

Sex disparity in COVID infection: a retrospective study using serum electrophoretic analysis (SPE) in men and women infected by COVID-19

Flaminia Tomassetti^{1,2*}, Edoardo Cappa^{1,2*}, Roberta Salierno^{1,2*}, Vanessa Rossi^{1,2}, Francesca Pacifici^{1,2}, Massimo Pieri^{1,2}, Sergio Bernardini^{1,2}, and Maria Morello^{1,2}

¹Department of Laboratory Medicine, "Tor Vergata" University Hospital, Rome, Italy

²Department of Experimental Medicine, University of "Tor Vergata", Rome, Italy

Introduction

- Several epidemiological studies demonstrated differences in the severity of symptoms and in the clinical course of the infection between females and males affected by **COVID-19** [1–3].
- Although men and women show the same incidence of being infected by COVID-19, men are more likely to experience severe symptomatology and exhibit higher mortality [2–4].
- Nevertheless, nowadays the biological mechanisms driving these differences are still poorly understood and **sex disparity** may be explained because females compared to men have a stronger immune response and focus more on health prevention. As reported, several inflammatory biomarkers, mainly used to measure the size of the severity of infection resulted in higher in men than in women [5,6].
- Our work focused on the **alteration of inflammatory serum proteins**, and it was performed a retrospective analysis of **serum protein electrophoresis (SPE)** respectively in women and men infected by COVID-19.

Methods

- Samples from COVID-19 hospitalized patients were collected.
- Inflammatory proteins, such as Protein C (CRP), Neutrophil-to-lymphocyte ratio (NLR), interleukin (IL) 6, fibrinogen and D-dimer, performed by Alinity c-series (Abbott, Chicago, Illinois, US), and the analysis of SPE, performed by Capillarys 3 TERA (Sebia, Lisses, France), were indagated.
- The samples were divided into group of **survived (S, n=140)** and **not survived (NS, n=33)** patients respectively subdivided into men and women. Also, 82 healthy patients with negative COVID-19 molecular swabs, were enrolled as a control group.

- Statistical analyses were performed by MedCalc (MedCalc Software Ltd, Ostend, Belgium).

Results

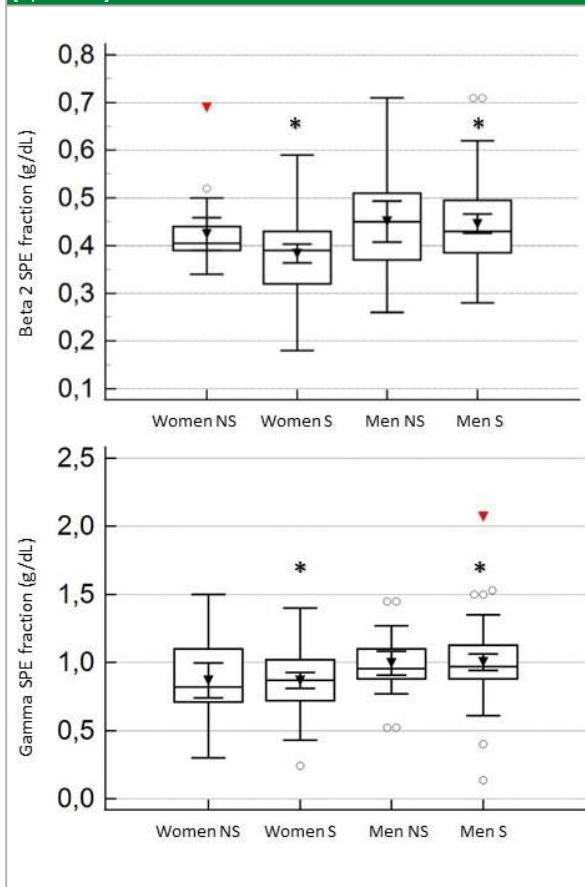
SPE DIFFERENCES IN GENDER

- In the SPE analysis, we noticed different values of **beta 2 and gamma** that were **significantly different** just in S patients ($p < 0.001$) linked to the sex of patients.

Figure 1 For Beta 2 SPE fraction: women S median value 0.39 (IQR: 0.32 to 0.43), women NS median value 0.41 (IQR: 0.38 to 0.48), men S median value 0.43 (Interquartile Range, IQR: 0.39 to 0.5), men NS median value 0.41 (IQR: 0.37 to 0.49).

For Gamma SPE fraction: women S median value 0.90 (IQR: 0.73 to 1.02), women NS median value 0.86 (IQR: 0.77 to 1.13), men S median value 0.98 (Interquartile Range, IQR: 0.89 to 1.15), men NS median value 0.98 (IQR: 0.89 to 1.10).

[* $p < 0.001$]



SPE DIFFERENCES IN SURVIVED vs NOT SURVIVED PATIENTS

- All the SPE fractions of the S and NS groups lead to significant results compared to the control group.

OTHER BIOMARKERS

- It was observed that **CRP and NLR** showed significantly **higher** values in men than in **women** for both S and NS groups ($p < 0.05$)

Conclusion

- This observational study for the first time lighted the **sex disparity in COVID-19** by serum SPE analysis.
- Considering that:
 - the proteins that migrate in these areas are involved in the immune response
 - the size of areas is statistically different in S and NS respectively women and men patients.
- This retrospective work could offer clinicians a new consideration about the prognosis and for a better pharmacological choice in depending on the sex of patients.

References

- Meng Y, Wu P, Lu W, Liu K, Ma K, Huang L, et al. Sex-specific clinical characteristics and prognosis of coronavirus disease-19 infection in Wuhan, China: A retrospective study of 168 severe patients. *PLoS Pathog* 2020;16:e1008520. <https://doi.org/10.1371/journal.ppat.1008520>.
- Sylvester S V, Rusu R, Chan B, Bellows M, O'Keefe C, Nicholson S. Sex differences in sequelae from COVID-19 infection and in long COVID syndrome: a review. *Curr Med Res Opin* 2022;38:1391–9. <https://doi.org/10.1080/03007995.2022.2081454>.
- Massion SP, Howa AC, Zhu Y, Kim A, Halasa N, Chappell J, et al. Sex differences in COVID-19 symptom severity and trajectories among ambulatory adults. *Influenza Other Respir Viruses* 2023;17:e13235. <https://doi.org/10.1111/irv.13235>.
- Garg S, Singh VK, Sonkar SC, Kelkar H, Singh S, Garg S, et al. Pattern of serum protein capillary electrophoretogram in SARS- CoV-2 infection. *Clinica Chimica Acta* 2022;527:11–6. <https://doi.org/10.1016/j.cca.2022.01.003>.
- Navarro SL, Kantor ED, Song X, Milne GL, Lampe JW, Kratz M, et al. Factors Associated with Multiple Biomarkers of Systemic Inflammation. *Cancer Epidemiol Biomarkers Prev* 2016;25:521–31. <https://doi.org/10.1158/1055-9965.EPI-15-0956>.
- Akkurt ES, Sahin Ozdemirel T, Ertan O, Unal E, Akinci Özyürek B. Is There a Gender Difference in Terms of Inflammatory Biomarkers in Patients With Severe Covid-19 Pneumonia? *Cureus* 2022;14:e32541. <https://doi.org/10.7759/cureus.32541>.