ORIGINAL ARTICLE

Severity of COVID-19 infection in vaccinated and unvaccinated patients and their outcome - a local experience

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ABSTRACT

Background: The COVID-19 pandemic continues to pose a significant global health threat. In late 2020 and early 2021, multiple vaccines were authorized for emergency use, enabling mass vaccination campaigns. This study aimed to evaluate factors influencing COVID-19 severity (mild, moderate, severe) and outcomes (death or discharge) in vaccinated individuals presenting to a tertiary care hospital.

Material and Methods: An observational study was conducted at Dr. Ziauddin Hospital Clifton, Karachi, Pakistan, from June to September 2021. We included patients aged 16 and above with RT-PCR-confirmed COVID-19 infection, categorized by vaccination status (unvaccinated, partially or fully vaccinated). The study analyzed variables such as age, gender, vaccination status, vaccine type, disease severity, day of presentation, hospital stay, and breakthrough infection duration. Data were analyzed using chi-square tests. A total of 341 patients were enrolled, with 219 vaccinated (V1) and 73 unvaccinated (V2).

Results: The median age was 65 years, with 61% males. Among the patients, 45% were fully vaccinated, 13.2% partially vaccinated, and 41% unvaccinated. Disease severity was mild in 17.9%, moderate in 50.1%, and severe in 32%. Disease severity was significantly associated with age (p=0.01), vaccination status (p=0.00), and vaccine type (p=0.00). Time since the last vaccination also influenced breakthrough infections (p=0.00). Of the patients, 76.5% survived and 23.5% died. Disease outcomes were associated with age (p=0.02), severity (p=0.00), hospital stay (p=0.01), and vaccine type (p=0.01).

Conclusion: Age and vaccine-related factors significantly influence disease severity, while additional factors beyond vaccination may impact disease outcomes. Further research is needed to explore these variables.

Keywords: Vaccination, COVID-19, Severity, Immunization, SARS-CoV-2

BACKGROUND

With nearly 500 million cases and more than six million fatalities reported to the World Health Organization (WHO), the coronavirus disease 2019 (COVID-19) epidemic continues to be a major public health emergency worldwide.[1] About 15% to 30% of patients infected with the wild-type variant of SARS-CoV2 developed acute respiratory distress syndrome, and the clinical spectrum of COVID-19 varies from mild to critical.[2] People with underlying illnesses and compromised immune systems were more likely to develop life-threatening illnesses.[3]

In 2020, the prevention of the pandemic's spread was largely accomplished through non-pharmaceutical interventions, which also helped to lessen the severity of illness and keep health services from becoming overburdened.[4,5] Although this strategy was generally successful, it had negative fiscal and social effects. Numerous vaccines were authorized for use in late 2020 and early 2021, demonstrating unmatched development speeds that allowed many nations to launch mass vaccination programs as a form of mitigation. As of November 21st, 2021, eight billion doses of the COVID-19 vaccine had been distributed across the globe in an attempt to reduce the COVID-19 rate.

In addition, it was also found that a UK-based case-control research verified the findings of a previous community-based investigation, which demonstrated a substantial decrease in the acquisition of infection following vaccination from 12 days after the first dose.[7,8] Two doses of BNT162b2 decreased the

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acquisition of infection either symptomatic or asymptomatic.

The main objective of COVID-19 vaccination is to mitigate the severity of the disease rather than achieving complete prevention of all infections. As a result, some vaccinated individuals may still experience breakthrough infections.[10] However, it is anticipated that these people will experience less serious infections, fewer hospitalizations, and fewer admissions to the intensive care unit (ICU). This may be accomplished by the vaccine's capacity to elicit antibodies and immunological memory.[11,12] This theory is supported by several studies of COVID-19 infections in individuals who received vaccinations. Therefore, Understanding the potential effects of vaccination on COVID-19 transmission and disease outcomes at the community level is an area of interest for clinicians and researchers. This study aims to determine the COVID-19 disease severity and outcomes among vaccinated individuals and unvaccinated individuals presenting to a tertiary care hospital.

MATERIAL AND METHODS

This observational study was conducted at the Covid-19 ward, Dr. Ziauddin Hospital Clifton Campus, Karachi, Pakistan from June 2021 to Sept 2021 after takin the approval from institutional Ethical Review Committee (vide reference number 4050721MAPUL). Infection was confirmed using RT-PCR on a nasopharyngeal or oropharyngeal swab. Patients of any gender, 16 years or above who had RT-PCR-confirmed COVID-19 infection, were unvaccinated, fully or partially vaccinated (who had received at least one dose of the vaccine) were included in this study. The variables used were age, gender, vaccination status (unvaccinated, fully or partially vaccinated), type of vaccine administered, disease severity (mild, moderate, and severe) as per the defined criteria mentioned below, day of disease presentation to the hospital, length of hospital stay and duration of breakthrough infection from last vaccine dose. Categorical variables were reported as frequencies and percentages. The chi-square test was used to determine the association of patient variables with disease severity and infection outcome (discharge or death). Consecutive sampling was employed to enroll participants. IBM SPSS (version 21) was used for analysis. Statistical significance was based on two-tailed p-values less than or equal to 5% level of significance.

Disease severity was classified using the following criteria by Wu *et al*.[13] Mild: Characterized by mild clinical symptoms and no evidence of pneumonia on lung Computed Tomography (CT) scan. Moderate: Manifesting with fever, cough, and lung CT revealing pneumonia. Severe: Involving respiratory distress, indicated by a respiratory rate exceeding 30 breaths per minute, resting oxygen saturation (O2Sat) of 93% or lower, and/or a ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FIO2) of 300 mmHg or less.[24]

Group sample sizes of (V1)219 and (V2)73 produce a two-sided 95% confidence interval for the difference in population proportions with a width that is equal to 0.200 when the estimated sample proportion (V1) is 0.85, the estimated sample proportion (V2) is 0.75, and the difference in sample proportions is 0.10.

RESULTS

A total of 341 patients were enrolled with a median age of 65 (IQR=51-76) year (range 24-94**)** Mean age 62yrs with SD of 16.8. Table-I is the frequency table of study variables. Table-II is a comparison of study variables with disease severity. Table-III compares study variables with disease outcomes.

Figure-I show infection cases since vaccination status, with the onset of symptoms since the last dose of vaccine for fully and partial vaccinated individuals. Figure-II shows breakthrough infections with vaccination status whereas figure-III shows vaccination status with disease severity. The differences in the group were statistically significant (p=0.00). Interestingly partially vaccinated group fared better than the fully vaccinated. Also, most cases in both the fully and partially vaccinated occurred within 1-3 months, and beyond the 3rd month were better for both groups. Mild, moderate, and severe disease numbers were 61 (17.9%), 171 (50.1%), and 109 (32%) respectively. Disease severity differed on the basis of age (p0.01), vaccination status (p0.0), vaccine type (p0.0), day of disease presentation (p0.02), and onset of infection since the last dose but did not differ on the basis of gender (p0.79). In our study variable of Gender (p0.27), Vaccine status (p0.58), and Day of Disease presentation (p0.51) was not associated with outcome but Age (p0.02), type of

vaccine (p0.01), Disease severity (p0.0), and length of hospital (p0.01) was associated with outcome of death

Table-I: Frequency table of study variables.

Variable	Frequency (%)
Age groups	
≤50 years	79 (23%)
>50 years	262 (77%)
Gender	
Male	208 (61%)
Female	133(39%)
Vaccination Status	
Full	155 (45%)
Partial	45 (13.2%)
No Vaccination	141 (41%)
Vaccine Type (Total 200)	
Sinopharm	121 (35%)
Sinovac	54 (15.8%)
Cansino	16 (4.7%)
Moderna	6 (1.8%)
Pfizer	1 (0.3%)
Pakvac	1(0.3%)
Astrazeneca	1(0.3%)
Severity of Disease	
Mild	61 (17.9%)
Moderate	171 (50.1%)
Severe	109 (32%)
Symptoms After Vaccination	
<1 month	25 (7.3%)
1-2 months	76 (22.3%)
2-3 months	77 (22.6%)
>3months	22 (6.5%)
Unvaccinated	141 (41.3%)
Outcome	
Discharged	261 (76.5%)
Death	80 (23.5%)

Table-II: Comparison of Study Variables with Disease Severity

Patients' features	Disease severity			p-Value
	Mild (%)	Moderate (%)	Severe (%)	
Age groups				
≤50 years	20	43	16	**0.01**
>50 years	41	128	93	
Gender				
Male	39	105	64	**0.79**
Female	22	66	45	
Type of vaccine				
Unvaccinated	4	86	51	
Sinopharm	35	47	39	
Sinovac	11	27	16	
Cansino	7	8	1	**0.0**
Astrazaneca	0	1	0	
Moderna	4	1	1	
Pfizer	0	1	0	

Pakvac	0	0	1	
Vaccination status				
Complete	46	66	43	
Nil	4	86	51	**0.0**
Partial	11	19	15	
Disease Day				
<5	44	84	62	
5-10	17	66	38	**0.02**
11-15	0	20	9	
>15	0	1	0	
Onset of symptoms from last vaccine				
<1 Month	8	97	61	
1-2 Months	22	32	22	
2-3 Months	27	30	20	**0.0**
>3 months	4	12	6	

Table-III: Comparison of study variables with Covid-19 infection outcomes.

Patients' features	Alive (%)	Dead (%)	p-value
Age groups			
≤50 years	68	11	**0.02**
>50 years	193	69	
Gender			
Male	155	53	**0.27**
Female	106	27	
Vaccination Status			
Complete	116	39	
Nil	108	33	**0.58**
Partial	37	8	
Type of vaccine			
Unvaccinated	108	33	
Sinopahrm	85	36	
Sinovac	45	9	
Cansino	16	0	
Astrazaneca	0	1	**0.01**
Moderna	6	0	
Pfizer	1	0	
Pakvac	0	1	
Disease severity			
Mild	58	3	
Moderate	156	15	**0.00**
Severe	47	62	
Disease Day			
<5	140	50	
5-10	96	25	
11-15	24	5	**0.5**
>15	1	0	
Length of Stay			
<5 days	41	5	
5-10 days	111	24	
10-14 days	72	26	**0.01**
14-21 days	32	18	
>21 days	6	7	

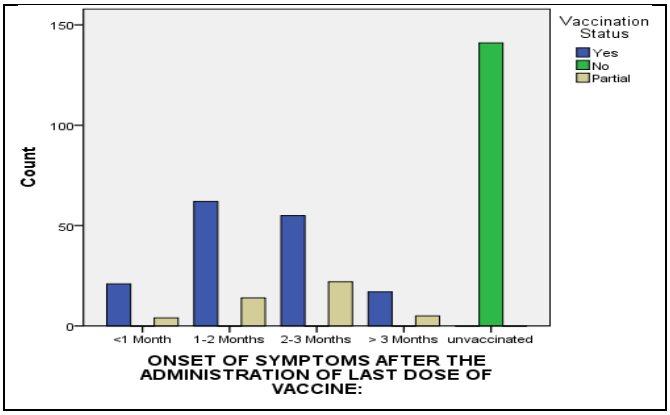

Figure-I: Infection cases with vaccination status.

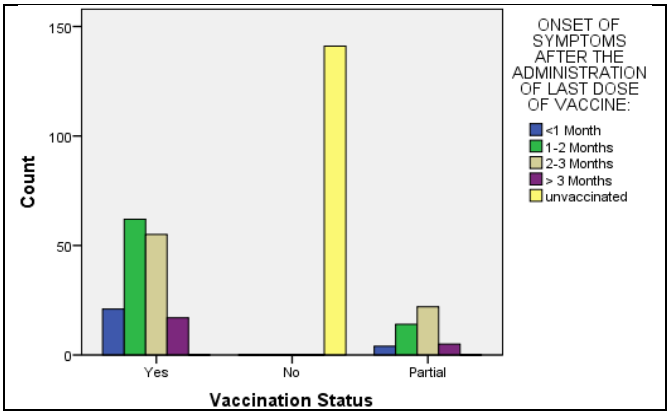

Figure-II: Vaccination status and breakthrough infections.

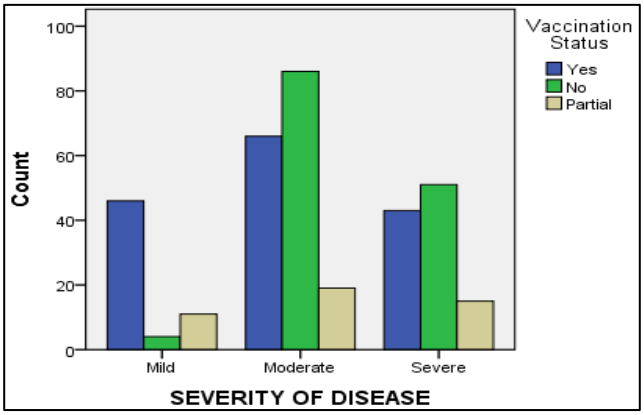

Figure-III: Severity of disease and vaccination status.

DISCUSSION

The COVID-19 vaccination campaign was launched in Pakistan in February 2021. The COVID-19 vaccine aids in avoiding fatalities, serious illness, and hospitalization.[14,15] The Centers for Disease Control and Prevention (CDC) recently defined "breakthrough infection" (BTI) as an infection happening two weeks after receiving the full dose of an approved vaccine.[16] During the implementation of the vaccination program, it is crucial to carry out surveillance of the general population to ensure effective monitoring of the situation.

In this study, we observed some very intriguing trends in relation to patient variables and disease severity and outcomes in both vaccinated and unvaccinated patients. The noticeable point is age is associated with both disease severity and disease outcomes. Most of the infected cases were elderly patients with a median age of 65 years and also had severe disease. Also, day of disease presentation was associated with disease severity but not with outcome. Delay in seeking treatment usually results in the worsening of the disease and hence disease severity

Secondly, in our study, few patients developed breakthrough infections after 3 months of vaccination. The total number of breakthrough infections was much less in the partially vaccinated group compared to the fully vaccinated group at all times from vaccination. On a similar note, an Italian study found that, compared to protection following the first booster dose, the relative effectiveness of a second booster dose against severe COVID-19 in persons 80 and older is only about 30% after 2 to 4 months.[17]

Third, an observable pattern in this study was a smaller proportion of mild disease presentation. This fact conflicts with many other studies evaluating the vaccine effectiveness and reporting that vaccinated individuals acquire mild disease.[18,19,20] The plausible reason for the reverse finding in our study could be the fact that most of the patients in our study were elderly who have a higher likelihood of developing moderate disease and healthcare-seeking behavior of the Pakistani population. One in six adults in Pakistan believe they and their families are safe from SARS-CoV-2 even without taking any preventive measures, according to a survey that was performed during the COVID-19 pandemic. Delayed presentation resulting in severe disease. The Sinopharm COVID-19 vaccine, also known as BBIBP-CorV in Pakistan, received approval for emergency use on January 18, 2021, and the vaccination program began on February 2, 2021.[21,22] Six COVID-19 vaccine types have recently received approval in Pakistan: Sinopharm (BBIBP-CorV), CanSino (AD5-nCOV), Sinovac (PiCoVacc), Sputnik (Gam-COVID-Vac), Pfizer (BNT162b2), and AstraZeneca (AZD1222, ChAdOx1

nCoV-19). Later, other vaccines were also introduced.[23,24] In the research, it has been demonstrated that each of these vaccines can reduce the severity of COVID-19 infection.[8-10,18] We found a strong association not only between vaccination status and disease severity but also between vaccine type and severity. Vaccination status was not associated with disease outcome but vaccine type was strongly associated keeping in mind that only 3 out of 7 the seven vaccines had reasonable numbers in the study. This would mean that outcome is influenced by a lot of factors and vaccine type is one of them. We would like to believe that it favored discharge but if it affected mortality then the safety of the vaccine would come into question. Numerous reports in the literature have suggested complications like stroke, MI, inflammation, and death. This is a very important area of research as novel vaccines were introduced without long-term safety data because of the urgency of the situation and hence this data is essential. Although many studies evaluating the vaccine effectiveness reported that there were no or few mortalities among vaccinated individuals and their disease was mild in nature[8-9] our data suggests otherwise. Possible causes for this could be coincidental events, such as deaths occurring shortly after vaccination due to unrelated causes, can mistakenly be attributed to the vaccine. Individuals with underlying health conditions, although vaccination significantly reduces their risk of severe outcomes from Covid-19, may still succumb to the virus, leading to the appearance of increased mortality rates among vaccinated individuals. Additionally, emerging variants of the virus may pose challenges in vaccine efficacy, potentially rendering vaccines less effective against certain variants and leaving vaccinated individuals at risk of severe illness and death, albeit at a lower rate compared to unvaccinated individuals. Furthermore, incomplete vaccination coverage within the population can contribute to ongoing transmission of the virus, heightening the risk of severe outcomes for both vaccinated and unvaccinated individuals. An interesting observation from table 3 is that “Sinopharm” vaccine had higher mortality (29%) compared to unvaccinated group (23%). Possible explanation for this could be vaccine related death or unrelated causes attributed to vaccine like age and comorbidities.

One-third of the patients in our study did not survive. Patients’ age and gender were not associated with outcome and interestingly not even with the vaccination status. However, as pointed out earlier the outcome was associated with vaccine type with disease severity.

The current study provides valuable insights into the severity of COVID-19 and the outcomes observed in vaccinated individuals. It specifically focuses on the experience of a single tertiary care hospital in Karachi. However, to obtain a more reliable and comprehensive understanding of disease severity among the vaccinated population, it would be beneficial to combine the results of similar studies conducted in different settings.

CONCLUSION

In conclusion, COVID for vaccinated individuals, age affects both severity of disease and disease outcomes, while day of disease presentation, vaccination status, and type of vaccine affect disease severity and not disease outcome. This means there may be additional factors beyond disease that may be contributory.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Namirah Iftikhar: Main conception of the study, study design, data collection, data analysis, manuscript writing, final approval, agreement to be accountable for all aspects of the work

Muhammad Osama Rehman Khalid: Data collection, data analysis, manuscript writing, final approval, agreement to be accountable for all aspects of the work

Ashar Ekhlaq Ahmed: Study design, manuscript writing, final approval, agreement to be accountable for all aspects of the work

Uzma Ghori: Final approval, agreement to be accountable for all aspects of the work

REFERENCES

1. Li M, Liu Q, Wu D, Tang L, Wang X, Yan T, *et al*. Association of COVID-19 vaccination and clinical severity of patients infected with Delta or Omicron variants—China, May 21, 2021–February 28, 2022. China CDC Wkly. 2022; 4(14): 293-7.
DOI: https://doi.org/10.46234/ccdcw2022.074

2. Attaway AH, Scheraga RG, Bhimraj A, Biehl M, Hatipoğlu U. Severe COVID-19 pneumonia: pathogenesis and clinical management. BMJ. 2021; 372: n436. DOI: https://doi.org/10.1136/bmj.n436
3. Formica N, Mallory R, Albert G, Robinson M, Plested JS, Cho I, *et al*. Different dose regimens of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373) in younger and older adults: A phase 2 randomized placebo-controlled trial. PLoS Med. 2021; 18(10): e1003769. DOI: https://doi.org/10.1371/journal.pmed.1003769
4. Vardavas CI, Nikitara K, Aslanoglou K, Hilton-Boon M, Phalkey R, Leonardi-Bee J, *et al.* Effectiveness of non-pharmaceutical measures (NPIs) on COVID-19 in Europe: A systematic literature review. medRxiv. 2021. DOI: https://doi.org/10.1101/2021.11.11.21266216
5. Cowling BJ, Ali ST, Ng TW, Tsang TK, Li JC, Fong MW, *et al.* Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: An observational study. Lancet Pubic Health. 2020; 5(5): e279-88. DOI: https://doi.org/10.1016/s2468-2667(20)30090-6
6. Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, *et al.* A global database of COVID-19 vaccinations. Nat Hum Behav. 2021; 5(7): 947-53. DOI: https://doi.org/10.1038/s41562-021-01122-8
7. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, *et al.* Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID symptom study app in the UK: A prospective observational study. Lancet Infect Dis. 2021; 21(7): 939-49. DOI: https://doi.org/10.1016/s1473-3099(21)00224-3
8. Bernal JL, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, *et al*. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on COVID-19-related symptoms, hospital admissions, and mortality in older adults in England: A test-negative case-control study. BMJ. 2021; 373: n1088. DOI: https://doi.org/10.1136/bmj.n1088
9. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, *et al*. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: An observational study using national surveillance data. Lancet. 2021; 397(10287): 1819-29. DOI: https://doi.org/10.1016/s0140-6736(21)00947-8
10. Singh C, Naik BN, Pandey S, Biswas B, Pati BK, Verma M, *et al.* Effectiveness of COVID-19 vaccine in preventing infection and disease severity: A case-control study from an Eastern State of India. Epidemiol Infect. 2021; 149: e224. DOI: https://doi.org/10.1017/s0950268821002247
11. Sanders RW, de Jong MD. Pandemic moves and countermoves: vaccines and viral variants. Lancet. 2021; 397(10282): 1326-7. DOI: https://doi.org/10.1016/s0140-6736(21)00730-3
12. Thompson MG, Burgess JL, Naleway AL, Tyner H, Yoon SK, Meece J, *et al*. Prevention and attenuation of COVID-19 with the BNT162b2 and mRNA-1273 vaccines. N Engl J Med. 2021; 385(4): 320-9. DOI: https://doi.org/10.1056/nejmoa2107058
13. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, *et al.* Clinical characteristics of imported cases of COVID-19 in Jiangsu province: A multicenter descriptive study. Clin Infect Dis. 2020. DOI: https://doi.org/10.1093/cid/ciaa199
14. Hashim A. Pakistan received the first COVID-19 vaccine shipment from China [Internet]. Al Jazeera; 2021 [cited 2022 Oct 28]. Available from: https://www.aljazeera.com/news/2021/2/1/pakistan-receives-first-shipment-of-coronavirus-vaccine
15. Shahzad A. Pakistan launches COVID-19 vaccination drive, starting with elderly [Internet]. Reuters; 2021 [cited 2022 Oct 28]. Available from: https://www.reuters.com/article/us-health-coronavirus-pakistan-vaccine-idUSKBN2B219K
16. Centers for Disease Control and Prevention. COVID-19 breakthrough case investigations and reporting [Internet]. CDC; 2021 [cited 2022 Oct 28]. Available from: https://www.cdc.gov/vaccines/covid19/health-departments/breakthrough-cases.html
17. Fabiani M, Mateo-Urdiales A, Sacco C, Rota MC, Petrone D, Bressi M, *et al*. Relative effectiveness of a 2nd booster dose of COVID-19 mRNA vaccine up to four months post administration in individuals aged 80 years or more in Italy: A retrospective matched cohort study. Vaccine. 2023; 41(1): 76-84. DOI: https://doi.org/10.1016/j.vaccine.2022.11.013
18. Arregocés-Castillo L, Fernández-Niño J, Rojas-Botero M, Palacios-Clavijo A, Galvis-Pedraza M, Rincón-Medrano L, *et al*. Effectiveness of COVID-19 vaccines in older adults in Colombia: A retrospective, population-based study of the ESPERANZA cohort. Lancet Healthy Longev. 2022; 3(4): e242-52. DOI: https://doi.org/10.1016/s2666-7568(22)00035-6
19. Ranzani OT, Hitchings MD, Dorion M, D'Agostini TL, de Paula RC, de Paula OF, *et al*. Effectiveness of the CoronaVac vaccine in older adults during a Gamma variant-associated epidemic of COVID-19 in Brazil: A test-negative case-control study. BMJ. 2021; 374: n2015. DOI: https://doi.org/10.1136/bmj.n2015
20. Li Y, Tenchov R, Smoot J, Liu C, Watkins S, Zhou Q. A comprehensive review of the global efforts on COVID-19 vaccine development. ACS Cent Sci. 2021; 7(4): 512-33. DOI: https://doi.org/10.1021/acscentsci.1c00120
21. Crasto DAM. BBIBP-CorV, Sinopharm COVID-19 vaccine. Greenfield C. 2021.
22. Muhammad SZ, Shaikh N, Asad D, Fatima N. Challenges to mass immunization against COVID-19 in Pakistan: A lower-middle-income vaccine-hesitant country. J Glob Health. 2022; 12: 03006. DOI: https://doi.org/10.7189/jogh.12.03006
23. Zayed NE, Abbas A, Lutfy SM. Criteria and potential predictors of severity in patients with COVID-19. Egypt J Bronchol. 2022; 16(1): 11. DOI: https://doi.org/10.1186/s43168-022-00116-y
24. Matta S, Chopra KK, Arora VK. Morbidity and mortality trends of COVID-19 in top 10 countries. Indian J Tuberc. 2020; 67(4): S167-72. DOI: https://doi.org/10.1016/j.ijtb.2020.09.031