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OPEN PEER REVIEW

Investigation of Biochemical and Inflammatory Markers in COVID-19 Patients Hospitalized in the Intensive Care Unit: An Observational Study in Northern Iran

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

4 comments · 20 Jun 2024 – 26 Jun 2024

Samaneh Naeimi Reviewer — ACCEPT — 20 Jun 2024

The article is generally acceptable, but it is not among the research priorities of the day.

Ebrahim Kharazinejad Reviewer — MINOR REVISION — 25 Jun 2024

This article needs minor revision.

Associate Editor — MAJOR REVISION — 25 Jun 2024

This article needs major revision.

Editor-in-Chief — MAJOR REVISION — 26 Jun 2024

This article needs major revision.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editor in chief,
Once again, we appreciate your kindness in considering our article. We read the reviewers' comments and responded to them carefully. We hope that the reviewer will be satisfied with our answers to the questions.

Reviewers' Comments:

Reviewer 1:

1. The title of manuscript is confusing.

A. we revised the title. **Investigation of Biochemical and Inflammatory Markers in COVID-19 patients hospitalized in the Intensive Care Unit: An observational study in Northern Iran.**

2. The Abstract and conclusion should be rewritten.

A: we revised it.

Abstract

Background: Since the first documentation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there has been a notable emphasis on it in a brief period, especially as the mortality rate and confirmed cases steadily rise. The rapid and accurate laboratory identification of an ongoing COVID-19 infection is essential for efficient pandemic control. For diagnostic purposes, various testing methods have been developed to detect the severity of COVID-19. These diagnostic methods play a crucial role in identifying and managing the spread of the virus within communities worldwide.

Methods: This cross-sectional observational study was conducted from February to June 2020, spanning four months. Patient clinical records and laboratory biomarkers data were collected.

Results: In this study, 263 patients were involved, with an average age of 59.38 ± 15.26 years, and 51.3% of them (135 patients) were male. The typical hospital stay was 9.25 ± 6.9 days. The patients were divided into three groups: those who survived (49.4%), those receiving treatment (4.9%), and those who did not survive (45.6%), with all treated patients surviving. An important connection was observed between serum lactate dehydrogenase (LDH), creatine phosphokinase (CPK), urea, leukocytosis, lymphopenia, high polymorphonuclear neutrophil (PMN) counts, and poor patient outcomes (p-value<0.05). Elevated aspartate transaminase (AST) levels also showed a close relationship with adverse outcomes (p-value 0.05). Furthermore, most patients with hyponatremia, high fasting blood glucose, and elevated serum creatinine levels did not survive despite lacking statistical significance.

Conclusion: Serum biomarkers serve as prognostic indicators for the severity of COVID-19 patients. Leveraging these markers aids in promptly diagnosing patients at high mortality risk and facilitates more effective treatments in the disease's initial phases. These biomarkers can help healthcare providers identify patients at higher risk of complications and guide the implementation of targeted interventions to improve patient outcomes.

5. Conclusion

In this research, we investigated the impact of serum biomarkers measured during hospitalization on the poor prognosis of high-risk COVID-19 patients. Our results suggest that elevated levels of serum LDH, CPK, urea, WBC, and PMN, along with lymphopenia during hospitalization, correlated with an increased risk of in-hospital mortality and anticipated severe respiratory failure in COVID-19 patients. This study highlights the importance of monitoring serum biomarkers during hospitalization to help identify patients at elevated risk of adverse outcomes and inform clinical management approaches. The findings indicate that early identification of these biomarkers could aid healthcare providers in stratifying high-risk COVID-19 patients for more intensive monitoring and timely interventions.

3. The introduction section is very brief.

A: we add new details to the introduction.

Clinical observations of COVID-19 patients have unveiled patterns of biochemical and inflammatory marker levels across various disease stages. Notably, heightened levels of markers such as CRP, D-dimer, and IL-6 have consistently manifested in severe cases with respiratory compromise, underscoring their potential as predictors of respiratory failure. Longitudinal studies monitoring changes in these markers in COVID-19 patients have offered valuable insights into their evolving relationship with respiratory function. Fluctuations in marker levels have mirrored shifts in respiratory status, furnishing crucial prognostic data for healthcare providers. The recognition of these markers as predictors of respiratory failure in COVID-19 patients stems from extensive research endeavors aimed at unraveling the intricate interplay among these markers, respiratory function, and disease outcomes.

4. Figures should be improved.

A: we improved them.

5. The English language must be corrected and improved by a native speaker. The goal of manuscript and novelty must be rewritten. It is not clear. Please check your manuscript thoroughly and carefully to refine the language. If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised

manuscript. Also, please highlight the changes made in the revised MS.
Major Revision

A: The revision was conducted to address language and grammar issues in the English text, resulting in comprehensive corrections being made to the entirety of the manuscript. Enhancing our understanding of the potential implications of serum inflammatory biomarker levels is crucial for developing novel approaches to enhance diagnosis and treatment efficacy in future pandemics or analogous crises. The primary objective of this investigation was to assess the influence of Biochemical and Inflammatory Markers on COVID-19 patients receiving care in the Intensive Care Unit. Consequently, recognizing the significance of serum inflammatory biomarker levels in diagnosing, promptly treating, and predicting outcomes for COVID-19 patients could assist healthcare authorities in readiness for forthcoming pandemics or inevitable global emergencies.

Reviewer 2:
This article need minor revision.

A: thanks for your time. We responded and revised the manuscript based on reviewers' requests and concern. We rewrite the abstract and conclusion part. We also improved English language of the manuscript as well.

Reviewer 3:
The article is generally acceptable, but it is not among the research priorities of the day

A: thanks for your time.

Systematic analysis of fluctuations in serum inflammatory biomarkers throughout the disease course can provide valuable insights into the pathophysiological mechanisms underlying severe COVID-19 manifestations. This understanding enhances knowledge of disease progression and aids in identifying potential therapeutic targets to address hyper-inflammatory responses in severe cases. Integrating biomarker data into clinical frameworks could transform patient management by enabling risk stratification, optimizing resource allocation in intensive care, and facilitating personalized treatment regimens for high-risk patients. Furthermore, the insights gained from studying these biomarkers are applicable beyond COVID-19, informing strategies for other infectious diseases and health crises. Establishing standardized protocols for biomarker assessment will strengthen healthcare systems' preparedness for future pandemics, ultimately improving global patient outcomes. In summary, investigating serum inflammatory biomarkers is crucial for advancing our understanding of critical illness in infectious diseases and developing effective diagnostic and therapeutic strategies for future health emergencies.

Reviewer attachment file

Dear Professor

The topic of the proposed work is interesting but it should be taken into account some considerations and modifications, that could improve the quality of the research, in agreement with the aim and the prestige of Journal. The manuscript is not well written and the text should be revised carefully.

1. The title of manuscript is confusing.
   A. we revised the title. **Investigation of Biochemical and Inflammatory Markers in COVID-19 patients hospitalized in the Intensive Care Unit: An observational study in Northern Iran.**
2. The Abstract and conclusion should be rewritten.
   A. We revised them.

   Abstract

   Background: Since the first documentation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there has been a notable emphasis on it in a brief period, especially as the mortality rate and confirmed cases steadily rise. The rapid and accurate laboratory identification of an ongoing COVID-19 infection is essential for efficient pandemic control. For diagnostic purposes, various testing methods have been developed to detect the severity of COVID-19. These diagnostic methods play a crucial role in identifying and managing the spread of the virus within communities worldwide.
   Methods: This cross-sectional observational study was conducted from February to June 2020, spanning four months. Patient clinical records and laboratory biomarkers data were collected.
   Results: In this study, 263 patients were involved, with an average age of 59.38 ± 15.26 years, and 51.3% of them (135 patients) were male. The typical hospital stay was 9.25 ± 6.9 days. The patients were divided into three groups: those who survived (49.4%), those receiving treatment (4.9%), and those who did not survive (45.6%), with all treated patients surviving. An important connection was observed between serum lactate dehydrogenase (LDH), creatine phosphokinase (CPK), urea, leukocytosis, lymphopenia, high polymorphonuclear neutrophil (PMN) counts, and poor patient outcomes (p-value<0.05). Elevated aspartate transaminase (AST) levels also showed a close relationship with adverse outcomes (p-value 0.05). Furthermore, most patients with hyponatremia, high fasting blood glucose, and elevated serum creatinine levels did not survive despite lacking statistical significance.
   Conclusion: Serum biomarkers serve as prognostic indicators for the severity of COVID-19 patients. Leveraging these markers aids in promptly diagnosing patients at high mortality risk and facilitates more effective treatments in the disease's initial phases. These biomarkers can help healthcare providers identify patients at higher risk of complications and guide the implementation of targeted interventions to improve patient outcomes.

Conclusion

In this research, we investigated the impact of serum biomarkers measured during hospitalization on the poor prognosis of high-risk COVID-19 patients. Our results suggest that elevated levels of serum LDH, CPK, urea, WBC, and PMN, along with lymphopenia during hospitalization, correlated with an increased risk of in-hospital mortality and anticipated severe respiratory failure in COVID-19 patients. This study highlights the importance of monitoring serum biomarkers during hospitalization to help identify patients at elevated risk of adverse outcomes and inform clinical management approaches. The findings indicate that early identification of these biomarkers could aid healthcare providers in stratifying high-risk COVID-19 patients for more intensive monitoring and timely interventions.

3. The introduction section is very brief.
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Clinical observations of COVID-19 patients have unveiled patterns of biochemical and inflammatory marker levels across various disease stages. Notably, heightened levels of markers such as CRP, D-dimer, and IL-6 have consistently manifested in severe cases with respiratory compromise, underscoring their potential as predictors of respiratory failure. Longitudinal studies monitoring changes in these markers in COVID-19 patients have offered valuable insights into their evolving relationship with respiratory function. Fluctuations in marker levels have mirrored shifts in respiratory status, furnishing crucial prognostic data for healthcare providers. The recognition of these markers as predictors of respiratory failure in COVID-19 patients stems from extensive research endeavors aimed at unraveling the intricate interplay among these markers, respiratory function, and disease outcomes.

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   A: The revision was conducted to address language and grammar issues in the English text, resulting in comprehensive corrections being made to the entirety of the manuscript.

   Enhancing our understanding of the potential implications of serum inflammatory biomarker levels is crucial for developing novel approaches to enhance diagnosis and treatment efficacy in future pandemics or analogous crises. The primary objective of this investigation was to assess the influence of Biochemical and Inflammatory Markers on COVID-19 patients receiving care in the Intensive Care Unit.

Consequently, recognizing the significance of serum inflammatory biomarker levels in diagnosing, promptly treating, and predicting outcomes for COVID-19 patients could assist healthcare authorities in readiness for forthcoming pandemics or inevitable global emergencies.

Major Revision

Reviewer attachment file

Dear Authors

Greetings

I have commented on the manuscript entitled “Investigation of Serum Laboratory Biomarkers in Patients with COVID19 Hospitalized in the Intensive Care Unit; an Observational Study in North of Iran.;;” You can find them below.

I would be grateful to review the manuscript which has been submitted to the **Comprehensive Health and Biomedical Studies**. thank you for giving me to review the manuscript.

- Abstract should be revised

  A. We revised it.

  B.

  Abstract
  Background: Since the first documentation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there has been a notable emphasis on it in a brief period, especially as the mortality rate and confirmed cases steadily rise. The rapid and accurate laboratory identification of an ongoing COVID-19 infection is essential for efficient pandemic control. For diagnostic purposes, various testing methods have been developed to detect the severity of COVID-19. These diagnostic methods play a crucial role in identifying and managing the spread of the virus within communities worldwide.
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Conclusion: Serum biomarkers serve as prognostic indicators for the severity of COVID-19 patients. Leveraging these markers aids in promptly diagnosing patients at high mortality risk and facilitates more effective treatments in the disease's initial phases. These biomarkers can help healthcare providers identify patients at higher risk of complications and guide the implementation of targeted interventions to improve patient outcomes.

- Introduction should be major revised

We revised it and added new paragraph. Clinical observations of COVID-19 patients have unveiled patterns of biochemical and inflammatory marker levels across various disease stages. Notably, heightened levels of markers such as CRP, D-dimer, and IL-6 have consistently manifested in severe cases with respiratory compromise, underscoring their potential as predictors of respiratory failure. Longitudinal studies monitoring changes in these markers in COVID-19 patients have offered valuable insights into their evolving relationship with respiratory function. Fluctuations in marker levels have mirrored shifts in respiratory status, furnishing crucial prognostic data for healthcare providers. The recognition of these markers as predictors of respiratory failure in COVID-19 patients stems from extensive research endeavors aimed at unraveling the intricate interplay among these markers, respiratory function, and disease outcomes.

- New references should be used

A. We included new references as well.

- Discussion should be revised

A. We revised it carefully and we checked for English language efficiency as well.

Furthermore, research conducted by Letelier et al., 2021, and Ponti et al, 2020, identified elevated levels of inflammatory serum markers (including ESR, CRP, and LDH), hepatic markers (AST and ALT), cardiac biomarkers (pro-BNP and CK-MB), and renal function indicators (urea and creatinine) in patients diagnosed with COVID-19. Additionally, they observed that patients in more critical conditions exhibited significantly higher levels of inflammatory serum markers, which correlated with an increased likelihood of organ damage and further elevation of these markers (32,33).

Best regards

2 Revision 1

0 comments

No public comments in this round.