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RESPONSE TO LETTER Healthcare Workers' Vulnerability to SARS-CoV-2 in Western Romania: A Study on Incidence and **Risk Factors for Non-Vaccination and Reinfection** [Response to Letter]

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Dear editor

Thank you for the interest shown by Mr. Fikri Elanda regarding our study. Concerning the limitations mentioned in the letter addressed to the Editor of the International Journal of General Medicine, we provide the following clarifications: The limitations 1, 2, 3, 4 mentioned by Mr. Fikri Elanda were specified by the authors in the original article:

Limitations of the study: [...] No data regarding the clinical form, hospitalization, or long-COVID status were available for the study, and cases were not investigated by sequencing (to confirm the type of variant). Also, the level of anti-spike/antinucleocapsid antibodies was not monitored (to reveal the post-vaccinal or natural post-disease protection). The recorded comorbidities were at very low levels of fact which supports under-reporting.¹

• These limitations partially stem from the study's design, utilizing data provided by the national SARS-CoV-2 infection surveillance system "Corona Forms" (where at the onset of infection, data about long-COVID, defined after a minimum of 4 weeks from the initial infection,² or in the case of post-COVID syndrome, after 3 months,³ cannot be collected). They also arise from the fact that many cases were outpatient, lacking classification into clinical forms and without additional biochemical (CRP, fibrinogen), hematological (platelet count), immunological or radiological investigations.

• Regarding sequencing, a technical report by the ECDC in February 2021, at the beginning of our study, indicated that only three countries in the EU had a sequencing capacity of over 10% of positive samples. Two others reached a maximum of 5%, while the majority of states (including Romania) had a sequencing capacity below the range recommended by the European Commission - between 5-10%.⁴ Thus, in Romania, according to the national methodology, the SARS-CoV-2 strains sequenced originate from:

- "Cases with failure to detect the S gene target during pre-screening using RT-PCR;
- Confirmed cases with a travel history outside or inside the country or direct contact with individuals returning from other countries within the period of 2–14 days prior to onset or within 14 days before confirmation (for asymptomatic cases);
- Confirmed cases originating from areas where a rapid increase in the number of cases is detected;
- Direct symptomatic/asymptomatic contacts of confirmed cases with any of the new variants;
- Up to 5 direct contacts from outbreaks where a case with a new variant has been detected;
- Reinfected cases (at least 180 days after recovery from the initial infection);
- Symptomatic cases fully vaccinated, at least 10 days after completing the vaccination"⁵

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The predominant circulating strains in certain pandemic waves have been identified based on data provided by the National Institute of Public Health, following the centralization of sequencing results at the national level.

• The average age across all four samples being under 50 years, sustained activity, including low fatality of 0.085% [95% CI 0.02–0.31], suggests a lower comorbidity compared to community cases occurring in older age groups. However, the obtained values (E1=2.06%; E2=2.14%; E3=3.22%; E4=5.30%) were considered affected by underreporting, which led to the possible bias reported in the article.¹ Under pandemic circumstances, in which saving lives was a priority, the quality of surveillance data is not similar to normal periods, in which there is sufficient time to apply standardized protocols.

Regarding Limit No.5 ("The study did not include observations related to the type of vaccine used, level of adherence to hygiene protocols, or environmental factors that may influence infection risk"), we specify that Figure No. 3 presents the types of vaccines used in the active immunization of the personnel. The statistical analysis retained vaccination with the messenger RNA Comirnaty vaccine (Pfizer-BioNTech) and the viral vector Janssen vaccine (Johnson & Johnson). These two types were also the most used in vaccinating the subjects included in the study (see Tables No. 2 and 3).

Considering Romania faced high levels of vaccine hesitancy (both among the population and among medical staff), the study focused on differences regarding vaccination and professional factors identified in the four categories of personnel, given that all subjects included in the study were confirmed COVID-19 cases. In a case-control design, differences regarding adherence to Standard Precautions or nosocomial environmental factors would have been really important. Furthermore, airborne transmission through Flugge droplets and aerosols is difficult to prevent in a closed environment, even with good hand hygiene adherence. Additionally, the analysis of external environmental factors in augmenting the transmission of COVID-19 infection at the community level in the same geographic region is the subject of an ongoing study, especially since the intertwining of community transmission with nosocomial transmission among medical staff has been highlighted.

Disclosure

The author reports no conflicts of interest in this communication.

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