## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Characteristics, Complications and Outcomes Among 1,549 Patients Hospitalized with COVID-19 in a Secondary Hospital in Madrid, Spain: a Retrospective Case Series Study |
| **AUTHORS** | Jiménez, Eva; Fontán-Vela, Mario; Valencia, Jorge; Fernandez-Jimenez, Ines; Álvaro-Alonso, Elena Alba; Izquierdo-García, Elsa; Lazaro Cebas, Andrea; Gallego Ruiz-Elvira, Elisa; Troya, Jesús; Tebar-Martinez, Ana Josefa; Garcia-Marina, Belén; Peña-Lillo, Gabriela; Abad-Motos, Ane; Macaya, Laura; Ryan, Pablo; Pérez-Butragueño, Mario |

## VERSION 1 – REVIEW

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| **REVIEWER** | William G Henderson<br>Adult and Child Consortium for Research and Delivery Science<br>University of Colorado Anschutz<br>USA |
| **REVIEW RETURNED** | 30-Jul-2020 |

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| **GENERAL COMMENTS** | This is a useful review of a secondary hospital's experience managing an influx of covid-19 patients during the pandemic in Spain. The manuscript could be improved in the following ways:<br>1. The manuscript would benefit from review by an English major. The authors sometimes use past tense and present tense. This should all be changed to past tense in most instances.<br>2. In the abstract, it would be useful to present the % of patients admitted to ICU and the ICU length of stay. Also, the % of patients on ventilator.<br>3. On page 8, lines 26-33, it is not very clear why they present characteristics of patient admitted or not admitted to ICU only for patients <65. I would either present this for all patients, or better explain why they did what they did.<br>4. In the Discussion section, it would be useful to describe how they expanded hospital and ICU capacity to handle the large influx of covid-19 patients. |

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| **REVIEWER** | Win Sen Kuan<br>National University Hospital, Singapore |
| **REVIEW RETURNED** | 05-Aug-2020 |

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| **GENERAL COMMENTS** | Thank you for the opportunity to review the manuscript entitled "Characteristics, Complications and Outcomes Among 1,549 Patients Hospitalized with COVID-19 in a Secondary Hospital". It is predominantly a descriptive study on hospitalized patients with COVID-19 at Infanta Leonor<br>University Hospital, Vallecas, Spain. |

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| | The manuscript is largely well-written with easy readability and minor grammatical errors.<br><br>I have several minor comments:<br>1. Please justify the meaning of “disproportionate number” (Page 7 Line 18). What is the comparator?<br>2. As most readers may not be familiar with the Spanish health care system, it would be useful for the authors to define what constitutes a secondary level hospital there.<br>3. Please state types (e.g. manufacturer, supplier) of RT-PCR assay and nasopharyngeal swabs used (Page 8 Line 14).<br>4. Please explain why 48 hours was used as a cut-off for exclusion of subjects from final analysis (Page 8 Line 21).<br>5. How was the selection for ICU admission opportunity made at ILUH? Were there fixed criteria (e.g. age, comorbidity and severity scores) or were they arbitrary?<br>6. More details about the logistic regression are required. What was the level of statistical significance required to be included into the model?<br>7. Suggest changing the word “global” (page 12, lines 29 and 41; Table 1) to “overall”.<br>8. The overcapacity situation of both ward and ICU beds is an important issue encountered during this period. It would be informative if the authors could provide further description on how the hospital handled this overcapacity in terms of space, manpower, equipment availability, isolation capabilities and protocols, and handling of concurrent non-COVID-19 patients. This could have been a factor that determined some of the the results obtained compared to other levels of care elsewhere in Spain. |

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| **REVIEWER** | David Murdoch<br>University of Otago, Christchurch<br>New Zealand |
| **REVIEW RETURNED** | 16-Aug-2020 |

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| **GENERAL COMMENTS** | This is a fairly straightforward description of one institution's experience during the early satages of the COVID-19 pandemic. While there is little in the report that is completely novel, it is still useful to document these sort of data at this stage. My comments mainly relate to the description and characteristics of the study site, as it is essential that readers who are unfamiliar with the location can make cross-site comparisons.<br><br>Specific comments:<br>(1) The introduction can be updated with the most recent global situation of the pandemic.<br>(2) I assume all patients with COVID-19 who were admitted to the study site were included in the analysis? This is implied, but it is important to be clear that no-one was excluded.<br>(3) What are the criteria for admission to the ICU during the study period? These criteria vary greatly with geographic location around the world, so it is important to understand the local criteria and thresholds. Did this change during the pandemic due to increasing demand? The total number admitted to ICU appear to be relatively small proportionately. Can the authors comment on this point?<br>(4) What is the age range of cases?<br>(5) This case series is from the early stages of the pandemic in Spain. Can the authors comment on whether there is any reason |

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| | to believe that the findings would be different were the study to be repeated now? |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer 1:

This is a useful review of a secondary hospital's experience managing an influx of covid-19 patients during the pandemic in Spain. The manuscript could be improved in the following ways:

1. The manuscript would benefit from review by an English major. The authors sometimes use past tense and present tense. This should all be changed to past tense in most instances.

Thanks for the suggestion. The manuscript has been reviewed and changed into past tense.

2. In the abstract, it would be useful to present the % of patients admitted to ICU and the ICU length of stay. Also, the % of patients on ventilator.

The requested information has been included in the abstract and in results.

3. On page 8, lines 26-33, it is not very clear why they present characteristics of patient admitted or not admitted to ICU only for patients <65. I would either present this for all patients, or better explain why they did what they did.

Thanks for the question. We describe characteristics of patient admitted or not admitted to ICU only for patients <65 because age was a major variable to decide admission or not admission to ICU in our hospital and we want avoid this selection bias. We added the explanation of the age threshold for the ICU analysis has been added in Methods / Statistical analysis.

4. In the Discussion section, it would be useful to describe how they expanded hospital and ICU capacity to handle the large influx of covid-19 patients.

The requested information has been included at the beginning of the Discussion: “During the outbreak, hospital wards almost doubled their capacity (702/361), with the number of patients in ICU quadrupling its capacity (32/8). Beds were brought from other hospitals (antique not working hospitals) to turn single rooms into double rooms and to make surge beds in large waiting room areas, which became ward beds. A cohort system (confirmed cases located together and patients with similar suspect degree too) was followed during the early stages of the epidemic in order to avoid hospital transmission. Some weeks after the beginning of the pandemic the Gym used for patient's rehabilitation, was transformed into a semi-critical unit where patients discharged from the ICU or patients needing closer monitoring or High Flow Oxygen were admitted. The ordinary activity in consultations and elective surgery was canceled, the pediatric emergencies were referred to other hospitals and all doctors attended patients with COVID-19 exclusively. All physicians and nursing staff were organized into two groups: the COVID Assistance group, led by the internal medicine department: they attended COVID-19 patients; and the COVID Non-Assistance group which gave all the administrative support: requesting laboratory tests, writing clinical reports, informing about clinical evolution to patient's relatives, etc.

Regarding Critical Care beds: our hospital regular capacity comprises 8 beds for ICU, and 6 for the Surgical Critical Care. Surge critical care beds where made available in the Post Anesthesia Care Unit (6) and the Outpatient Surgery Post-Anesthesia Care Unit (12 beds), to a maximum of 32 critical care beds."

Reviewer 2:

Thank you for the opportunity to review the manuscript entitled "Characteristics, Complications and Outcomes Among 1,549 Patients Hospitalized with COVID-19 in a Secondary Hospital". It is predominantly a descriptive study on hospitalized patients with COVID-19 at Infanta Leonor University Hospital, Vallecas, Spain.

The manuscript is largely well-written with easy readability and minor grammatical errors.
I have several minor comments:

1. Please justify the meaning of "disproportionate number" (Page 7 Line 18). What is the comparator?

We have included a comparison between the number of beds per 1000 inhabitants in our district and the same indicator for the whole region of Madrid, in the Background section.

2. As most readers may not be familiar with the Spanish health care system, it would be useful for the authors to define what constitutes a secondary level hospital there.

We have provided a brief description with the indicators used to determine the level of complexity of hospitals in our country, in the Background section:

"Hospitals of the various regional health services of Spain are categorized into different complexity levels depending on their size, technological resources and the availability of clinical services or departments which could attend patients coming from different parts of the country, thus, in ascending order of complexity we have primary, secondary and tertiary level hospitals".

3. Please state types (e.g. manufacturer, supplier) of RT-PCR assay and nasopharyngeal swabs used (Page 8 Line 14).

The requested information has been included at Methods / Study design and participants:

"SARS-CoV-2 infection was confirmed by real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay (FTD SARS-CoV-2 Assay by SIEMENS) from nasopharyngeal swabs (Deltaswab by Deltalab)."

4. Please explain why 48 hours was used as a cut-off for exclusion of subjects from final analysis (Page 8 Line 21).

We have included the explanation of this cut-off on the paper (Methods/ Study design and participants):

“Patients discharged from the emergency department and those transferred to another hospital in the first 48 hours were not included in the final analysis; although these patients were hospitalized at ILUH, they didn’t stay enough time to record all the relevant clinical data due to the hospital overcapacity context.”

5. How was the selection for ICU admission opportunity made at ILUH? Were there fixed criteria (e.g. age, comorbidity and severity scores) or were they arbitrary?

We extended the explanation “The selection for ICU admission opportunity was made individually, based on each patient’s comorbidities, functional capacity, age (never solely age as a criteria) and depending on the availability of critical care beds at the moment. A local guideline for patient admission on critical care unit was made, based on the consensus document released by the Spanish Society of Intensive and Critical Care (SEMICYUC) and other 17 medical societies.

6. More details about the logistic regression are required. What was the level of statistical significance required to be included into the model?

Information about the statistical significance has been included in Methods/Statistical Analysis. The statistical significance level used for the univariate and multivariate analysis was $p<0.05$.

7. Suggest changing the word “global” (page 12, lines 29 and 41; Table 1) to “overall”.

We appreciate your suggestion and accepted the change.

8. The overcapacity situation of both ward and ICU beds is an important issue encountered during this period. It would be informative if the authors could provide further description on how the hospital handled this overcapacity in terms of space, manpower, equipment availability, isolation capabilities and protocols, and handling of concurrent non-COVID-19 patients. This could have been a factor that determined some of the the results obtained compared to other levels of care elsewhere in Spain.

The requested information has been included at the beginning of the Discussion:

“During the outbreak, hospital wards almost doubled their capacity (702/361), with the number of patients in ICU quadrupling its capacity (32/8). Beds were brought from other hospitals (antique not working hospitals) to turn single rooms into double rooms and to make surge beds in large waiting room areas, which became ward beds. A cohort system (confirmed cases located together and patients with similar suspect degree too) was followed during the early stages of the epidemic in order to avoid hospital transmission. Some weeks after the beginning of the pandemic the Gym used for patient's rehabilitation, was transformed into a semi-critical unit where patients discharged from the ICU or patients needing closer monitoring or High Flow Oxygen were admitted. The ordinary activity in consultations and elective surgery was canceled, the pediatric emergencies were referred to other hospitals and all doctors attended patients with COVID-19 exclusively. All physicians and nursing staff were organized into two groups: the COVID Assistance group, led by the internal medicine department: they attended COVID-19 patients; and the COVID Non-Assistance group which gave all

the administrative support: requesting laboratory tests, writing clinical reports, informing about clinical evolution to patient's relatives, etc.

Regarding Critical Care beds: our hospital regular capacity comprises 8 beds for ICU, and 6 for the Surgical Critical Care. Surge critical care beds where made available in the Post Anesthesia Care Unit (6) and the Outpatient Surgery Post-Anesthesia Care Unit (12 beds), to a maximum of 32 critical care beds."

Reviewer: 3

This is a fairly straightforward description of one institution's experience during the early satages of the COVID-19 pandemic. While there is little in the report that is completely novel, it is still useful to document these sort of data at this stage. My comments mainly relate to the description and characteristics of the study site, as it is essential that readers who are unfamiliar with the location can make cross-site comparisons.

Specific comments:
(1) The introduction can be updated with the most recent global situation of the pandemic.

Thanks for the suggestion. The most recent data on the pandemic in Spain have been included in the Background section.

(2) I assume all patients with COVID-19 who were admitted to the study site were included in the analysis? This is implied, but it is important to be clear that no-one was excluded.

We have included a sentence in Methods / Study design and participants, declaring that no-one was excluded.

(3) What are the criteria for admission to the ICU during the study period? These criteria vary greatly with geographic location around the world, so it is important to understand the local criteria and thresholds. Did this change during the pandemic due to increasing demand? The total number admitted to ICU appear to be relatively small proportionately. Can the authors comment on this point?
The following explanation has been included in the Discussion:
"During the study, criteria for ICU admission was the need for mechanical ventilation. Due to the number of ICU beds made available for the number of patients admitted to hospital, which doubled the usual hospital capacity, during the study period 22 patients were transferred to other ICUs of Madrid, to make ILUH's ICU beds available for other patients. In the same way, due to the scarce ICU bed capacity, triage of patients had to be done. The selection for ICU admission opportunity was made individually, based on each patient's comorbidities, functional capacity, age (never solely age as a criteria) and depending on the availability of critical care beds at the moment. A local guideline for patient admission on critical care unit was made, based on the consensus document released by the Spanish Society of Intensive and Critical Care (SEMICYUC) and other 17 medical societies. On the other hand, Non Invasive Mechanical Ventilation or High Flow Oxygen, managed by pneumologists, was available in the ward for selected patients not admitted to ICU".

(4) What is the age range of cases?

Age range of cases is included in the Results.

(5) This case series is from the early stages of the pandemic in Spain. Can the authors comment on whether there is any reason to believe that the findings would be different were the study to be repeated now?

We are now attending a second outbreak of COVID-19 in Madrid. Compared to the first outbreak, the speed of community transmission is lower, the case detection capacity is higher, there is more knowledge of the disease and the possible treatments and healthcare settings are better prepared. All these factors will probably have a great impact on the analysis if the study were to be repeated now. Future analysis comparing results from first and consecutive waves of COVID-19 pandemic at ILUH would be interesting to make.

## VERSION 2 – REVIEW

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| **REVIEWER** | Win Sen Kuan<br>National University Hospital and National University of Singapore, Singapore |
| **REVIEW RETURNED** | 19-Sep-2020 |

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| **GENERAL COMMENTS** | Thank you for addressing my comments. |

## VERSION 2 – AUTHOR RESPONSE

Thank you for your review. We have made the requested changes to our manuscript.

Editors Comments to Author: Please revise the title of your manuscript to include the research question, study design and setting. This is the preferred format of the journal.

The new title is “Characteristics, Complications and Outcomes Among 1,549 Patients Hospitalized with COVID-19 in a Secondary Hospital in Madrid, Spain: a Retrospective Case Series Study”

Reviewer(s)' Comments to Author. Reviewer: 2: Please state any competing interests or state ‘None declared’.

We have stated “none declared” instead of “none to declare”.