Adherence of Physicians to Local Guideline Recommendations among Patients with COVID-19 in Two Tertiary Public Hospitals in Metro Manila, Philippines: A Rapid Assessment Study

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ABSTRACT

Objectives. Adherence to clinical practice guidelines (CPG) has been shown to reduce inter-physician practice variation and improve quality of care. This study evaluated guideline adherence of physicians in two tertiary public hospitals to local CPG on COVID-19.

Methods. This was a multicenter, retrospective chart review, rapid assessment method study. Guideline adherence and non-adherence (overuse and underuse) to 15 strong recommendations in the prevailing Philippine COVID-19 Living Recommendations were assessed among a sample of patients admitted in two centers from July to October 2021. Differences in adherence across COVID-19 disease severities and managing hospital units were analyzed.

Results. A total of 723 patient charts from two centers were reviewed. Guideline adherence to dexamethasone use among patients with hypoxemia is 91.4% (95% CI 88.6 to 93.6) with 9.2% overuse. Tocilizumab was underused in 52.2% of patients with indications to receive the drug. There was overuse of empiric antibiotics in 43.6% of patients without suspicion of bacterial coinfection. Lowest adherence to antibiotic use was seen among patients with critical disease severity and those managed in the intensive care unit. None of the other non-recommended treatment modalities were given.

Conclusion. Management of COVID-19 in both centers was generally adherent to guideline recommendations. We detected high underuse of tocilizumab probably related to the global supply shortage during the study period and high overuse of antibiotics in patients without suspicion of bacterial coinfection. While the results of this study cannot be generalized in other healthcare settings, we recommend the application of similar rapid assessment studies in guideline adherence evaluation as a quality improvement tool and to identify issues with resource utilization especially during public health emergencies.

Keywords: guideline adherence, COVID-19, rapid assessment, quality improvement

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INTRODUCTION

The importance of developing clinical practice guidelines (CPG) has been magnified during the initial period of the COVID-19 pandemic given the constant barrage of new information. In principle, CPGs provide a summary of evidence-based recommendations and reduce practice variation between healthcare providers.[1] Adherence to guidelines has been associated with improved quality and cost-effectiveness of care by increasing utilization of effective therapies and reducing use of ineffective ones.[2,3] Factors affecting physician adherence include awareness, familiarity, and agreement with the CPG document. External barriers, including lack of resources and organizational constraints, also limit physicians' ability to adhere to the recommendations.[4]

Published data on adherence to COVID-19 guidelines is currently limited. In 2020, a questionnaire-based study was conducted to look into the perceptions of physicians regarding COVID-19 management in relation to the Indian National Task Force Guidelines for COVID-19. The researchers found out that only about half of the respondents said they would prescribe treatment (e.g., hydroxychloroquine and azithromycin) in accordance with their local recommendations.[5] To our knowledge, there have been no prior studies which looked at physician adherence to COVID-19 guidelines in the Philippines. We therefore aimed to evaluate physician adherence in two tertiary public hospitals in Metro Manila to the Philippine COVID-19 Living Recommendations, which is published online by the University of the Philippines National Institutes of Health (UP-NIH) and the Philippine Society of Microbiology and Infectious Disease (PSMID).[6]

METHODS

Study Design

This is a multicenter retrospective chart review.

As a quality improvement initiative, the information derived from this study is intended to be communicated individually with the hospital administrators of participating centers, policy makers from the Philippine Department of Health, and developers of the Philippine COVID-19 Living Recommendations to guide specific interventions in terms of guideline implementation, dissemination, and future revisions of the CPG. This entailed using a rapid assessment method by adapting the following concepts: 1) funding and institutional approvals facilitated by a multidisciplinary team, 2) short and adaptive study protocol, 3) simplified sampling method and data collection, and 4) rapid implementation and analysis of the project.[7,8] As part of the COVID-19 REsponse Assessment TEam (CREATE), the investigators invited centers who were willing to develop and adopt a uniform study protocol.

Study Population

Two tertiary public hospitals in Metro Manila agreed to participate in the study. Center A used electronic medical records (EMR) while Center B used pen and paper charts. Patients in both centers were included if the following criteria were satisfied: 1) admitted from July 1 to October 31, 2021; 2) age of at least 19 years at the time of admission; 3) laboratory-confirmed COVID-19 with SARS-CoV-2 detection using reverse transcription polymerase chain reaction (RT-PCR) upon admission; and 4) managed by a COVID-19 designated unit within the hospital. Patients were excluded if they were transfers from another institution other than the two participating centers.

Data Collection and Management

Prevailing guideline recommendations (June 2021 update of the Philippine COVID-19 Living Recommendations) during the study period (July 1 to October 31, 2021) were reviewed. "Strong recommendations" regarding screening and diagnosis, treatment, and critical and respiratory management of COVID-19 were listed. Only specific guideline recommendations which were deemed to be relevant among hospitalized patients were included in the data analysis. The specific conditions when treatment modalities were recommended for or against were identified, and these were used as the basis for extraction of data during records review. Data on demographics (age, sex), managing hospital unit (ward, intensive care unit [ICU]) and clinical outcomes (discharged, transferred, or died) were also collected.

We generated a list of patients who were consecutively admitted in COVID-19 designated units in the two participating centers within the period of interest. Using these lists as our sampling frame, a random sample of 384 patients for each center was computed at 95% confidence level with a margin of error of 5%. Given lack of prior data, we assumed the percentage of physician adherence to each guideline recommendation in our target population to be 50%. Charts of patients who belong to the sample were reviewed.

A password-protected electronic form using Google Forms was created and provided to the research assistants (RAs) for data collection and encoding. Prior to starting data collection and throughout the validation process, all RAs were trained and given a manual with standard operating procedure (SOP) on how to collect and encode relevant study data. The investigators reviewed 20% of the total data collected by the RAs against the source documents. Any inconsistencies in the data were discussed with the RAs to identify and address the sources of the discrepancies. This validation process was done by systematically selecting 10 patient records every 50 charts until the 20% of total collected data (125 charts) were evaluated. The SOP manual was continuously updated for uniformity of subsequent data collection. Upon reaching the target sample size, data collected via Google Forms were exported into a password-protected Microsoft Excel

sheet accessible only to the study investigators. Codes and data validation were embedded in the Excel database.

Data Analysis

Data were analyzed using Stata 17. Qualitative variables such as sex and severity were described using frequencies and percentages. Quantitative variables were described using mean, standard deviation, and minimum and maximum values.

Guideline adherence was defined as the proportion of patients who were appropriately managed based on the conditions specified in the CPG (Appendix A). Adherence rates were estimated together for both centers at 95% confidence level using disproportionate stratified random sampling with the participating center as the stratification variable. Finite population correction was done given a population size of 1475 and 580 in Center A and B, respectively. While sample size is sufficient to determine strata-specific estimates, these were no longer done since we deemed that the overall adherence in the two centers will better guide policy. Data on non-adherence were further analyzed as overuse (i.e., proportion of patients given a drug for whom it is not indicated) and underuse (i.e., proportion of patients who did not receive a drug indicated for that specific patient group). The operational definitions of guideline adherence and formulas used for computing adherence, overuse, and underuse are available under Appendices A and B.

Prespecified subgroup analyses were conducted to determine differences in adherence across COVID-19 disease severity categories (asymptomatic, mild, moderate, severe, and critical) and between locations where patients were primarily managed (ward and ICU). Considering that the COVID-19 disease severity on admission may change throughout the hospital course thereby possibly necessitating additional interventions, we used the worst severity in the entire duration of hospitalization for the subgroup analysis.

Ethical Considerations

This study was approved by the respective institutional ethics review boards of both participating centers. Permissions to conduct the study were granted on the condition that the names of the hospitals will be anonymized.

RESULTS

Guideline Recommendations

We identified 61 "strong recommendations" in the June 2021 update of the Philippine COVID-19 Living Recommendations. Of these, only 15 were relevant to hospitalized patients (Table 1). The rest of the recommendations were appropriate for the outpatient and community settings, spanning topics on COVID-19 infection prevention and vaccination. There were recommendations for use of certain treatments (positive recommendations) and recommendations against use of certain drugs (negative recommendations). These are summarized in Table 1. For simplification of analysis, the recommendations on empiric antibiotics and azithromycin were considered overlapping and were analyzed as a single data set.

Characteristics of Study Population

A total of 723 patients were included in the study, 338 in Center A and 385 in Center B. Of these 723 patients, 381 (52.7%) are males (Table 2). The mean age is 53.2 years. Most of the patients admitted were classified to have severe COVID-19 (30.7%).

Adherence to Guideline Recommendations

Guideline adherence to dexamethasone use is high for both patients with hypoxemia (91.4%; 95% CI 88.6 to 93.6)

Table 1. Strong recommendations from the June 2021 update of the Philippine COVID-19 Living Recommendations relevant to hospitalized patients

Therapy	Guideline Recommendation
Positive recommendations	
Dexamethasone	Dexamethasone recommended among patients who require supplemental O_2
Tocilizumab	Tocilizumab recommended among patients showing rapid respiratory deterioration and/or requiring high doses of oxygen and with elevated biomarkers of inflammation
Negative recommendations	
Dexamethasone	Dexamethasone not recommended among patients who do not require supplemental O_2
Tocilizumab	Tocilizumab not recommended among patients who do not require supplemental O_2
Empiric antibiotics	Routine antibiotics not recommended among patients with severe and critical COVID-19 unless with suspicion of bacterial coinfection
Azithromycin	Azithromycin not recommended as treatment for patients with COVID-19
Hydroxychloroquine or chloroquine	Hydroxychloroquine or chloroquine not recommended as treatment for patients with COVID-19
Ibuprofen	Ibuprofen not recommended as treatment for patients with COVID-19
Oseltamivir	Oseltamivir not recommended as treatment for patients with COVID-19
Lopinavir/ritonavir	Lopinavir/ritonavir not recommended as treatment for patients with COVID-19
Bamlanivimab	Bamlanivimab not recommended as treatment for patients with COVID-19
Etoposide	Etoposide not recommended as treatment for patients with cytokine storm
Convalescent plasma	Convalescent plasma not recommended as treatment for patients with COVID-19
Ivermectin	Ivermectin not recommended as treatment for patients with COVID-19
Lianhua	Lianhua not recommended as treatment for patients with COVID-19

Table 2. Characteristics of patients admitted in the two centers from July to October 2021

Characteristics	Total patients admitted n=723 (%)
Sex	
Male	52.7
Female	47.3
Severity	
Asymptomatic	0.7
Mild	22.8
Moderate	20.3
Severe	30.7
Critical	24.9
No information	0.6
Hospital unit	
General ward	85.9
Intensive care unit	14.1
Outcomes	
Discharged	81.8
Transferred	0.3
Died	17.9

Table 3. Adherence of physicians to COVID guideline recommendations

Therapy	Number of observations	Adherence (%) (95% CI)[a]
Positive recommendations		
Dexamethasone only if hypoxemic	408/446	91.4 (88.6, 93.6)
Tocilizumab only if indicated	136/323	47.8 (42.7, 52.9)
Negative recommendations		
Dexamethasone if not hypoxemic	258/277	90.8 (86.5, 93.9)
Tocilizumab if not indicated	383/400	94.1 (91.1, 96.2)
Empiric antibiotics if with no suspicion of bacterial coinfection	163/322	56.4 (51.6, 61.1)
Ibuprofen if not indicated	703/703	100.0[b]
Hydroxychloroquine	723/723	100.0[b]
Oseltamivir	723/723	100.0[b]
Lopinavir/Ritonavir	723/723	100.0[b]
Bamlanivimab	723/723	100.0[b]
Etoposide	723/723	100.0[b]
Convalescent plasma	723/723	100.0[b]
Ivermectin	723/723	100.0[b]
Lianhua	723/723	100.0[b]

[a]Weight-adjusted based on disproportionate stratified random sampling across two centers. [b]Exact binomial estimation method yielded a lower limit of 99% in each center. CI, confidence interval.

Table 4. Comparison of guideline adherence across severity and hospital unit where patients were managed

Therapy	Adherence (%) (95% CI)[a]					
	Severity				Hospital unit	
	Mild	Moderate	Severe	Critical	Ward	Intensive care unit
Positive recommendations						
Dexamethasone only if hypoxemic	[b]	[b]	96.5 (93.3, 98.2)	96.4 (92.7, 98.3)	90.7 (87.4, 93.2)	94.8 (88.5, 97.7)
Tocilizumab only if indicated	[b]	[b]	40.0 (32.5, 48.1)	57.4 (50.5, 64.1)	46.1 (40.2, 52.1)	53.8 (44.2, 63.1)
Negative recommendations						
Dexamethasone if not hypoxemic	95.6 (90.3, 98.1)	89.3 (81.9, 93.9)	[b]	[b]	90.7 (86.3, 93.8)	100.0
Tocilizumab if not indicated	100	99.2 (98.3, 99.7)	[b]	[b]	94.3 (91.2, 96.4)	86.5 (70.1, 94.6)
Empiric antibiotics if with no suspicion for bacterial coinfection	78.1 (72.3, 83.0)	50.4 (39.8, 61.0)	27.6 (17.2, 41.2)	11.2 (2.2, 41.8)	59.2 (54.2, 64.0)	4.4 (1.4,12.7)

[a]Weight-adjusted based on disproportionate stratified random sampling across two centers. [b]Recommendation not applicable to disease severity group. CI, confidence interval

and those without hypoxemia (90.8%; 95% CI 86.5 to 93.9). Meanwhile, adherence to tocilizumab use is lower primarily driven by underuse (52.2%) rather than overuse (5.9%) of the drug (Table 3). Use of empiric antibiotics was non-adherent to guidelines in 43.6% of patients. Notably, worse COVID-19 disease severity and admission in the intensive care unit are associated with decreased guideline adherence to antibiotic use (Table 4). None of the other treatment modalities that were not recommended to be used among hospitalized patients with COVID-19 were given.

DISCUSSION

Overall, guideline-adherent care was high for both centers. Adherence to dexamethasone use in this study was similar to prescription patterns reported in other COVID-19 centers globally (70 to 95%),[9-12] with the high utilization rate being influenced significantly by the result of the RECOVERY trial.[9] Underuse of tocilizumab appears to be related to supply issues during the study period. Coinciding with the surge of the B. 1.617.2 (Delta) variant in September

2021, the Philippine Department of Health reported a national and global shortage of tocilizumab.[13] Despite the aforementioned shortage, the adherence to tocilizumab seen in this study is higher than the prescription patterns reported in other COVID-19 centers across the world (0.5 to 40%).[9,14-16]

Overuse of empiric antibiotics is associated with disease severity (i.e., more severe cases are given antibiotics without sufficient indication) and location of treatment (i.e., ICU patients are given antibiotics without sufficient indication). A similar trend was observed in the use of azithromycin where highest adherence rates were seen in mild cases and the lowest adherence seen in critical cases. This observation is consistent with other studies on bacterial pneumonia showing higher guideline-nonadherent antibiotic use among those with worse pneumonia severity and in those admitted in the ICU.[17,18] This practice may also reflect the difficulty in differentiating patients with COVID-19 and those with bacterial coinfection, such as community-acquired pneumonia, given their overlapping clinical and radiographic chest findings.[19]

Physicians from both tertiary public hospitals seem to follow guideline recommendations. This could be partly attributable to the COVID-19 protocols in place in both centers. The use of well-designed protocolized pathways has been shown to standardize care processes and improve quality of care in terms of reducing unnecessary testing, decreasing length of stay, and reducing medical errors.[20] Considering that this study was conducted during a COVID-19 surge in two urban training institutions, results cannot be generalized to other healthcare settings.

The study has several limitations. As a retrospective chart review, data quality may be affected by completeness of physician charting, legibility of handwriting on paper charts in Center B, and reliability of data extractors. To mitigate risk of incomplete data, we simplified data collection to include only the most essential information and trained RAs to check all sections of the medical chart (e.g., physicians' notes, nurses' notes, and medication sheet). To address legibility in one center which used paper records, illegible chart entries were referred by the RAs to the investigators for adjudication. The other center which made use of an EMR system was able to use a search function for ease of data collection and reported no issues on legibility. Uniformity of data extraction among RAs was ensured using a SOP manual. Data quality was assured by validation of the data collected wherein we found high concordance rates between the RAs and the study investigators.

The current study presents the application of a rapid assessment method in guideline adherence evaluation to identify and address issues with resource utilization. We employed an adaptive study protocol, simplified the sampling method and data collection, and had weekly meetings with a multidisciplinary team to speed up data collection and analysis. We also had meetings with potential funders, publishers, and policy makers to facilitate approval, eventual dissemination, and utilization of the study. The same protocol may be employed in other settings and in other diseases with existing CPGs. It may also be utilized as a post-intervention evaluation to assess the impact of guideline adherence on quality of care. To investigate the reasons for non-adherence, future studies may include key informant interviews and focus group discussions to complement the chart review. Clinical practice may benefit from regular assessment of guideline adherence by addressing the following issues: to prevent underuse, adequate supplies of recommended treatments should be ensured by facilities; and to minimize overuse, timely and adequate dissemination of CPG to physicians may be helpful.

CONCLUSION

We evaluated physician adherence in two tertiary public hospitals in Metro Manila to the Philippine COVID-19 Living Recommendations using a rapid assessment method. Guideline adherence to relevant recommendations was high for the two centers. There was high underuse of tocilizumab which appears to be related to the local and global supply shortage of the drug in September 2021. Among patients without suspicion for bacterial coinfection, there was high overuse of empiric antibiotics especially among those with severe to critical disease severity and those in the intensive care unit.

Recommendations

Based on our findings, we recommend that hospital administrators institutionalize similar types of research as quality improvement initiatives. We recommend that policy makers consider the use of rapid assessments as a possible way to detect supply chain issues to guide resource allocation, which is especially useful during a public health emergency. Guideline adherence studies may also give feedback to guideline developers on how to improve clarity and timeliness of dissemination of CPGs, and to hospital administrators on how to improve strategies to facilitate guideline adaptation in practice.

Statement of Authorship

AGE contributed in the conceptualization, methodology, validation, formal analysis, writing the original draft, review and editing, and project administration; CPC contributed in the methodology, validation, formal analysis, writing the original draft, review and editing; LMPV contributed in the conceptualization, methodology, writing the original draft, review and editing, and supervision; NTCC contributed in the conceptualization, methodology, writing the original draft, review and editing; MTBA contributed in the methodology, validation, review and editing, and project administration; JBCB, VAST, JALM, BFE and CLCA contributed in the conceptualization, methodology,

validation, writing the original draft, review and editing; RNVJ and LOP contributed in the methodology, validation, review and editing; LFD contributed in the review and editing; AMLD contributed in the conceptualization, methodology, formal analysis, writing the original draft, supervision, project administration, and funding acquisition.

Author Disclosure

All authors declared no conflicts of interest.

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APPENDICES

Appendix A. Operational definitions of guideline adherence

Therapy	Conditions needed to satisfy to be considered adherent to guidelines
Positive recommendations	
Dexamethasone only if hypoxemic	Received dexamethasone if patient required O_2 support
Tocilizumab only if indicated	Received tocilizumab if patient required HFNC or mechanical ventilation regardless of CRP levels OR Received tocilizumab if patient was given conventional O_2 support and with elevated CRP (≥75 mg/dL) levels
Negative recommendations	
Dexamethasone if not hypoxemic	Did not receive dexamethasone if patient did not require O_2 support
Tocilizumab if not indicated	Did not receive tocilizumab if patient was not given supplemental O_2 OR Did not receive tocilizumab if with non-elevated CRP (<75 mg/dL) and did not require HFNC or mechanical ventilation
Empiric antibiotics if with no suspicion of bacterial coinfection	Did not receive antibiotics if with no suspicion of concomitant bacterial infection[a]
Hydroxychloroquine	Did not receive hydroxychloroquine if with no other diagnosis for which hydroxychloroquine would be indicated (malaria, systemic lupus erythematosus, rheumatoid arthritis)
Ibuprofen	Did not receive ibuprofen if with no other diagnosis for which ibuprofen would be indicated (rheumatoid arthritis, osteoarthritis, dysmenorrhea, pain)
Oseltamivir	Did not receive oseltamivir if with no other diagnosis for which oseltamivir would be indicated (influenza)
Lopinavir/ritonavir, bamlanivimab, etoposide, convalescent plasma, ivermectin, lianhua	Did not receive any of these interventions

[a]Patients were assumed to have no suspicion of bacterial coinfection if their charts did not explicitly state a diagnosis of a bacterial infection. Data extractors (RAs) were given an exhaustive list of bacterial infections which they were to look for in each of the charts. The data collected underwent the same validation process (20% of total charts) by the study investigators who were physicians. HFNC, high-flow nasal cannula; CRP, C-reactive protein.

Appendix B. Formulas used for computing adherence, overuse, and underuse

Positively stated recommendations (dexamethasone and tocilizumab)

	Intervention given	Intervention not given
Intervention indicated	A	B
Intervention not indicated	C	D

Adherence = A ÷ (A + B)
Underuse = B ÷ (A + B)

Negatively stated recommendations with other possible indications for use (dexamethasone, tocilizumab, empiric antibiotics, azithromycin, hydroxychloroquine, ibuprofen, and oseltamivir)

	Intervention given	Intervention not given
Intervention indicated	A	B
Intervention not indicated	C	D

Adherence = D ÷ (C + D)
Overuse = C ÷ (C + D)

Negatively stated recommendations with no other common indications for use (lopinavir/ritonavir, bamlanivimab, etoposide, convalescent plasma, ivermectin, and lianhua)

Intervention not given	A
Intervention given	B

Adherence = A ÷ (A + B)
Overuse = B ÷ (A + B)