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Vaccination history in covıd 19 cases: Observational study

Ahmet Doğan[1*], **Taliha Karakök**[2], **Yakup Gezer**[3], **Süleyman Değermenci**[4]

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Authors' Affiliation:
[1]Ordu State Hospital, Department of Infectious Diseases and Clinical Microbiology, Ordu, Turkey
[2]Fatsa State Hospital, Department of Infectious Diseases and Clinical Microbiology, Ordu, Turkey
[3]Konya City Hospital, Department of Infectious Diseases and Clinical Microbiology, Konya, Turkey
[4]Ünye State Hospital, Department of İnternal Medicine, Ordu, Turkey

[*]**Corresponding Author**
Ordu State Hospital, Department of Infectious Diseases and Clinical Microbiology, Ordu, Turkey
Orcid: 0000-0001-51104027
Email: drahmtdgn@gmail.com

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ABSTRACT

Background: The lack of an effective antiviral treatment in the COVID 19 pandemic is increasing the importance of vaccines day by day. *Materials and Methods*: The study was scheduled between October 1, 2021 and January 7, 2022. COVID-19 PCR negative cases, cases whose vaccine information could not be reached, and cases under 18 years of age were excluded from the study. The cases in the service and the ICU, the cases that died and did not die during the follow-up in the ICU, and the vaccinated and unvaccinated cases were compared among themselves by dividing them into two groups. *Results:* The mean age, presence of comorbid conditions, length of stay, time elapsed after the last dose of vaccine and some laboratory values were found to be higher in ICU cases than in cases hospitalized in the service. The mean age and intubation rate were higher in the patients who died in the ICU compared to the survivors. The intubation rate was higher and the length of stay in the ICU was longer in unvaccinated cases compared to vaccinated cases. *Conclusion:* In our study, it was determined that the COVID 19 vaccines reduced the hospitalization of the patients in the early age groups, the length of stay in the ICU, and the admission to intubation. The reason for the significant difference in terms of mortality was thought to be due to the excess of comorbid conditions and higher average age in vaccinated cases.

Keywords: biontech, covid-19 vaccine, mortality, sinovac

1. INTRODUCTİON

As of January 2, 2022, a total of approximately 289 million cases and just over 5.4 million deaths have been reported globally, according to the World Health Organization (WHO) weekly Covid 19 epidemiological update report. In recent days, a rapid increase of up to 71% in the number of cases has been detected, while a 10% decrease in death rates has been observed. The weekly case incidence increased by 100% in the Americas, the Southeast Asian Region (78%), the European Region (65%), and the African Region (22%) (WHO TEAM, 2022). The pandemic continues to be the greatest threat to humanity, with a serious impact on politics, economy and culture on a global scale (Wang et al., 2020). Because SARS-CoV-2 is transmitted more quickly than other strains, the need for vaccines is increasing day by day (Zhu et al., 2020). Especially in elderly patients, since the risk of mortality due to sub-diseases

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increases significantly, protection with vaccination has become inevitable (Chan et al., 2020).

Inactivated vaccines, recombinant spike protein vaccines, viral vector vaccines, RNA vaccines, live attenuated vaccines, and virus-like particle vaccines are the COVID 19 vaccines that are actively used worldwide (Sharma et al., 2020; Korang et al., 2020; Mohapatra et al., 2021). The effectiveness of actively used vaccines against COVID 19 is demonstrated by studies. Especially in the young population, the vaccine response is higher (Wang et al., 2021; Liu et al., 2021; Sharif et al., 2021; Frenck et al., 2021). The aim of this retrospective observational multicenter study is to examine the vaccination history of cases followed in the service or ICU due to COVID 19 and to analyze the clinical reflection of vaccinations.

2. MATERIALS AND METHODS

The research was carried out in three State Hospitals in the Ordu region from October 1, 2021 - January 7, 2022. A total of 400 cases were examined, by randomly selecting 200 cases from the pandemic services of the centers and 200 cases from the pandemic ICUs. All of the included cases have COVID-19 PCR positivity. Data were obtained from the hospital information management system (HIMS). Demographic characteristics, length of stay, comorbid conditions, vaccination status, intubation status, mortality status and laboratory values of the cases were recorded. The cases taken from the service to the ICU due to clinical worsening were examined in the ICU group. COVID-19 PCR negative cases, cases whose vaccine information could not be reached, and <18 years cases were excluded from the study. The cases who went to the clean service after the isolation period of 21 days while being followed up in the ICU, or the follow-up information of the cases who were discharged were included in the study. The service and ICU patients, those who died during their stay in the ICU and those who lived and those who had COVID 19 vaccine and those who were not, were compared.

Statistical analysis

Research findings were collected retrospectively from three centers and uploaded to the IBM SPSS v.26 package program. Mean and min-max values were given for quantitative variables, and numerical (percentage) values were given for qualitative variables. Differences between groups of categorical variables were tested using Fisher's exact and Pearson's Chi-square tests. For independent quantitative data not normally distributed, they were analyzed using the Mann-Whitney U test. A value of $p<0.05$ was considered significant.

3. RESULTS

The mean age (mean±SD) of all cases was (71.7±13.9). 50.2% (201) of the cases were male and 49.8% (199) were female. When the vaccination history of all cases was examined, 20.2% (81) of the patients were unvaccinated, 5.3% (21) had a single dose, 40.2% (161) had a double dose, and 34.3% (137) had three doses. Of the service patients, 114 (57%) had only sinovac vaccine, and 18 (9%) had only biontech vaccine. Of the ICU patients, 113 (56.5%) had only sinovac and 14 (7%) only biontech vaccine. Other patients had a combination of both vaccines. Mortality was observed in 137 (34.3%) of all cases. When service and ICU patients were compared; the age, comorbid conditions, length of stay, time from the last dose of vaccine to the disease and some laboratory values watched higher in ICU patients. The findings of the two groups are compared in Table 1.

Table 1 Comparison of Patients in the Service and ICU

Case	Service (n=200)	ICU (n=200)	p value
Age (Mean±SD)	68.2±14.5	75.2±12.4	0.000
Sex Male Female	 93 (%46.5) 107 (%53.5)	 108 (%54) 92 (%46)	 0.134
İntubation	0	127 (%63.5)	0.000
Presence of comorbid disease	176 (%88)	194 (%97)	0.001
COVID vaccine status Unvaccinated Vaccinated	 40 (%20) 160 (%80)	 41 (%20.5) 159 (%79.5)	 0.901
Time after last dose of vaccination (Mean±SD)	151.3±77	192.7±271.6	0.031
Length of Hospitalization (Mean±SD)	7.1±3.7	9.9±6.4	0.000

Laboratory values (Mean±SD)			
WBC (10^3/μL)	8.7±5	11.6±5.6	0.000
Hemoglobin (Hb) (g/dL)	12.2±2.2	11.9±2	0.110
Platelet (Plt) (10^3/μL)	218±104.9	226.4±102.1	0.232
Ne (10^3/μL)	6.9±4.6	10.3±5.3	0.000
Lymphocyte (Le) (10^3/μL)	1.2±0.7	0.8±0.8	0.000
Urea (mg/dl)	52.8±36.5	81.3±52.5	0.000
Creatinine (mg/dl)	1.1±0.7	1.5±1.1	0.000
Alanine aminotransferase (ALT) (U/L)	22.8±18	40.6±110.4	0.095
Aspartate Aminotransferase (AST) (U/L)	32.6±27.6	80.5±285.4	0.000
Gamma Glutamyl Transferase (GGT) (U/L)	37.5±47.4	40.9-31.4	0.042
Alkaline Phosphatase (ALP) (U/L)	99.8±221.2	83.4±46.3	0.132
C-Reactive Protein (CRP) (mg/dl)	120.7±82.2	133±96.3	0.433
D-dimer (ng/ml)	1194±1640	2288±2641	0.000
Ferritin (μg/L)	471.9±485	755.3±1045	0.000
CK-MB (ng/ml)	4.3±23.7	5.3±9	0.000
Troponin (ng/ml)	0.1±0.1	0.5±2.1	0.000

Mortality and survivors of 200 cases followed up in the ICU were compared among themselves. It was observed that intubation rate and mean age were higher in the mortal group. The findings of the two groups are summarized in Table 2. When the vaccinated and unvaccinated cases are compared among themselves; some laboratory values such as WBC, Ne and comorbidity rates were higher in vaccinated cases. In unvaccinated cases, it was observed that the average age at admission to the hospital was lower and ICU duration was longer. The findings of the two groups are summarized in Table 3.

Table 2 Comparison of Cases Survivors and Died in ICU

Case	Survivor, (n=64)	Died, (n=136)	p value
Sex Male Female	 40 (%62.5) 24 (%37.5)	 68 (%50) 68 (%50)	0.098
İntubation	13 (%20.3)	114 (%83.8)	0.000
Presence of comorbid disease	61 (%95.3)	133 (%97.8)	0.387
Age (Mean±SD)	72.3±12.9	76,6±11.9	0.023
Laboratory values (Mean±SD)			
WBC (10^3/μL)	10.8±4.9	12±5.8	0.213
Hb (g/dL)	11.9±2.1	12±2	0.889
Plt (10^3/μL)	235.1±104	222.4±101.3	0.540
Ne (10^3/μL)	9.3±4.6	10.7±5.6	0.106
Le (10^3/μL)	0.9±1	0.8±0.7	0.552
Urea (mg/dl)	81.4±48.5	81.2±54.4	0.878
Creatinine (mg/dl)	1.6±1.3	1.4±1.1	0.868
ALT (U/L)	27.1±30.7	47±131.9	0.215
AST (U/L)	31.4±26	103.1±343.2	0.000
GGT (U/L)	41.9±38.3	40.5±28.7	0.575
ALP (U/L)	84.7±52.3	82.8±43.9	0.654
CRP (mg/dl)	125±95.7	136.8±96.8	0.336
D-dimer (ng/ml)	2197±2801	2330±2574	0.127
Ferritin (μg/L)	622.7±549.3	819.4±1211.9	0.174
CK-MB (ng/ml)	4.7±9.7	5.5±8.5	0.062
Troponin (ng/ml)	0.3±0.9	0.6±2.5	0.049

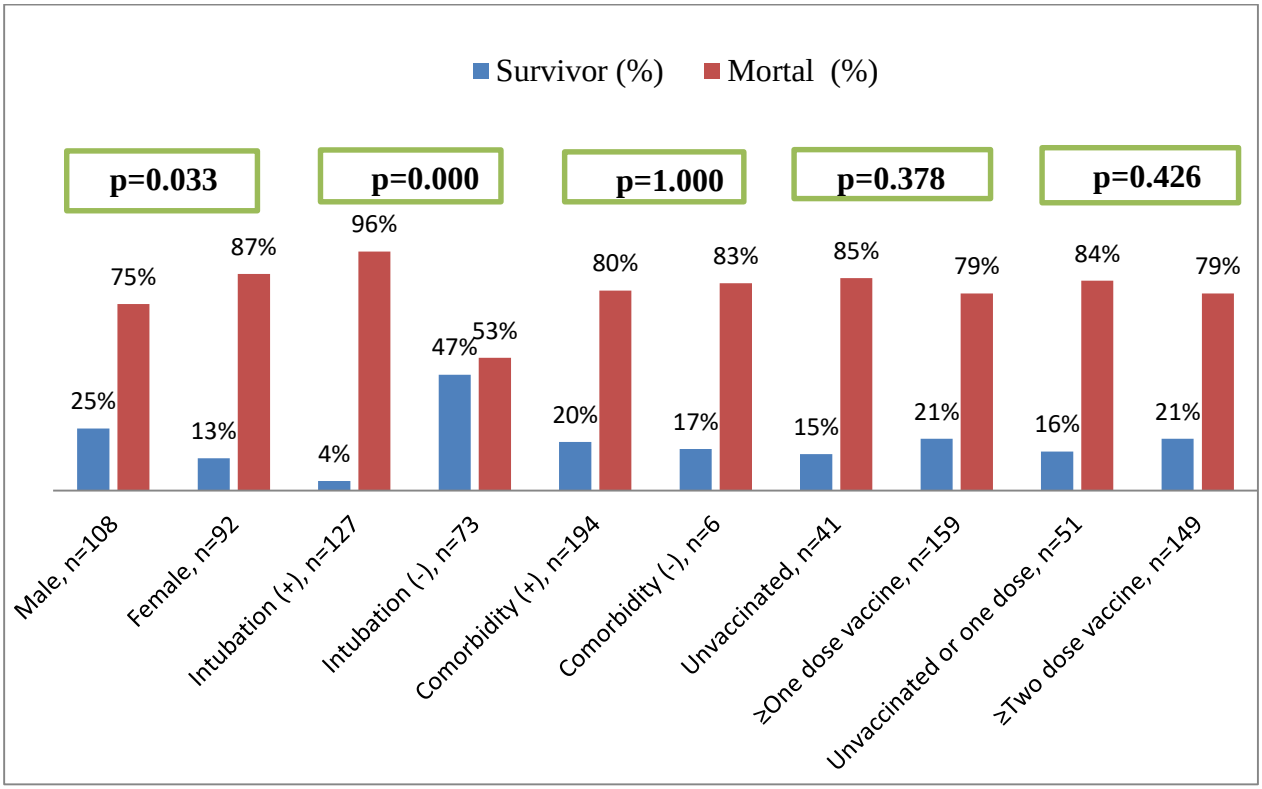
Table 3 Comparison of Unvaccinated and Vaccinated Cases

Case	Unvaccinated (n=81)	Vaccinated (n=319)	p value
Sex Male Female	 37 (%45.7) 44 (%54.3)	 164 (%51.4) 155 (%48.6)	0.357
Presence of comorbid disease	62 (%15.5)	308 (%84.5)	0.000
İntubation	31 (%38.3)	96 (%30.1)	0.158
Mortality	32 (%39.5)	105 (%32.9)	0.264
Age (Mean±SD)	63.5±17.5	73.8±12	0.000
Service length of stay (Mean±SD)	3.8±4.7	3.5±4.3	0.638
ICU length of stay (Mean±SD)	6.1±7.7	4.7±6.4	0.012
Laboratory values (Mean±SD)			
WBC (10^3/μL)	8.7±5.5	10.5±5.4	0.001
Hb (g/dL)	12.3±2.1	12±2.1	0.274
Plt (10^3/μL)	228.9±117.3	220.6±99.8	0.772
Ne (10^3/μL)	7.3±5.4	8.9±5.2	0.001
Le (10^3/μL)	0.9±0.6	1±0.8	0.932
Urea (mg/dl)	54.3±33.6	70.3±49.8	0.003
Creatinine (mg/dl)	1±0.6	1.4±1	0.002
ALT (U/L)	31.9±31.4	31.7±87.6	0.004
AST (U/L)	43-42	56.4±213.3	0.010
GGT (U/L)	52.6±59	35±37.3	0.002
ALP (U/L)	79.6±36.2	96.4-191.4	0.390
CRP (mg/dl)	121.6±98	128.2±87.5	0.251
D-dimer (ng/ml)	1861±2465	1737±2234	0.602
Ferritin (μg/L)	709.4±614.2	602.4±897.2	0.072
CK-MB (ng/ml)	3.4±3.8	5.2±18.5	0.864
Troponin (ng/ml)	0.2±0.4	0.4±1.8	0.622

The 60-day long-term prognosis of the cases followed in the ICU was evaluated. Mortality rate was found to be higher in female gender (p=0.033) and intubated cases (p=0.000). The mean age of the survivors and those who died was (71.1±12.9 and 76.2±12.1), respectively. In addition, the age was higher in mortal cases (p=0,034). The long-term prognoses of the cases are shown in Graph 1.

4. DISCUSSION

There have been many studies on the protection of COVID-19 vaccines in the world (Lu et al., 2008; Zhu et al., 2020; Sağlık Bakanlığı, 2021). In a study published in the UK between 8 December 2020 and 19 February 2021, the efficacy of single-dose Pfizer-BioNTech and Oxford-AstraZeneca vaccines against symptoms, emergency hospitalization and mortality in COVID 19 cases aged 70 and over was investigated. A single dose of both vaccines reduced hospitalizations with COVID-19 by 80%. It has also been reported that only one dose of Biontech vaccine is 85% effective in preventing mortality associated with COVID-19. Efficacy increased even more at the second dose (Bernal et al., 2021). Intermediate results reported during Phase III studies of the BioNTech and AstraZeneca vaccines were highly effective when administered at intervals of three and four weeks, respectively, between doses (Polack et al., 2020; Voysey et al., 2021). Using national surveillance data in Israel, the effect of Pfizer-BioNTech vaccine on hospitalization and mortality in cases aged 16 years and over was investigated. Two doses of Pfizer-BioNTech vaccine; It has been found to be highly effective in all age groups (including adults ≥16 years) in preventing hospitalization of COVID-19 patients with and without symptoms, serious illness, and death (Haas et al., 2021).



Graph 1 Long-Term Effects of Vaccines in the ICU

In another mini-review discussing the COVID-19 vaccines, 19 articles were reviewed. In the review of eleven vaccines, it was concluded that Oxford-AstraZeneca was 81% effective, Pfizer-BioNTech 95%, Moderna 94% and Sputnik V 92% effective (Doroftei et al., 2021). Sinovac is 65.9% effective for symptomatic cases. It is not a live vaccine, it is inactivated. Its side effects are quite limited (Duarte et al., 2021). A 75% antibody seroconversion was reported in the phase I study of the Sinovac vaccine in 144 subjects aged 18-59 years. Sinovac's Phase II study was conducted in 600 subjects and improved purification, resulting in efficacy >95%. In the Phase III study, seroversion increased to 100% and 97% with 2 doses between days 0 and 28 (Pijls et al., 2021; Zhang et al., 2021). In the interim data obtained from the Phase III studies of Sinovac in our country, an efficacy of 91.25% was reported (Turkey, 2020).

In our study, data were collected from three major centers in the Ordu region. When the vaccination history of all cases is examined, 20.2% of the cases are still unvaccinated and 5.3% are single-dose vaccines. When vaccinated cases and unvaccinated cases are compared; It was determined that the average age of admission to the hospital was higher and ICU duration was shorter in vaccinated cases. Mortality was 39.5% in unvaccinated cases, while it was 32.9% in vaccinated cases. But there was no significant difference. We think that the lack of significant difference in mortality is due to the higher mean age and comorbidity rate in vaccinated cases. The 60-day long-term mortality status of the cases followed in the ICU was evaluated. While the mean age and intubation rate were higher in mortal cases, there was no significant difference in COVID 19 vaccine doses.

There are different risk factors directly related to severity of illness and death in cases followed up in the ICU due to COVID 19. In a meta-analysis of 59 studies, the relationship of age and gender with ICU admission, severity of illness and death was evaluated. It has been observed that the male gender has more risks of COVID 19 than females. In addition, the direct relationship of severity of illness and death with male gender was shown. In the same study, the risk of infection, severity of illness and death were higher in cases aged 70 and over. In another study, in which data from 2491 adults hospitalized with laboratory-confirmed COVID-19 between March 1 and May 2, 2020 were analyzed, advanced age, immunosuppression, and presence of chronic disease were directly associated with mortality (Kim et al., 2021). In a similar study describing the clinical features and laboratory values of 201 patients with COVID-19 pneumonia who developed or died of acute respiratory distress syndrome (ARDS), comorbid conditions, ARDS, advanced age, neutrophilia, LDH and high D-Dimer were linked to a high death rate (Wu et al., 2020).

In our study, the cases followed in the service and ICU was compared among them. The rate of presence of comorbid conditions was substantially more in cases followed up in the ICU. In addition, the interval between the last vaccine dose and the disease was longer in ICU cases. When the laboratory values were compared, it was seen that the D-Dimer, Ferritin, CK-MB and Troponin

values were higher together with neutrophilia and lymphopenia in the cases in the ICU. In our study, patients who were followed up in the ICU with and without mortality were compared among themselves. It was observed that intubation rate and mean age were higher in mortal cases. Comorbid conditions and sexes were similar. Troponin from laboratory values was higher in mortal cases.

5. CONCLUSION

Sinovac and Biontech vaccines reduce hospital admissions due to COVID 19 in the younger age group, shorten the ICU duration and reduce the intubation rate. The number of comorbid conditions and advanced age are two factors that could potentially reduce vaccine efficacy. Neutrophilia, Lymphopenia, Troponin and D-Dimer elevation are important laboratory values that affect the prognosis during hospitalization. Intubation is directly related to mortality in ICU cases. According to our study, gender is not a factor that significantly affects vaccine effectiveness. ICU cases are older than service cases and comorbid conditions are more common. In addition, the length of hospital stay and the time after the last dose of vaccination are again longer in ICU cases.

Author Contributions

Ahmet DOĞAN; Corresponding author: Writing the article, collecting data, generating hypotheses, applying for ethical permission. Taliha KARAKÖK: Data collection, hypothesis generation, Final check of manuscript. Yakup GEZER: Statistical analysis of data, Final check of manuscript. Süleyman DEGERMENCİ: Data collection, Final control of the manuscript,

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Ethical approval

The study was approved by the Medical Ethics Committee of Ordu University (ethical approval code: 2022/21).

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW, Tsoi HW, Lo SK, Chan KH, Poon VK, Chan WM, Ip JD, Cai JP, Cheng VC, Chen H, Hui CK, Yuen KY. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020; 395(10223):514-523 doi: 10.1016/S0140-6736(20)30154-9.
2. Doroftei B, Ciobica A, Ilie OD, Maftei R, Ilea C. Mini-Review Discussing the Reliability and Efficiency of COVID-19 Vaccines. Diagnostics (Basel) 2021; 11(4):579 doi: 10.3390/diagnostics11040579.
3. Duarte LF, Gálvez NMS, Iturriaga C, Melo-González F, Soto JA, Schultz BM, Urzúa M, González LA, Vázquez Y, Ríos M, Berríos-Rojas RV, Rivera-Pérez D, Moreno-Tapia D, Pacheco GA, Vallejos OP, Hoppe-Elsholz G, Navarrete MS, Rojas Á, Fasce RA, Fernández J, Mora J, Ramírez E, Zeng G, Meng W, González-Aramundiz JV, González PA, Abarca K, Bueno SM, Kalergis AM. Immune Profile and Clinical Outcome of Breakthrough Cases After Vaccination With an Inactivated SARS-CoV-2 Vaccine. Front Immunol 2021; 12:742914 doi: 10.3389/fimmu.2021.742914.
4. Frenck RW Jr, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, Perez JL, Walter EB, Senders S, Bailey R, Swanson KA, Ma H, Xu X, Koury K, Kalina WV, Cooper D, Jennings T, Brandon DM, Thomas SJ, Türeci Ö, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. N Engl J Med 2021; 385(3):239-250 doi: 10.1056/NEJMoa2107456.
5. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, Brooks N, Smaja M, Mircus G, Pan K, Southern J,

Swerdlow DL, Jodar L, Levy Y, Alroy-Preis S. 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):1819-1829 doi: 10.1016/S0140-6736(21)00947-8.

6. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. WHO TEAM. 6 January 2022. Emergency Situational Updates.
7. Kim L, Garg S, O'Halloran A, Whitaker M, Pham H, Anderson EJ, Armistead I, Bennett NM, Billing L, Como-Sabetti K, Hill M, Kim S, Monroe ML, Muse A, Reingold AL, Schaffner W, Sutton M, Talbot HK, Torres SM, Yousey-Hindes K, Holstein R, Cummings C, Brammer L, Hall AJ, Fry AM, Langley GE. Risk Factors for Intensive Care Unit Admission and In-hospital Mortality Among Hospitalized Adults Identified through the US Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET). Clin Infect Dis 2021; 72(9):e206-e214 doi: 10.1093/cid/ciaa1012.
8. Korang SK, Juul S, Nielsen EE, Feinberg J, Siddiqui F, Ong G, Klingenberg S, Veroniki AA, Bu F, Thabane L, Thomsen AR, Jakobsen JC, Gluud C. Vaccines to prevent COVID-19: a protocol for a living systematic review with network meta-analysis including individual patient data (The LIVING VACCINE Project). Syst Rev 2020; 9(1):262 doi: 10.1186/s13643-020-01516-1.
9. Liu Q, Qin C,Liu M, Liu J. Efectiveness and safety of SARS-CoV-2 vaccine in real-world studies: a systematic review and meta-analysis. Inf Dis Povert 2021; 10:132 https://doi.org/10.1186/s40249-021-00915-3.
10. Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, Simmons R, Cottrell S, Roberts R, O'Doherty M, Brown K, Cameron C, Stockton D, McMenamin J, Ramsay M. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021; 373:n1088 doi: 10.1136/bmj.n1088.
11. Lu Z, Kou W, Du B, Wu Y, Zhao S, Brusco OA, Morgan JM, Capuzzi DM. Chinese Coronary Secondary Prevention Study Group, Li S. Effect of Xuezhikang, an extract from red yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction. Am J Cardiol 2008; 101(12):1689-93 doi: 10.1016/j.amjcard.2008.02.056.
12. Mohapatra TK, Nayak RR, Mondal A, Nanda SS. A novel and Emerging Coronavirus Infection: Repurposing and Scale of Advances of Therapeutics, Immunotherapeutics and Vaccine Development. Drug Discov 2021;15(35):06-33
13. Pijls BG, Jolani S, Atherley A, Derckx RT, Dijkstra JIR, Franssen GHL, Hendriks S, Richters A, Venemans-Jellema A, Zalpuri S, Zeegers MP. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. BMJ Open 2021; 11(1):e044640 doi: 10.1136/bmjopen-2020-044640.
14. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020; 383(27):2603-2615 doi: 10.1056/NEJMoa2034577.
15. Sharif N, Alzahrani KJ, Ahmed SN, Dey SK. Efficacy, Immunogenicity and Safety of COVID-19 Vaccines: A Systematic Reviewand Meta-Analysis. Front Immunol 2021; 12:714170 doi: 10.3389/fimmu.2021.714170.
16. Sharma O, Sultan AA, Ding H, Triggle CR. A Review of the Progress and Challenges of Developing a Vaccinefor COVID-19. Front Immunol 2020; 11:585354 doi: 10.3389/fimmu.2020.585354
17. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü. COVID-19 (SARS-CoV-2 Enfeksiyonu) Temaslı Takibi, Salgın Yönetimi, Evde Hasta İzlemi ve Filyasyon (2 Ekim 2021). https://covid19.saglik.gov.tr/Eklenti/41623/0/covid-19rehberitemaslitakibievdehastaizlemivefilyasyon-021021pdf.pdf
18. Turkey says China's Sinovac COVID vaccine 91.25% effective in late trials. Reuters [Internet] 2020; Available from: https://www. reuters.com/article/health-coronavirus-turkey-chinaint-idUSKBN28Y1R3.
19. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, Angus B, Baillie VL, Barnabas SL, Bhorat QE, Bibi S, Briner C, Cicconi P, Collins AM, Colin-Jones R, Cutland CL, Darton TC, Dheda K, Duncan CJA, Emary KRW, Ewer KJ, Fairlie L, Faust SN, Feng S, Ferreira DM, Finn A, Goodman AL, Green CM, Green CA, Heath PT, Hill C, Hill H, Hirsch I, Hodgson SHC, Izu A, Jackson S, Jenkin D, Joe CCD, Kerridge S, Koen A, Kwatra G, Lazarus R, Lawrie AM, Lelliott A, Libri V, Lillie PJ, Mallory R, Mendes AVA, Milan EP, Minassian AM, McGregor A, Morrison H, Mujadidi YF, Nana A, O'Reilly PJ, Padayachee SD, Pittella A, Plested E, Pollock KM, Ramasamy MN, Rhead S, Schwarzbold AV, Singh N, Smith A, Song R, Snape MD, Sprinz E, Sutherland RK, Tarrant R, Thomson EC, Török ME, Toshner M, Turner DPJ, Vekemans J, Villafana TL, Watson MEE, Williams CJ, Douglas AD, Hill AVS, Lambe T, Gilbert SC, Pollard AJ; Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine

(AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021; 397(10269):99-111 doi: 10.1016/S0140-6736(20)32661-1.

20. Wang C, Horby PW, Hayden FG, Gao GF. A Novel Coronavirus Outbreak of Global Health Concern. Lancet 2020; 395:470–73 doi: 10.1016/S0140-6736(20)30185-9
21. Wang J, Tong Y, Li D, Li J, Li Y. The Impact of Age Difference on the Efficacy and Safety of COVID-19 Vaccines: A Systematic Review and Meta-Analysis. Front Immunol 2021; 12:758294. doi: 10.3389/fimmu.2021.758294.
22. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020; 180(7):934-943. doi: 10.1001/jamainternmed.2020.0994.
23. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, Han W, Chen Z, Tang R, Yin W, Chen X, Hu Y, Liu X, Jiang C, Li J, Yang M, Song Y, Wang X, Gao Q, Zhu F. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis 2021; 21(2):181-192 doi: 10.1016/S1473-3099(20)30843-4.
24. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, Lei F, Wang H, Xie J, Wang W, Li H, Zhang P, Song X, Chen X, Xiang M, Zhang C, Bai L, Xiang D, Chen MM, Liu Y, Yan Y, Liu M, Mao W, Zou J, Liu L, Chen G, Luo P, Xiao B, Zhang C, Zhang Z, Lu Z, Wang J, Lu H, Xia X, Wang D, Liao X, Peng G, Ye P, Yang J, Yuan Y, Huang X, Guo J, Zhang BH, Li H. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. Cell Metab 2020; 31(6):1068-1077.e3 doi: 10.1016/j.cmet.2020.04.021.
25. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020; 382(8):727-733 doi: 10.1056/NEJMoa2001017.