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# Exploring the Trends of Acute Appendicitis Following Recovery or Vaccination From COVID-19

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ABSTRACT

*Introduction:* The relationship that vaccination against corona virus disease 19 (COVID-19) or recovery from the acute form of the illness may have with the incidence or severity of acute appendicitis (AA) has not been explored. The aim of this study was to evaluate this relationship.

*Methods:* A single centre retrospective study of all consecutive adult patients presenting with AA in the 6 mo after the initiation of a national vaccination program was performed. The presenting characteristics and pathological data of patients who had either been vaccinated against or recovered from COVID-19 were compared with those who had not. In addition, historical data from the equivalent period 12 and 24 mo beforehand was also extracted. The incidence of AA was compared between each of these time-frames.

*Results:* Of the 258 patients initially identified, 255 were included in the analysis of which 156 had either been vaccinated and/or recovered from COVID-19 (61.2%) whilst 99 (38.8%) patients had not. When comparing these two groups, there were no significant differences in the presenting characteristics, operative findings or postoperative courses. There was also no significant change in the incidence of AA when comparing the study dates with historical data (median weekly incidence of AA 8.0 *versus* 8.0 *versus* 8.0 respectively, $P = 0.672$).

*Conclusions:* Based on the data presented here, we failed to find a relationship between a national vaccination program and both the nature and incidence of AA presenting to a busy urban hospital.

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## Introduction

The spread of the novel severe acute respiratory syndrome coronavirus two, also known as Corona Virus Disease 19 (COVID-19), has been associated with a decrease of up to 60% in the number of emergency surgery admissions.[1,2] Similarly, following the onset of the pandemic a decrease in the number of patients presenting with acute appendicitis (AA) was

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also noted.[3,4] A concurrent increase in the proportion of delayed presentations and the incidence of complicated disease has also been described.[5-8] These changes, as well as concerns for the safety of those operating on COVID-19 positive patients, have ushered in a trend towards managing AA nonoperatively with antibiotics as opposed to with surgery.[9,10]

The impact of COVID-19 has also been felt in other areas of general surgery. For instance, delays in diagnosing cancer as a result of lockdowns is associated with greater disease burden and poorer overall survival.[11] Finally, some cancer patients were offered nonsurgical intervention for resectable disease to prevent a delay in intervention caused by a reduction in resources during the pandemic.[12]

It has been postulated that patient's fear of contracting COVID-19 is partly responsible for the increase in the number of patients with suspected AA delaying or avoiding their presentation to the department of emergency medicine (ED).[2] However, the growing availability of vaccines effective against COVID-19 may represent an opportunity to mitigate these concerns.[13] This reflects evidence that vaccination against COVID-19 reduces the incidence of infection with severe forms of the disease.[14,15] In addition, recovery from COVID-19 is thought to provide a degree of protection from future re-infection and as such, may also affect healthcare seeking behaviours.[16]

As a large number of people are willing to accept the vaccine if offered and an increasing number of people are recovering from acute COVID-19 infection, the incidence and severity of AA may similarly be affected as patients may no longer fear attending the ED.[13,17] Moreover, as some countries have started rolling back public health measures aimed at curbing the spread of COVID-19, access to healthcare for this group of patients may well be improved. The aim of this study was to explore whether vaccination against COVID-19 or recovery from the acute illness was associated with a change in the incidence, presenting characteristics and severity of AA.

## Materials and Methods

### *Setting*

This retrospective single centre study was performed in a general surgery department based in a busy urban university affiliated hospital. Whilst this hospital is one of three within close geographical proximity, it houses the most active regional acute surgical service. Referral to the acute surgical service can either be via primary care physicians or self-presentation to the ED.

### *Patient selection*

Institutional ethics board approval was sought and obtained and the requirement for informed consent waived in light of the anonymous nature of the study. Using the ICD-9 diagnostic codes for appendicitis (540-542), all consecutive patients who presented via the ED between the 1st of January and the 31st of July 2021 were identified. These dates were chosen as they covered the period of time that a national vaccination program opened to all adults aged 18 y and over was being rolled out administering over 150,000 doses daily.[18] Although there was no formal algorithm for diagnosis AA at our centre, patients rarely proceed to surgery without radiological findings in keeping with AA. The decision to perform either abdominal ultrasonography or computed tomography was based on clinical suspicion and/or raised inflammatory markers.

Once identified, these patients were verified according to the following inclusion criteria: Patients must have been aged 18 y or older; must have presented emergently via the ED; have had their surgery performed for a clinically or radiologically presumed AA; and have medical records available for review including documentation of their COVID-19 immunization or recovery status. Patients could have been treated surgically with either a laparoscopic or open appendectomy or conservatively with intravenous antibiotics. Patients who underwent surgery for a presumed AA in whom a normal appendix was ultimately found were also included in the study.

### *Data extraction*

The data extracted from the patients' electronic hospital records included patient age and gender and the length of symptoms before presentation to the ED. The incidence of delayed presentation was noted and defined as presentation to the ED $\geq$ 72 h following the onset of symptoms. The intraoperative findings were recorded and classified as follows. Uncomplicated AA referred to acute inflammation of the appendix whilst complicated AA included gangrene, perforation or peri-appendicular abscess. A normal appendix was defined by the absence of gross inflammation. The length of hospital stay was extracted and recorded in days. In addition, patients who were given antibiotics following discharge for $>$72 h were also identified. Finally, post-operative complications of Clavien-Dindo grade $\geq$3 that occurred within 30 d following surgery were also recorded.

The primary aim of the study was to compare whether immunization status or recovery from COVID-19 affected the presenting characteristics and severity of AA presenting to the ED. The secondary outcome was to assess whether the incidence of AA changed following the implementation of a national policy of vaccination against COVID-19 in comparison to historical data.

In order to assess whether vaccination status or recovery from COVID-19 affected the presenting characteristics or the severity of AA, all patients identified between the study dates were stratified according to vaccination or recovery status. Patients were considered to have been vaccinated if they had received any brand of vaccination according the prescribed dosing recommendations. Similarly, only patients with serological proof of previous COVID-19 infection were counted as having recovered. Patients who had been both vaccinated and had serological proof of previous infection were also included in the analysis. Once allocated to the vaccinated/recovered group, the clinicopathological and surgical data of these patients was compared with those who had not been vaccinated nor recovered from COVID-19.

With regards to the secondary outcome, the incidence of patients presenting to hospital during the study period was compared with historical data from the same institution both 1 and 2 y prior (equivalent to January 1, 2019 until July 31, 2019 and January 1, 2020 until July 31, 2020). A search of these equivalent time-periods before the study dates enabled a year-on-year comparison, compensating for seasonal or temporal changes in the incidence of AA both before and during the COVID-19 outbreak.

### *Statistical analysis*

All statistical analysis was performed using SPSS version 27 (IBM SPSS Statistics for Windows, Version 21.0. Released 2020. Armonk, NY: IBM Corp). Descriptive statistics are displayed as median or N with interquartile range or percentage in parenthesis unless stated otherwise. Univariate comparisons between the two groups were performed using Fishers exact test or Chi squared for ordinal or categorical variables and Mann Whitney *U*-test for continuous variables. In order to compare the incidence of AA before and after COVID-19 vaccination became widely available, a comparison was made between the average monthly incidence of AA during the study period with equivalent time periods 12 and 24 mo beforehand using ANOVA. For all analyses, a *P* value of $<0.05$ was considered significant.

## Results

Between the study dates, 258 patients were admitted via the ED with a presumed diagnosis of AA. Data was available for 255 patients (98.8%). In order to assess the primary outcome, a comparison was made between patients who had either been vaccinated or recovered from COVID-19 and those who had not. The results of this analysis are described in Table 1. There were 156 patients allocated to the vaccinated or recovered group (61.2%) and 99 (38.8%) patients allocated to the non-vaccinated or recovered group. In the former, 125 (80.1%) of patients had been fully vaccinated with greater than 2 wk elapsing between their second dose and presentation to the ED. There were no significant differences in terms of the presenting characteristics, severity or treatment modality when comparing between the two groups. Furthermore, no differences were noted neither in terms of the postoperative length of stay nor the need for postdischarge antibiotic therapy.

The description of the monthly incidence of AA throughout the study period is presented in Figure along with the historical data from the equivalent periods 12 and 24 mo earlier. This graph shows that there were generally less cases of AA in the 2020 and 2021 time periods in comparison to 2019, especially during April. However, these differences were not sustained and the trend appears to be that the incidence of AA was similar between the three time periods.

To further assess whether there was a difference in the distribution of the incidence of AA between the study dates in comparison with historical data, an ANOVA analysis was performed. The results of this are shown in Table 2. There was no significant difference between the median weekly incidence of AA when comparing between the three time periods included in the analysis ($P = 0.672$).

## Discussion

In this study we have shown that, for the cohort presented here, when comparing patients who had been vaccinated against or recovered from COVID-19 with those who had not, there were no differences in terms of their presenting characteristics or severity of their AA. Furthermore, there was no difference in the incidence of AA following the roll out of a national vaccination program in comparison with an equivalent pre-COVID-19 period. Considering that previous studies have described an increase in the incidence of delayed presentations of AA alongside an overall decrease in the incidence of AA presenting to the ED, we expected that the role out of a national vaccine program would be associated with a reverse in this trend.

Whilst the seasonal changes in the incidence of AA have been previously described with fewer cases in the winter and a peak in the summer, this was not a trend noted in our cohort.[19] Some of the factors that are thought to underpin seasonal changes may have been affected by the COVID-19 outbreak. These include national lockdowns, closure of educational systems and insistence on social distancing as they may have influenced behavioural and dietary habits previously been associated with the incidence of AA.[20] However, with regards to other factors associated with the temporal changes in the incidence of AA this may not be the case. This includes factors such as changes in the weather and temperature that are less likely to have been affected by COVID-19.[21]

Previous studies have described a decline in the incidence of AA during the outbreak of COVID-19 with a concurrent increase in the number of patients presenting with complicated AA.[6-8,10] Several theories have been proposed to explain these changes. Anxiety regarding patient-to-patient transmission of COVID-19 may prevent presentation to the ED.[22,23] As such, more patients may be inclined to treat themselves symptomatically at home only presenting to hospital when their symptoms fail to resolve.[24] Evidence also suggests that lockdown policies aimed at stemming the spread of COVID-19 negatively affects access to healthcare resulting in delayed presentation of common illnesses due to cancelled appointments due to limited public transport.[25-27]

In light of these explanations, it could be expected that the initiation of a national vaccination program would be associated with a reverse in the aforementioned trends in AA noted during COVID-19. However, the data presented here fails to demonstrate this. There are several possible reasons why this may be the case. Firstly, there is growing evidence concerning ‘pandemic fatigue’ and nonadherence to lock-down policies.[28] While intention to adhere to governmental guidelines remains high,[29] up to 92.8% of people have been found to not adhere to all social distancing rules.[30] As a result, the proposed public health theories thought to affect the declining incidence of AA may become less relevant as the pandemic continues. This may

**Table 1 – Analysis of the characteristics and severity of AA of patients identified during the study period.**

| Variable | Vaccinated/recovered | Non-vaccinated/non-recovered | *P* value |
|---|---|---|---|
| | N = 156 | N = 99 | |
| | N/median (%/IQR) | N/median (%/IQR) | |
| Vaccinated | 125 (80.1%) | - | - |
| Gender: | | | |
| Male | 78 (50.0%) | 50 (50.5%) | |
| Female | 78 (50.0%) | 49 (49.5%) | 0.937 |
| Age (y) | 28.0 (15.5) | 29.0 (17.0) | 0.701 |
| Length of symptoms (d) | 1.0 (1.0) | 1.0 (1.0) | 0.250 |
| Delayed presentation (>3 d) | 13 (8.3%) | 9 (9.1%) | 0.834 |
| Leucocytosis ($\times 10^9$/L) | 13.2 (6.3) | 12.8 (7.6) | 0.511 |
| C Reactive protein (1 mg/L) | 1.9 (5.0) | 1.5 (2.9) | 0.780 |
| Non-surgical treatment | 3 (1.9%) | 2 (2.0%) | 0.957 |
| Severity of appendicitis: | | | |
| Normal appendix | 0 (0.0%) | 2 (2.0%) | |
| Uncomplicated appendicitis | 117 (75.0%) | 75 (75.8%) | |
| Complicated appendicitis | 39 (25.0%) | 22 (22.2%) | 0.748 |
| Laparoscopic appendectomy | 152 (97.4%) | 95 (96.0%) | 0.927 |
| Percutaneous/laparoscopic drainage of peri-appendicular abscess | 2 (1.3%) | 1 (1.0%) | >0.999 |
| Length of surgery (min) | 37.0 (22.0) | 33.5 (23.5) | 0.373 |
| Post-operative peritoneal drain | 21 (13.5%) | 5 (5.1%) | 0.316 |
| Length of stay (d) | 1.0 (1.0) | 1.0 (1.0) | 0.121 |
| Patients given antibiotic treatment on discharge | 21 (13.5%) | 15 (15.2%) | 0.532 |
| Post-operative complication | 0 (0.0%) | 1 (1.0%) | >0.999 |

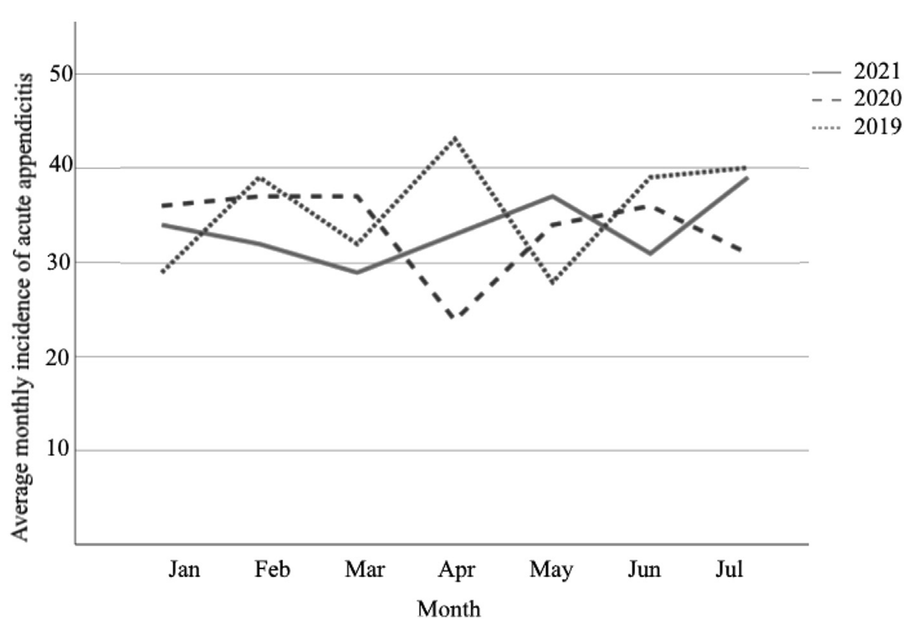


**Fig. – The average monthly incidence of acute appendicitis cases during the study group and historical time periods.**

**Table 2 – A comparison of the weekly incidence of AA presenting to the department of emergency medicine during the study period with historical data.**

| Time period | Median weekly incidence of AA (IQR) | P value |
|---|---|---|
| January 01, 2021-July 01, 2021 | 8.0 (4.0) | |
| January 01, 2020-July 31, 2020 | 8.0 (4.25) | |
| January 01, 2019-July 31, 2020 | 8.0 (5.0) | 0.672 |

also explain why the incidence of AA presented here, almost a year after the onset of COVID-19, is so similar to the historical data from 24 mo previously.

Secondly, the current literature that explores the relationship between COVID-19 and the changing nature of AA does not consider the impact successful vaccination or post-infection status on the incidence or characteristics of AA. There is preliminary evidence that suggests that adherence to hygiene behaviours fluctuates with the incidence of COVID-19.[31] Similarly, as the incidence of COVID-19 declines, the fear of transmission may be lessened. Furthermore, the fear of transmission is maximal amongst a group of patients who tend not to suffer from AA. Those found to be most at fear include the elderly, the unemployed, and those with a history of psychiatric illness.[26] We propose that a potential change in public perception, possibly reinforced following vaccination or recovery from COVID-19 may also, to an extent, explain why there was also no difference in the presenting characteristics or severity of AA in the cohort presented here.

It is important to differentiate whether the changes in the incidence of AA that have been observed elsewhere are due to the changes in the incidence of COVID-19 or due to the effect of a national lockdown. Understanding this differentiation is important for healthcare resource planning and allocation as it may affect the timing of when acute care services are restored. If acute surgical care has been rationalized during the pandemic, restoration of these services will need to be timed for either downturns in the prevalence of COVID-19 or the ending of national lockdowns aimed at stemming the spread of COVID-19. This is vital to ensure appropriate provision of acute surgical care services for the projected future work-load at the appropriate time.

There are several limitations to this study. The data was collected retrospectively and was limited to the experience of a single centre. Although this study was performed in an urban hospital housing a busy acute surgical service, as hospitals within close geographic proximity were not included in the study a degree of referral bias will have been introduced. The data was also further limited by only exploring AA and did not include other acute surgical illnesses. In addition, other variables that could have been useful in understanding changes in patient behaviour, such as COVID-19 fear of transmission scale were not collected.[27] We also included those who had recovered from COVID-19 alongside those who had been vaccinated. Although there were only a few patients who recovered from COVID-19 who were not vaccinated, the inclusion of these patients affects the generalizability of the results. Finally, it is possible that by extending the time-period of the study changes in the incidence and severity of AA may have been noted.

### *Conclusions*

In the cohort of patients presented here, we were unable to demonstrate a relationship between vaccination against COVID-19 or recovery from acute infection and the incidence, severity or presenting characteristics of AA. This suggests that the implementation of a national vaccination program may not affect the nature nor volume of common surgical emergencies managed by acute general surgical services. As more countries start to vaccinate patients against COVID-19, further studies will be needed to understand how demands for acute care surgical services will be affected.

## Author Contributions

JT–literature search, study design, data collection, data analysis, data interpretation, writing, critical revision. AK–literature search, study design, data collection, data analysis, data interpretation, writing, critical revision. RG–data collection, data analysis, data interpretation, writing, critical revision. MG–data collection, data analysis, data interpretation, writing, critical revision. MY–data collection, data analysis, data interpretation, writing, critical revision. YT–data collection, data analysis, data interpretation, writing, critical revision. PR–study design, data analysis, data interpretation, writing, critical revision.

## Disclosure

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REFERENCES

1. Dick L, Green J, Brown J, et al. Changes in emergency general surgery during covid-19 in Scotland: a prospective cohort study. *World J Surg*. 2020;22:3590–3594.
2. Cano-Valderrama O, Morales X, Ferrigni CJ, et al. Acute Care Surgery during the COVID-19 pandemic in Spain: changes in volume, causes and complications. A multicentre retrospective cohort study. *Int J Surg*. 2020;80:157–161.

3. Tankel J, Keinan A, Blich O, et al. The decreasing incidence of acute appendicitis during COVID-19: a retrospective multi-centre study. *World J Surg*. 2020;26:1–6.
4. Fisher JC, Tomita SS, Ginsburg HB, Gordon A, Walker D, Kuenzler KA. Increase in pediatric perforated appendicitis in the New York City metropolitan region at the epicenter of the COVID-19 outbreak. *Ann Surg*. 2021;273:410–415.
5. Finkelstein P, Picado O, Muddasani K, et al. Retrospective analysis of the trends in acute appendicitis during the COVID-19 pandemic. *J Laparoendosc Adv Surg Tech A*. 2020;31:243–246.
6. Willms AG, Oldhafer KJ, Conze S, et al. Appendicitis during the COVID-19 lockdown: results of a multicenter analysis in Germany. *Langenbecks Arch Surg*. 2021;406:367–375.
7. Kvasnovsky CL, Shi Y, Rich BS, et al. Limiting hospital resources for acute appendicitis in children: lessons learned from the U.S. epicenter of the COVID-19 pandemic. *J Pediatr Surg*. 2020;56:900–904.
8. Snapiri O, Rosenberg Danziger C, Krause I, et al. Delayed diagnosis of paediatric appendicitis during the COVID-19 pandemic. *Acta Paediatr*. 2020;109:1672–1676.
9. Collard M, Lakkis Z, Loriau J, et al. Antibiotics alone as an alternative to appendectomy for uncomplicated acute appendicitis in adults: changes in treatment modalities related to the COVID-19 health crisis. *J Visc Surg*. 2020;157:S33–S42.
10. Solis E, Hameed A, Brown K, Pleass H, Johnston E. Delayed emergency surgical presentation: impact of corona virus disease (COVID-19) on non-COVID patients. *ANZ J Surg*. 2020;90:1482–1483.
11. Thierry A, Pastor B, Pisareva E, et al. Association of COVID-19 lockdown with the tumour burden in patients with newly diagnosed etestatic colorectal cancer. *JAMA Netw Open*. 2021;4:e2124483.
12. Kidane S, Spicer J, Kim J, et al. SABR-BRIDGE: stereotatic ablative radiotherapy before resection to avoid delay for easrly stage lung cancer oligomets during the COVID-19 pandemic. *Front Oncol*. 2020;10:580189.
13. Malik AA, McFadden SAM, Elharake J, Omer SB. Determinants of COVID-19 vaccine acceptance in the US. *EClinicalMedicine*. 2020;26:100495.
14. Knoll MD, Wonodi C. Oxford–AstraZeneca COVID-19 vaccine efficacy. *Lancet*. 2021;397:72–74.
15. Hall VJ, Foulkes S, Saei A, et al. Effectiveness of BNT162b2 mRNA vaccine against infection and COVID-19 vaccine coverage in healthcare workers in England, multicentre prospective cohort study (the SIREN study). *Lancet*. 2021;397:1725–1735.
16. SeyedAlinaghi S, Oliaei S, Kianzad S, et al. Reinfection risk of novel coronavirus (COVID-19): a systematic review of current evidence. *World J Virol*. 2020;9:79–90.
17. Reiter PL, Pennell ML, Katz ML. Acceptability of a COVID-19 vaccine among adults in the United States: how many people would get vaccinated? *Vaccine*. 2020;38:6500–6507.
18. Rosen B, Waitzberg R, Israeli A. Israel's rapid rollout of vaccinations for COVID-19. *Isr J Health Policy Res*. 2021;10:2–14.
19. Ahmed W, Akhtar MS, Khan S. Seasonal variation of acute appendicitis. *Pak J Med Sci*. 2018;34:564–567.
20. York TJ. Seasonal and climatic variation in the incidence of adult acute appendicitis: a seven year longitudinal analysis. *BMC Emerg Med*. 2020;20:24.
21. Ilves I, Fagerström A, Herzig KH, Juvonen P, Miettinen P, Paajanen H. Seasonal variations of acute appendicitis and nonspecific abdominal pain in Finland. *World J Gastroenterol*. 2014;20:4037–4042.
22. Alenazi TH, Al Arbash H, El-Saed A, et al. Identified transmission dynamics of Middle East respiratory syndrome coronavirus infection during an outbreak: implications of an overcrowded emergency department. *Clin Infect Dis*. 2017;65:675–679.
23. Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. *Lancet Child Adolesc Health*. 2020;4:e10–e11.
24. Cobben LP, De Mol Van Otterloo A, Puylaert JBCM. Spontaneously resolving appendicitis: frequency and natural history in 60 patients. *Radiology*. 2000;65:675–679.
25. Tankel JW, Ratcliffe D, Smith M, et al. Consequences of the emergency response to COVID-19: a whole health care system review in a single city in the United Kingdom. *BMC Emerg Med*. 2021;21:55.
26. Midorikawa H, Aiba M, Lebowitz A, et al. Confirming validity of The Fear of COVID-19 Scale in Japanese with a nationwide large-scale sample. *PLoS One*. 2021;16:e0246840.
27. Nguyen HT, Do BN, Pham KM, et al. Fear of COVID-19 scale—associations of its scores with health literacy and health-related behaviors among medical students. *Int J Environ Res Public Health*. 2020;17:4164.
28. Michie S, West R, Harvey N. The concept of "fatigue" in tackling covid-19. *BMJ*. 2020;371:m4171.
29. Davies R. Coronavirus and the social impacts on Great Britain data - office for national statistics. 2020. Available at: www.ons.gov.uk. Accessed August 1, 2021.
30. Hills S, Eraso Y. Factors associated with non-adherence to social distancing rules during the COVID-19 pandemic: a logistic regression analysis. *BMC Public Health*. 2021;21:352.
31. Huang F, Armando M, Dufau S, Florea O, Brouqui P, Boudjema S. COVID-19 outbreak and healthcare worker behavioural change toward hand hygiene practices. *J Hosp Infect*. 2021;111:27–34.