Research Article

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A Three Years Retrospective Study Of Covid-19 Patients And Cases Admitted At A Tertiary Greek Hospital

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1. Abstract:

1.1 Introduction:
The novel coronavirus SARS-CoV-2 was detected in December 2019 in Wuhan, China, and rapidly spread all over the world. It causes COVID-19 disease and WHO on 11 March 2020 declared the outbreak as a pandemic. Health care systems, the hospitals, the trade, the national economies, all aspects of human life and the societies globally faced an unexpected "earthquake" due to the asynchronous threat that had to deal with, unprepared for such situation.

1.2. Aim of the study:
The aim of our study was t to investigate the potential correlation between RT-PCR for SARS-CoV-2 results and Rapid Test results, with demographic characteristics, etiology for hospital admission, travel history, vaccination and number of vaccination doses in patients that were admitted to a tertiary care hospital and to examine a mathematical formula that might describe the correlation of the aforementioned parameters.

1.3. Material:
The population under study consisted of 2791 male and female patients who were admitted at the Emergency Department and the Pathology Department of Nikea General Hospital "Agios Panteleimon", Piraeus, Greece.

1.4. Results:
In our study we observed statistically significant correlation of both Rapid Test result and RT-PCR result with etiology for hospital admission, travel history, contact with a confirmed case and hospitalization. Relying on the descriptive statistics we observe that men were mostly affected by SARS-CoV-2. Neither of the two tests (RT-PCR and Rapid Test) correlated with patient gender or specimen type. RT-PCR positive results are slightly greater at January 2022, December 2022 and July and August 2022. As regards with the vaccination, only RT-PCR result is correlated with vaccination (yes/no). It was also observed that the cycles ORF1ab and N genes correlate with etiology of admission and pneumonia, while cycles N gene correlate additionally and with other diseases.

2. Key words:
SARS-VoV-2, COVID-19, pandemic, RT-PCR, Rapid Test, CTs

3. Introduction:

COVID-19 disease, leading to a worldwide pandemic, is caused by SARS-CoV-2 virus (Severe Acute Respiratory Syndrome Coronavirus-2) [1,2]. The impact of the ongoing pandemic to healthcare systems and public health worldwide dramatically increased the morbidity and mortality rates of the patients. Numerous vaccines have been developed in the past three years, thus providing increased immunity against the disease. Two COVID-19 mRNA vaccines were developed by Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273). Moreover, two viral vector vaccines were developed by Johnson & Johnson/Janssen (Ad26.COV2.S) and AstraZeneca (ChAdOx1 nCov-19). These four vaccines were the most widely applied worldwide and were approved by both the FDA (U.S. Food and Drug Administration) and EMA (European Medicines Agency) organizations. The effectiveness of those vaccines has been continuously evaluated and raised a lot of concerns due to emergence of several virus mutations [3,4,5]. The present study aimed to study the patients that were admitted to a tertiary care hospital and to investigate the potential correlation between RT-PCR for SARS-CoV-2 results and Rapid Test results, with demographic characteristics, etiology for hospital admission, travel history, vaccination and number of vaccination doses. Moreover, it aimed to examine a mathematical formula that might describe the correlation of the aforementioned parameters.

4. Aim Of The Study:

The aim of our retrospective study was to investigate any correlation of positive RT-PCR results for the SARS-CoV-2 virus causing COVID-19 disease with patient demographics (sex, age), contact with a confirmed COVID-19 case, recent travel history, vaccination and vaccine doses, rapid test results, disease (yes or no), hospitalization (in ward, or ICU, with or without mechanical support), etiology for hospital admission (from the ICU, inpatient clinics, for preoperative testing, or other reasons), hospitalization and genes' Cts. Moreover, we aimed to highlight the association of positive samples during the pandemic waves of COVID-19 and during the conducted time period under study.

5. Materials And Methods:

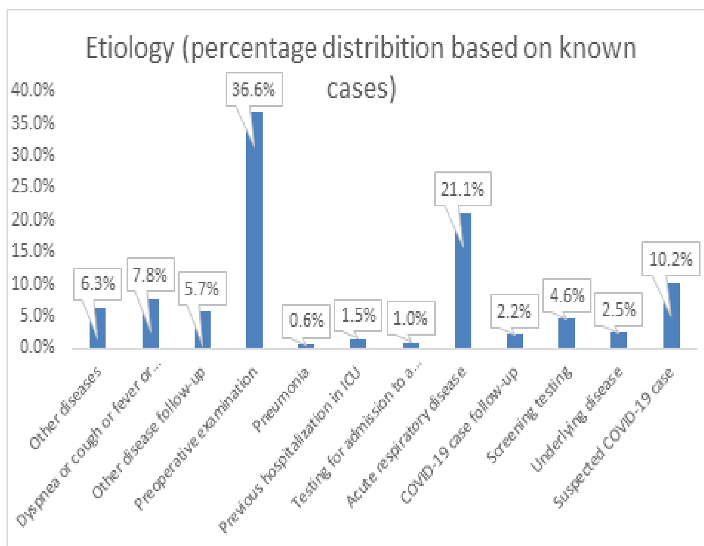
The population under study consisted of 2791 male and female patients who were admitted at the Emergency Department and the Pathology Department of Nikea General Hospital "Agios Panteleimon", Piraeus, Greece. All patients were informed about the study and gave their consent. The study was approved by the Hospital's Ethics Committee and carried out according to the Declaration of Helsinki. On admission, data as regards to the patients were collected from the referral notes and extracted from the Hospital Information System. Data were collected between December 2021 and January 2023. Real-time RT-PCR for SARS-CoV-2 tests were performed on Xiamen Zeesan Sanity 2.0 System, a fully automated and integrated molecular diagnostic platform. Nasopharyngeal, oropharyngeal or BAL samples from patients admitted to various departments of the hospital were tested within 3 hours for the presence of SARS-CoV-2 nucleocapsid gene (N) and open reading frame 1ab (ORF1ab) gene. To prevent PCR inhibition, synthetic swabs and 3 ml Citoswab Microbiology Transport Media, manufactured by Citotest Labware Manufacturing were used. BAL samples were pre-treated using 10ml water for injection. Before inserting the samples into the extraction cartridge, 30s vortexing was conducted. Then 1000uL and 500uL swab and BAL sample accordingly, were transferred into the lysis buffer of the extraction cartridge. Next, the extraction cartridge as well as the PCR reagents were inserted into Sanity 2.0 System, which uses magnetic particle method for the RNA extraction and multiplex TaqMan probe-base one-step real-time RT-PCR for target amplification and detection. PCR result interpretation was carried out automatically by instruments' software. Cutoff Ct for positive samples was 31 and 33 for N and ORF1ab gene respectively. In all samples, RNAse P was used as internal control to distinguish false negative results. The sensitivity of the test was 200 copies/ml. The study was conducted in the molecular laboratory of the hospital that is under Schem EQA (Lab Scala) quality control.

6. Results:

The study included 2791 patients, 1561 (55,9 %) male and 1216 (43,6 %) female. In 14 cases (0,5%) patient gender was not recorded in the referral form, due to administrative nonconformity. Patients were asked if they had a recent travel history. Only 31 patients (1,1 %) confirmed to have a recent travel history, 732 patients (26,2 %) did not have a recent travel history, while in 2028 cases (72,7%) information about travel history was missing, because these patients were admitted form mental health centers and nursing homes. However, due to their medical condition we as assume that they were not able to travel. Patients were asked if they had contact with a confirmed COVID-19 case. Among them, 157 (5,6%) patients had contact with a confirmed COVID-19 case and 450 patients (16,1%) did not have any contact with a confirmed COVID-19 case. Moreover, information about contact with a confirmed case for 2184 patients (78,3%) was missing, because these patients were admitted form mental health centers and nursing homes.

Etiology for hospital admission, as recorded in the referral note, included fever, cough and/or dyspnea (6,6%), preoperative examination (31,0%), pneumonia (0,5%), underlying disease (2,1%), acute respiratory disease (17,8%), testing for admission to a nursing home according to national guidelines (0,8%), screening testing for professional reasons (3,9%), suspected COVID-19 case (8,6%), COVID-19 case follow-up (1,8%) and other disease follow-up (4,8%), other diseases, such as orthopedic, digestive, neurologic and heart disease (5,4%), as well as previous hospitalization in ICU (1,3%). In 427 (15,3%) cases etiology for hospital admission was missing due to administrative nonconformity, (Figure 1). Rapid tests were performed for 2478 patients. Among them 2175 patients (77,9%) were negative, and 303 patients were positive (10,9%). For 313 patients Rapid tests were not performed, due to economic constraints in healthcare expenses.

Figure 1: Etiology distribution (percentage distribution based on known cases only)



RT-PCR for SARS-CoV-2 test was performed for all patients. Out of them, 2080 (74,5%) patients had a negative PCR result, 611 (21,9%) had a positive PCR result and 94 (3,4%) had a weak positive result. Invalid test results were recorded on 6 (0,2 %) cases and are attributed to inappropriate

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sample quality. The majority of RT-PCR tests (2708 tests, 97,0%) were performed in nasopharyngeal specimens, 72 (2,6%) were performed in bronchoalveolar lavage and 11 (0,4%) in oropharyngeal specimens. Out of the patients under study, 1511 (54,4%) were not hospitalized, 1217 (43,8%) were hospitalized and 51 (1,9%) were admitted to the ICU. We performed a chi-square of independence test to observe if RT-PCR result is correlated with any of the following parameters: etiology for hospital admission, gender, travel history, contact with a confirmed case, rapid test result, specimen type and hospitalization. RT-PCR result is correlated with etiology for hospital admission (p-value < 2.2e-16), travel history (p-value = 0.0006035), contact with a confirmed case (p-value < 2.2e-16), rapid test result (p-value < 2.2e-16) and hospitalization (p-value=0.04044). RT-PCR result is not correlated with gender (p-value=0.797) or with specimen type (p-value=0.7042). Out of the patients under study, 2198 (78,7%) were vaccinated with different vaccines. The data are presented in Table 1.

Table 1: Vaccine type, relevant frequencies and percentages

FREQUENCIES OF VACCINE TYPE		
Row Labels	**FREQUENCY**	**PERCENTAGE**
ASTRA ZENEKA	4	0.20%
JOHNSON	47	2.10%
JOHNSON+PFIZER	1	0.00%
MODERNA	169	7.70%
PFIZER	1960	89.20%
PFIZER+ MODERNA	1	0.00%
NOT RECORDED IN THE REFERRAL NOTE	16	0.70%
TOTAL	2198	100%

Moreover, the patients had received from 1 to 5 vaccination doses. The data are presented in Table 2.

Table 2: Vaccine doses, relevant frequencies and percentages

VACCINE DOSES		
Doses	**FREQUENCIES**	**PERCENTAGE**
1	102	4.60%
2	411	18.70%
3	1499	68.20%
4	152	6.90%
5	34	1.50%
TOTAL	2198	100%

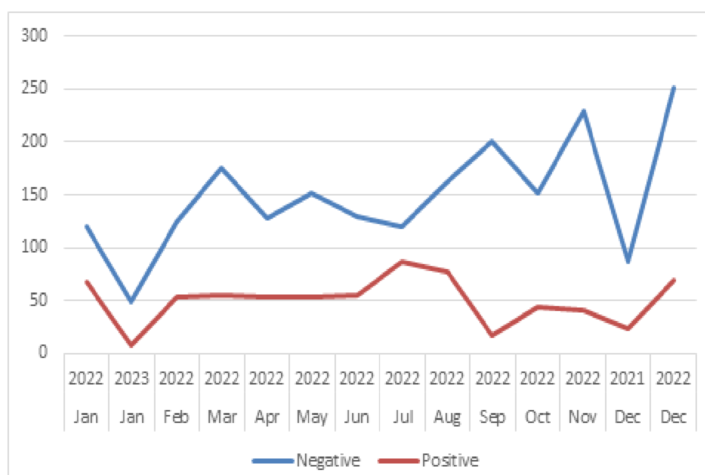
We performed a chi-square of independence test to observe if RT-PCR result is correlated with any of the following parameters: vaccination, vaccine type and vaccination doses. RT-PCR result is correlated with vaccination (p-value =0.002924). RT-PCR result is not correlated with vaccine type (p-value = 0.07989) or with number of vaccination doses (p-value = 0.2427). We performed an independent t-samples test to investigate whether there is any statistical significant difference of the mean age on the RT-PCR result (see table 3).

Table 3: Mean and Standard deviation of age for each PCR Result

PCR_RESULT	Frequency	Mean Age	Standard Deviation
Negative	1822	60.012	20.733
Positive	619	63.635	21.988
Unknown	3	67.667	12.097

Mean age of patients with a negative RT-PCR result was 60,01years, while mean age of patients with positive RT-PCR-result was 63,63 years. The difference between the two groups is statistically significant (p-value = 0.0003433). All RT-PCR tests were performed from December 2021 to January 2023, as presented in Figure 2. As seen in this figure, the number of positive test results seem not to be changed throughout the months. Positive results are slightly greater at January 2022, December 2022 and July and August 2022. We are seeing also a pick in the negative results for March 2022, May 2022, September 2022 November 2022 as well as December 2022. These were the months with the greater number of tests conducted. Also we can see that during July and August 2022, although we had a relative large number of positive results, the number of tests conducted seem not to be so much (at least for July 2022). We performed a chi-square of independence test to observe if Rapid Test result is correlated with any of the following parameters: etiology for hospital admission, gender, travel history, contact with a confirmed case, specimen type and hospitalization.

Figure 2: Distribution of PCR tests with negative and positive results per month. Blue line represents negative samples and orange line positive samples.



Rapid Test result is correlated with etiology for hospital admission (p-value < 2.2e-16), travel history (p-value = 0.006603), contact with a confirmed case (p-value < 2.2e-16) and hospitalization (p-value=0.01777).

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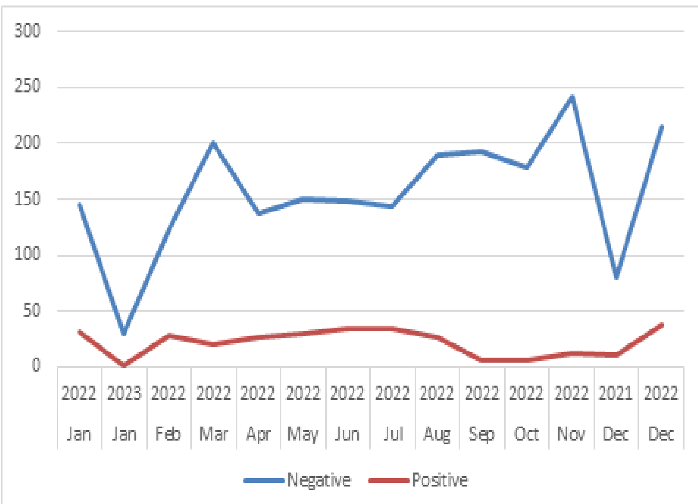
Rapid Test result is not correlated with gender (p-value = 0.4962) or with specimen type (p-value = 0.3696). Moreover, Rapid Test result is not correlated with vaccination (p-value = 0.05961), vaccine type (p-value = 0.9483) and vaccine doses (p-value = 0.06628). Distribution of Rapid Test results are presented in Figure 3. The view is more or less the same as the one we had with RT-PCR results (figure 2). However, here we can also observe a greater number of negative tests as compared to the RT-PCR ones that is generally high for all 2022. The picks are the same as we had with PCR tests.

Figure 3: Distribution of Rapid Test results during the time period under study. Blue line represents negative samples and orange line positive samples.



Mean age of positive patients was 57,75 years, while mean age of negative patients was 62,76 years. The difference between the two groups is statistically significant (p-value = 1.634e-06). Moreover, Rapid Test result is not correlated with gender (p-value = 0.1139). In this study we also examined the relationships between CYCLE ORF 1ab gene and CYCLE N GENE with etiology and vaccination dose. This examination was performed using Analysis of Variance. Specifically, in table 4 below we can see the results for the analysis of variance of CYCLE ORF 1ab gene as compared between the etiology grouped values.

Table 4: Anova results for CYCLE ORF 1ab gene between etiology groups.

	Df	DSum SQ	Mean SQ	F Value	Pr(>F)
Etiology	11	2020	183.60	3.69	0.000241
Residuals	521	29260	56.16		

Seems there is a statistically significant difference between the mean of CYCLE ORF 1ab gene as compared to the different etiology groups. According to the statistics presented in Table 5, Other diseases as well as Pneumonia do have the larger mean CYCLE ORF 1ab gene amongst the different level for Etiology.

Table 5: Means and Standard Deviations for CYCLE ORF 1ab gene between the etiology groups.

Etiology	Count	Mean	SD
Other diseases	150	29,56292	4,767713
Dyspnea or cough or fever or other COVID-19 related	185	24,73444	7,305803
Other disease follow-up	135	24,04889	6,527254
Preoperative examination	866	25,99419	7,887138
Pneumonia	14	27,475	8,896627
Previous hospitalization in ICU	35	24,38333	5,328289
Testing for admission to a nursing home	408	23,20512	8,127504
Acute respiratory disease	51	24,295	5,894491
COVID-19 case follow-up	108	21,52259	5,828136
Screening testing	58	24,12438	7,624072
Underlying disease	241	22,20953	7,698173
Suspected COVID-19 case	427	25,43451	7,588138

Additionally, the same view we are having for CYCLE_N_GENE also. According to the ANOVA Results (F= 4189 p.value<0.001), CYCLE_N_GENE is having significantly different mean values between the levels of etiology. Likewise the mean values for CYCLE ORF 1ab gene, the mean values for CYCLE_N_GENE are greater for Other diseases as well as Pneumonia. Furthermore, both the levels for CYCLE_N_GENE and for CYCLE ORF 1ab gene seems not to affected by the vaccination dose (F=0.348 with p-value=0.85 (CYCLE_N_GENE) and F=0.71 with p-value=0.58 (CYCLE ORF 1ab gene) Lastly, we fitted a logistic regression model to model the probability of hospitalization and controlling for this model all the other measuring variables.

The fitted model had the form:

logit(p)=0.03-0.01 Age +0.46 Vaccination - No-1.79 *Dyspnea or cough or fever or other COVID-19 related symptoms-1.26 * Acute respiratory disease -3.61 *Screening testing -1.25 Underlying disease - 1,5 * Suspected COVID-19 case. In summary among the measuring variables, we had provided during the fitting of the model, only the vaccination (baseline level YES), the Age and Etiology (baseline level other diseases) were came significant as of driving the probability for hospitalization. Interpretation of the above estimating logit equation brings us to the following notes:

1. The odds ratio for the probability of hospitalization for the change in age is equal to exp(-0.01)=0.99 when age is increasing for 1 year as compared to the odds of hospitalization for a person 1 year younger.
2. The odds ratio for the probability of hospitalization given that the person has not done the vaccine related to the odds of hospitalization when the person is having had the vaccine is exp(0.46)=1.58. This means that a person that has not done the vaccine is having 58% larger odd of hospitalization as related to the odd of a person that has done the vaccine.
3. exp (-1.79) =0.167 is the odds ratio for the probability of hospitalization given that the patient is having Dyspnea or cough or

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fever or other COVID-19 related symptoms as related to the odds ratio for hospitalization when the patient is having other diseases. This means that a patient that is having Dyspnea or cough or fever or other COVID-19 related symptoms has 83% smaller odds for hospitalization when this is compared to the odds of hospitalization for a patient that is having other diseases

4. exp (-1.26) =0.284 is the odds ratio for the probability of hospitalization given that the patient is having acute respiratory disease relative to the odd of hospitalization when the patient is having other diseases. In other words, a patient with acute respiratory disease is having 71% smaller odds for the probability of hospitalization when this is compared to the odd of hospitalization for a patient that is having other diseases.
5. Furthermore, exp (-1.25) =0.287 is the odds ratio for the probability of hospitalization given that the patient is having underlying diseases as related to the odds for hospitalization when the patient is having other diseases. In other words, a patient with underlying diseases is having 71% smaller odds for hospitalization as compared to the odds for a patient who is having other diseases.
6. Lastly, exp (-1.5) =0.22 is the odds for the probability of hospitalization given that the patient is suspected to have COVID-19, as compared to the odds for hospitalization when the patient is having other diseases. This means that the patient who is suspected to have COVID-19 is having 78% smaller odds for hospitalization as compared to the patient who is having other diseases.

Generally, as we can see from the output of the logistic model, a person who is having other disease is having a greater probability for hospitalization. This is also valid for a person who had not done the vaccine. As a conclusion we can say that we have not seen great probability for hospitalization for a person having symptoms for COVID-19, or underlying diseases or even acute respiratory disease. This means that the patients of our sample are mainly hospitalized due to having other diseases, and not due to any COVID-19 related symptoms, etc.

7. Discussion:

The new COVID-19 disease pandemic, caused due to infection by SARS-CoV-2 had serious consequences in all aspects of life, as well as in healthcare delivery worldwide. The pandemic has led to an unprecedented increase in the number of patients admitted to the hospitals and as soon as its early detection in the city of Wuhan, China, the need for effective and appropriate laboratory tests emerged [6, 7, 8]. Those tests, such as Rapid Test and RT-PCR test are very useful tools for the control of the disease and for patient monitoring, as well as for screening at the emergency department of hospitals [9]. In the present study we examined 2791 patients admitted in a tertiary care hospital in Greece and tried to evaluate the potential correlation between RT-PCR and Rapid Test results with demographic characteristics, etiology for hospital admission, travel history, vaccination and number of vaccination doses. Moreover, we tried to estimate a mathematical relation that describes the correlation of these parameters by means of ANOVA and logistic regression. In our study we observed statistically significant correlation of both Rapid Test result and RT-PCR result with etiology for hospital admission, travel history, contact with a confirmed case and hospitalization. Neither of the two tests was correlated with patient gender or specimen type [10,11,12,13,14,15,16]. Rapid Tests were found negative in 77,9%, that approximately correlates to the negative 74,5% RT-PCR tests [17,18]. The positive RT-PCR results were found in 21,9% and 3,4% weak positive, while positive Rapid Test was 10,9%, that leads to the so far well-known conclusion that molecular techniques represent the gold standard for the detection of viral genome [17,19, 22]. As regards with the vaccination, only RT-PCR result is correlated with vaccination (yes/no). Vaccine type or number of vaccination doses are not correlated with any of the two parameters [15, 23]. It was observed that the cycles ORF1ab and N genes correlate with etiology of admission and pneumonia, while cycles N gene correlate additionally and with other diseases [10, 20, 25]. Relying on the descriptive statistics we observe that men were mostly affected by SARS-CoV-2 [10,11,12,16]. No recent travel history was reported from the majority of patients, which correlates to the restricted measures and the decreased number of travelers [13]. This study has some limitations; first due to the heavy workload of the hospital on duty days, many referral forms had missing data and consequently the statistical analysis was difficult. Second, the data collection has not been designed as a prospective research tool but was based on review of medical files and referral notes a posteriori.

8. Conclusion:

The sudden and unexpected pandemic of COVID-19 left in its wake a wealth of research and clinical experience and useful tools for health care systems to use in order to be ready for future health crises. The COVID-19 pandemic appeared to affect preferentially men, aged people >55 years old with underlying diseases, causing severe pneumonia and increased mortality. Hospitals faced an urgent need for extension of intensive care departments, expenses for hospitalization of COVID-19 patients and medicaments, along with those for reagents and apparatus. The applied measures, lockdowns, transportation, traveling abroad and the vaccination programs aimed the limitation of coronavirus transmission.

9. Authors' contribution:

Antonia Mourtzikou conceived and designed the study, wrote the initial and final drafts of the article, and supervised the study. Antonia K. Korre statistically analyzed and interpreted the extracted data. Marilena Stamouli organized the data and contribute to manuscript editing. Antonia Mourtzikou, Panagiotis Koumpouros and Christina Seitopoulou carried out the RT- PCR tests. Georgia Kalliora provided research scope and literature references. Elpida Toka provided scientific and logistic support. Sofia Kasidiaraki collected the specimens, carried out the Rapid Tests, the data collection details. Maria Kimouli contributed to the project administration.

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References:

1. WHO Director-General's opening remarks at the media briefing on COVID-19-11 n.d. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-March 2020 19---11-march-2020N.
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020; 382(8):727-733. http://dx.doi.org/10.1056/NEJMoa2001017.
3. Fabiani M, Puopolo M, Morciano C, et al. Effectiveness of mRNA vaccines and waning of protection against SARS-CoV-2 infection and severe covid-19 during predominant circulation of the delta variant in Italy: retrospective cohort study. BMJ 2022; 376: e069052.
4. Thompson MG, Natarajan K, Irving SA, et al. Effectiveness of a Third Dose of mRNA Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance - VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal Wkly Rep 2022;71(4):139–45.
5. Naranbhai V, Garcia-Beltran WF, Chang CC, et al. Comparative immunogenicity and effectiveness of mRNA-1273, BNT162b2 and Ad26.COV2. S COVID-19 vaccines. J Infect Dis. 2021; jiab593
6. Pollard CA, Morran MP, Nestor-Kalinoski AL. The COVID-19 pandemic: a global health crisis. Physiol Genomics. 2020, 52(11):549-557. doi: 10.1152/physiolgenomics.00089.2020.
7. Hermann, B., Benghanem, S., Jouan, Y. et al. The positive impact of COVID-19 on critical care: from unprecedented challenges to transformative changes, from the perspective of young intensivists. Ann. Intensive Care, 2023, 13(28). https://doi.org/10.1186/s13613-023-01118-9
8. Myers LC, Liu VX. The COVID-19 Pandemic Strikes Again and Again and Again. JAMA Netw Open. 2022, 5(3):e221760. doi:10.1001/jamanetworkopen.2022.1760
9. Mourtzikou A, Tsiftsis D, Agrogianni M, Kasimatis N, Anthoula Dritsa A, Stamouli M, et al. A Synchronous Blind Test and Methodological Comparison Between Colloidal Gold Rapid Test vs RT-PCR For Sars-Cov-2 Detection. European Journal of Biomedical Research. 2022, 1(5). doi.org/10.24018/ejbiomed.2022.1.5.26
10. Percivale I., Danna P S C, Falaschi Z , Berardo S, Gangi S, Tricca S, et al. Men and women affected by Sars-CoV-2 pneumonia: same CT features but different outcome. Clin Radiol. 2021, 76(3):235.e25-235.e34.
11. Dubin JM, Bennett NE, Halpern JA. The adverse impact of COVID-19 on men's health. Curr Opin Urol. 2022, 32(2):146-151.
12. Conti P, Younes A. Coronavirus COV-19/SARS-CoV-2 affects women less than men: clinical response to viral infection. J Biol Regul Homeost Agents. 2020, 34(2):339-343.
13. Linka K, Peirlinck M, Costabal FS, Kuhl E. Outbreak dynamics of COVID-19 in Europe and the effect of travel restrictions. Comput Methods Biomech Biomed Engin. 2020, 23(11):710-717.
14. Shallie PD, Haffejee F. 100 DAYS OF COVID-19: RISK FACTORS AND CONFIRMED CASES IN 19 AFRICAN COUNTRIES. Afr J Infect Dis. 2021, 15(2):31-35.
15. Singanayagam A, Hakki S, Dunning J, Madon KJ, Crone MA, Koycheva A, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. Lancet Infect Dis. 2022, 22(2):183-195.
16. Statsenko Y, Al Zahmi F, Habuza T, Almansoori TM, Smetanina D, Simiyu GL, et al. Impact of Age and Sex on COVID-19 Severity Assessed From Radiologic and Clinical Findings. Front Cell Infect Microbiol. 2022, 11:777070. DOI: 10.3389/fcimb.2021.777070.
17. Fekete T. In adults and children in the ED with COVID-19 symptoms or a confirmed contact, a rapid POC antigen test had ≥72% sensitivity and ≥99% specificity vs. RT-PCR. Ann Intern Med. 2021, 174(7):JC83.
18. Möckel M, Corman VM, Stegemann MS, Hofmann J, Stein A, Jones TC, et al. SARS-CoV-2 antigen rapid immunoassay for diagnosis of COVID-19 in the emergency department. Biomarkers. 2021, 26:213-20.
19. Al-Hashimi OTM, Al-Ansari WIA, Abbas SA, Jumaa DS, Hammad SA, Hammoudi FA, Allawi AAD. The sensitivity and specificity of COVID-19 rapid anti-gene test in comparison to RT-PCR test as a gold standard test. J Clin Lab Anal. 2023, 37(3):e24844.
20. Mourtzikou A, Korre A, Stamouli M, Seitopoulou C, Petraki I, Kalliora G, et al. Suspected COVID-19 Cases Admitted in a Tertiary Care Hospital. Correlation of Demographic and Clinical Characteristics with Viral Load Results and Hospitalization. European Journal of Biomedical Research (EJ-BIOMED). 2022, 1(2), 2022. https://doi.org/10.24018/ejbiomed.2022.1.2.6
21. Mungomklang A, Trichaisri N, Jirachewee J, Sukprasert J, Tulalamba W, Viprakasit V. Limited sensitivity of a rapid Sars-Cov-2 antigen detection assay for surveillance of asymptomatic individuals in thailand. Am J Trop Med Hyg. 2021, 105(6):1505-1509. doi: 10.4269/ajtmh.21-0809. PMID: 34634778; PMCID: PMC8641330
22. Krüttgen A, Cornelissen CG, Dreher M, Hornef MW, Imöhl M, Kleines M. Comparison of the SARS-CoV-2 Rapid antigen test to the real star Sars-CoV-2 RT PCR kit. J Virol Methods. 2021, 288:114024. DOI: 10.1016/j.jviromet.2020.114024.
23. Papadopoulos VP, Emmanouilidou A, Yerou M, Panagaris S, Souleiman C, Varela D, et al. SARS-CoV-2 Vaccination Coverage and Key Public Health Indicators May Explain Disparities in COVID-19 Country-Specific Case Fatality Rate Within European Economic Area. Cureus. 2022, 14(3):e22989.
24. Mourtzikou A, Stamouli M, Toka E, Koumpouros P, Kalliora G, Seitopoulou C, et al. Seasonal Respiratory Virus Circulation in a Tertiary Care Hospital in Greece. EJ-BIOMED. 2023, 2(3). 10.24018/ejbiomed.2023.2.3.65
25. Macedo MCF, 1 , Pinheiro IM, Carvalho CJL, Fraga HCJR, Isaac P Araujo C, Montes SS, et al. (2020). Correlation between hospitalized patients' demographics, symptoms, comorbidities, and COVID-19 pandemic in Bahia, Brazil. PLoS One, 15(12):e0243966.