/National Police), years of experience ( $< 11$  years, 11-20 years,  $> 20$  years). The specialties (medical, surgical, clinical laboratory analysis) were defined according to the National Council of Medical Residency (CONAREME) of Peru<sup>(16)</sup>. Physicians with less patient interaction were categorized as clinical laboratory analysts (radiology and pathology). The classification of healthcare service levels (Level I, Level II, Level III) was based on criteria set by the Peruvian government, where Level I facilities have lower resolution capacity, while Level III facilities have higher resolution capacity<sup>(17)</sup>.

### Statistical analyses

We used RStudio (version 4) for statistical analysis.

Categorical variables were described using frequencies and percentages, while numerical variables were summarized using measures of central tendency and dispersion. Prevalence ratios (PR) were calculated using Poisson regression with robust variance, adjusting for sociodemographic factors. Statistical significance was set at a p-value of <0.05.

**Ethics statement**

The research protocol was approved by the Ethics Committee of the Peruvian Union University (Resolution Number: CEUPeU-0056). Participants were informed about the research's purpose and the voluntary nature of their participation through informed consent. Additionally, the questionnaire was confidential and anonymous, and the data collected were used exclusively for research purposes.

**RESULTS**

**General Characteristics of the Study Sample**

We received 339 responses from physicians across 20 different regions of Peru. Of these, 63.1% were male, with an average age of 41.8 years (SD: 11.8). Most physicians (67.6%) had graduated from a public university, and 73.7% were medical specialists. Additionally, 54.3% worked in a medical institution affiliated with MINSA, and 48.1% had less than 11 years of work experience. When asked to classify the hypothetical COVID-19 case, 89.7% of physicians correctly identified it as mild, 10% classified it as moderate, and 0.3% as severe (Table 1).

**Adherence to guideline recommendations**

The overall adherence rate to the guideline recommendations for managing mild COVID-19 cases was 85.0%. We observed that adherence was 16.5% lower among physicians over 60 years old compared to those aged 30-59 (p = 0.041). Physicians who graduated from private universities showed significantly higher adherence (91.8%) compared to those from public universities (81.7%; p = 0.022). Additionally, specialist physicians were more likely to adhere to the guidelines than general practitioners (87.5% vs. 79.4%; p = 0.026). We also found that physicians with 11-20 years of experience had 12.8% higher adherence compared to those with over 20 years of experience (p = 0.02) (Table 1)

**Medications prescribed**

The most commonly prescribed medication for the hypothetical mild COVID-19 case was acetaminophen (96.2%), followed by NSAIDs (11.5%) and ivermectin (6.8%). Among the NSAIDs, ibuprofen (59.0%) and naproxen (41.0%) were the most frequently prescribed. Additionally, 11 physicians prescribed antibiotics, with azithromycin being the most common. Nine physicians recommended oxygen therapy, and five prescribed oral corticosteroids such as dexamethasone or prednisone (Figure 1).

**Knowledge of the adverse effects**

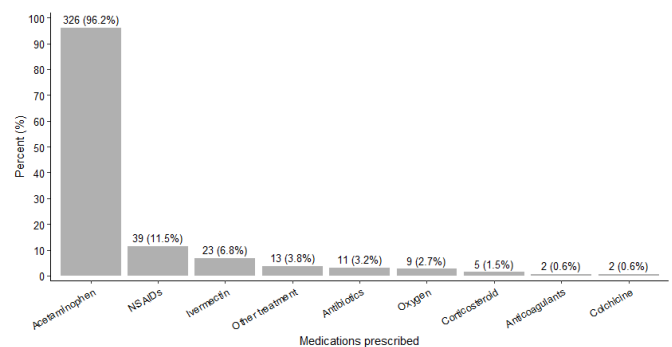
Among the physicians who prescribed acetaminophen, hepatotoxicity was the most frequently reported adverse effect (92.9%). For those prescribing NSAIDs, gastrointestinal irritation (94.9%) and renal insufficiency (46.2%) were the most commonly mentioned adverse effects. Physicians who

**Table 1. General characteristics of physicians according to adherence to recommendations from guidelines for mild COVID-19 cases (n=339).**

Characteristic	n (%)	Adherent n=288 (85.0%)	Non-adherent n= 51 (15.0%)	p-value
<b>Gender</b>				0.073
Male	214 (63.1)	188 (87.9)	26 (12.1)	
Female	125 (36.9)	100 (80.0)	25 (20.0)	
<b>Age (years)</b>				0.041
≤29	50 (14.8)	42 (84.0)	8 (16.0)	
30-59	255 (75.2)	222 (87.1)	33 (12.9)	
≥60	34 (10.0)	24 (70.6)	10 (29.4)	
<b>Undergraduate university</b>				0.022
Public	229 (67.6)	187 (81.7)	42 (18.3)	
Private	110 (32.4)	101 (91.8)	9 (8.18)	
<b>Academic degree</b>				0.026
General practitioner	141 (41.6)	112 (79.4)	29 (20.6)	
Resident physician	30 (8.8)	29 (96.7)	1 (3.33)	
Specialist physician	168 (49.6)	147 (87.5)	21 (12.5)	
<b>Specialty (n=198)</b>				0.012
Medical	146 (73.7)	135 (92.5)	11 (7.5)	
Surgical	43 (21.7)	35 (81.4)	8 (18.6)	
Clinical laboratory analysts	9 (4.6)	6 (66.7)	3 (33.3)	
<b>City of residence</b>				0.212
Province	252 (74.3)	210 (83.3)	42 (16.7)	
Lima	87 (25.7)	78 (89.7)	9 (10.3)	
<b>Medical institution affiliation</b>				0.007
MINSA	184 (54.3)	147 (79.9)	37 (20.1)	
ESSALUD	119 (35.1)	106 (89.1)	13 (10.9)	0.161
Private clinic	49 (14.5)	41 (83.7)	8 (16.3)	0.956
Private consultancy	34 (10.0)	29 (85.3)	5 (14.7)	1.000
FFAA/PNP	6 (1.8)	5 (83.3)	1 (16.7)	1.000
<b>Healthcare service levels</b>				0.297
Level I	66 (19.5)	54 (81.8)	12 (18.2)	
Level II	106 (31.3)	87 (82.1)	19 (17.9)	
Level III	167 (49.2)	147 (88.0)	20 (12.0)	
<b>Years of experience</b>				0.028
<11	139 (41.0)	121 (87.1)	18 (12.9)	
11-20	111 (32.7)	99 (89.2)	12 (10.8)	
>20	89 (26.3)	68 (76.4)	21 (23.6)	
<b>Clinical form</b>				0.003
Mild	304 (89.7)	265 (87.2)	39 (12.8)	
Moderate	34 (10.0)	22 (64.7)	12 (35.3)	
Severe	1 (0.3)	1 (100)	0 (0.00)	

MINSA: Peruvian Ministry of Health; ESSALUD: Peruvian Social Health Insurance; FFAA/PNP: Health Service of the Armed Forces and National Police of Peru.

\* p-values were calculated by Pearson's chi-squared test.



**Figure 1. Medications prescribed by physicians for the fictitious case of mild COVID-19.**

prescribed ivermectin primarily noted dizziness and nausea (65.2%) and diarrhea (47.8%) as side effects. For antibiotics, diarrhea was the most reported side effect (45.5%) (Table 2).

**Table 2. Knowledge of the side effects of medications prescribed by physicians for the fictitious case of mild COVID-19 (n=339).**

Category	n (%)
Acetaminophen	326 (96.2)
Hepatotoxicity	303 (92.9)
Rashes	47 (14.4)
Neutropenia	47 (14.4)
Kidney damage	39 (12.0)
NSAIDs	39 (11.5)
Digestive tube irritation	37 (94.9)
Renal insufficiency	18 (46.2)
Fluid retention	5 (12.8)
Arterial hypotension	2 (5.1)
Ivermectin	23 (6.8)
Dizziness and sickness	15 (65.2)
Diarrhea	11 (47.8)
Hepatotoxicity	8 (34.8)
Rash	8 (34.8)
Fever	1 (4.4)
Blisters / Peeling of skin	1 (4.4)
Antibiotics	11 (3.2)
Diarrhea	5 (45.5)
Microbiota changes	4 (36.4)
Abdominal pain	4 (36.4)
Development resistant bacteria	3 (27.3)
Muscular weakness	0 (0)
Fungi infections	0 (0)
Oral corticosteroids	5 (1.5)
Immunosuppression	3 (60.0)
Liquid retention	2 (40.0)
Hyperglycemia	2 (40.0)
Sepsis	1 (20.0)
Vomiting	0 (0)
Anticoagulants	2 (0.6)
Digestive bleeding	2 (100.0)
Epistaxis	1 (50.0)
Intracranial hemorrhage	1 (50.0)
Paradoxical thrombotic effects	1 (50.0)
Colchicine	2 (0.6)
Diarrhea	2 (100.0)
Abdominal pain	2 (100.0)
Nausea / Vomiting	1 (50.0)
Rashes	0 (0)
Hepatic / Kidney alteration	0 (0)

**Factors associated with adherence to Guidelines**

We found that physicians who graduated from private universities had an 11% higher prevalence of adherence to the guidelines compared to those from public universities (aPR: 1.11; 95% CI: 1.02-1.21). Physicians working in MINSA affiliated institutions had a 22% lower prevalence of adherence (aPR: 0.78; 95% CI: 0.67-0.90). Additionally, physicians who correctly classified the clinical severity of the case as mild COVID-19 had a 33% higher adherence to guidelines (aPR: 1.33; 95% CI: 1.06-1.65) (Table 3).

**DISCUSSION**

This study assessed the adherence of Peruvian physicians to international guidelines for the treatment of mild COVID-19 cases, as well as their knowledge of the adverse effects of commonly prescribed medications. We found that nearly 90% of physicians correctly classified the clinical severity of the case and followed the recommended treatment guidelines. However, certain sociodemographic factors, such as the physician's place of education and their affiliation with public institutions like MINSA, influenced adherence rates.

Our findings align with other research showing that most physicians generally adhere to treatment guidelines for mild COVID-19. However, some studies in Peru have reported different trends. For example, a study in Cajamarca between January and July 2021 found that, despite international recommendations, many physicians prescribed medications like azithromycin (72.3%) and dexamethasone (54.3%) for COVID-19<sup>(18)</sup>. Similarly, a study in Lima in early 2021 reported the frequent use of ivermectin (94%), acetaminophen (93.5%), aspirin (82.1%), and prednisone (81.6%), all of which are not recommended for mild COVID-19 by international health organizations<sup>(19,9)</sup>.

The inappropriate use of medications during the early stages of COVID-19 increases the risk of complications and hospitalization. A study conducted in a Peruvian hospital found that many patients who were later hospitalized had been treated with antibiotics, ivermectin, or corticosteroids

**Table 3. Sociodemographic factors associated with adherence to recommendations from guidelines for mild COVID-19 cases (n=339).**

Characteristic	Unadjusted analysis			Adjusted analysis*			
	PR	CI 95%	p	PR	CI 95%	p	
Gender	Female	Ref.		Ref.			
	Male	1.11	0.99-1.22	0.51	1.10	1.00-1.21	0.039
Age (years)	≤29	Ref.		Ref.			
	30-59	1.03	0.90-1.18	0.590	0.96	0.83-1.11	0.562
	≥60	0.84	0.65-1.07	0.171	0.81	0.62-1.05	0.112
Undergraduate university	Public	Ref.		Ref.			
	Private	1.12	1.03-1.22	0.004	1.11	1.02-1.21	0.016
Academic degree	General practitioner	Ref.		Ref.			
	Resident physician	1.23	1.09-1.38	<0.001	1.08	0.85-1.37	0.520
	Medical specialist	1.12	1.00-1.25	0.040	1.08	0.87-1.35	0.479
Specialty	Not having/ not carrying out	Ref.		Ref.			
	Have or carrying out	1.14	1.02-1.27	0.016	1.12	0.88-1.42	0.365
MINSA	Not working	Ref.		Ref.			
	Work	0.88	0.80-0.96	0.004	0.78	0.67-0.90	0.001
ESSALUD	Not working	Ref.		Ref.			
	Work	1.08	0.99-1.17	0.097	0.88	0.75-1.03	0.124
Private clinic	Not working	Ref.		Ref.			
	Work	0.98	0.86-1.22	0.793	0.89	0.76-1.04	0.142
Years of experience	≤10	Ref.		Ref.			
	11-20	1.09	0.99-1.19	0.084	1.02	0.93-1.13	0.658
	>20	0.93	0.83-1.03	0.172	0.93	0.82-1.04	0.209
City of residence	Lima	Ref.		Ref.			
	Province	1.08	0.98-1.19	0.113	1.01	0.92-1.11	0.778
Clinical form	Moderate/ Severe	Ref.		Ref.			
	Mild	1.33	1.04-1.69	0.023	1.33	1.06-1.65	0.013

PR: Prevalence Ratio. CI 95%: 95% confidence interval.  
\*PR was adjusted for all the sociodemographic variables.

before admission<sup>(20)</sup>. This highlights the importance of adhering to guidelines and avoiding the use of unproven therapies, as inappropriate prescriptions can lead to worsened patient outcomes and strain on healthcare resources.

Most physicians only recognized one adverse effect. This gap in knowledge, particularly concerning drugs like ivermectin and hydroxychloroquine, may be due to inadequate training or outdated information during medical school<sup>(21,22)</sup>. Previous reports have shown that a significant number of Peruvian medical students struggle with passing the National Medicine Exam (ENAM), which could point to deficiencies in their clinical education, particularly in pharmacology and patient safety<sup>(23)</sup>.

Previous reports have shown that a significant number of Peruvian medical students struggle with passing the National Medicine Exam (ENAM), which could point to deficiencies in their clinical education, particularly in pharmacology and patient safety<sup>(24)</sup>. In contrast, physicians working for MINSA-affiliated institutions had lower adherence rates, which could be attributed to challenges in keeping up with evidence-based practices, especially among older physicians who may find it difficult to access updated information through digital platforms<sup>(25)</sup>. Finally, physicians who accurately classified the case severity as mild COVID-19 showed significantly higher adherence to guidelines. This suggests that a thorough understanding of the clinical presentation of COVID-19 is crucial for ensuring appropriate treatment.

Our study highlights the importance of ongoing education and training in clinical guidelines to improve patient care during health crises like the COVID-19 pandemic. Our study has several limitations. First, we did not reach the optimal sample size to reduce the margin of error to 5%, mainly due to pandemic-related restrictions and difficulties in reaching physicians in remote areas. Second, we relied on self-reported data, which may be subject to bias, as we did not verify physician credentials due to confidentiality concerns. Additionally, as a cross-sectional study, we cannot establish causal relationships between the factors studied and adherence to guidelines. Despite the limitations, our study has some strengths, such as the use of an instrument validated by specialist physicians and the inclusion of participants from different regions of Peru.

## CONCLUSION

Our study shows that most Peruvian physicians adhere to international guidelines for the treatment of mild COVID-19. Factors associated with higher adherence include graduating from a private university and correctly identifying the clinical severity of the case. Conversely, working in a MINSA-affiliated institution was linked to lower adherence. Ongoing efforts to improve physician training and access to updated clinical information are crucial to ensuring optimal patient care during pandemics.

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