RESEARCH ARTICLE

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Suspected COVID-19 Cases Admitted in a Tertiary Care Hospital. Correlation of Demographic and Clinical Characteristics with Viral Load Results and Hospitalization

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ABSTRACT

***Background*: The current pandemic outbreak of COVID-19 due to the SARS-CoV-2 virus affected the health care systems, health services and economy globally. It also affected the health of the population worldwide, with high mortality and morbidity rates. The present study aimed to study the patients that were admitted to a tertiary care hospital and to investigate the potential correlation between hospitalization and RT-PCR for SARS-CoV-2 results with demographic characteristics and clinical characteristics. Moreover, it aimed to examine a mathematical formula that might describe the correlation of the aforementioned parameters.**

***Methods*: The study population included 1244 patients admitted to the Nikea General Hospital "Agios Panteleimon", Piraeus, Greece. Patient age, gender, underlying diseases, travel history, symptoms, etiology for hospital admission and contact with confirmed cases were recorded. Potential correlation of hospitalization and RT-PCR for SARS-CoV-2 results with the aforementioned characteristics were identified by chi-square test of independence and logistic regression analysis.**

***Results*: We observed significant correlation of hospitalization with fever, cough, dyspnea, pneumonia, travel history and etiology for hospital admission. We observed significant correlation of RT-PCR for SARS-CoV-2 results with rapid antigen test result, hospitalization etiology for hospital admission and contact with confirmed COVI-19 case.**

***Conclusions*: According to the logistic regression model, RT-PCR for SARS-CoV-2 result, fever, dyspnea, pneumonia, and underlying disease are the most important predictors for hospitalization in the population under study. Contact with confirmed COVID-19 case is the most important predictor for RT-PCR for SARS-CoV-2 result.**

Keywords: Greece, hospitalization, suspected COVID-19 cases, tertiary hospital, viral load results.

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I. INTRODUCTION

SARS-CoV-2 (severe acute respiratory syndrome caused by coronavirus 2) was first identified in the city of Wuhan, the capital of Hubei Province in the People's Republic of China, in December 2019 and since then has rapidly spread all over the world with approximately 5,1 million confirmed deaths and 410 million confirmed cases [1], [2]. On March 11, 2020, World Health Organization declared it as a pandemic [3]. The disease caused by SARS-CoV-2, called COVID-19 (Corona Virus Disease 2019) in most cases occurs with mild, influenza-like symptoms. However, in 10 to 15% of cases, it may progress to severe pneumonia, acute respiratory distress syndrome and death [4]-[6]. The most vulnerable population groups are the elderly and patients with underlying diseases, such as diabetes mellitus, obesity, hypertension, cardiovascular disease and renal disorders [7]-

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[13]. SARS-CoV-2 is a single-stranded positive (+) polarity RNA virus, with an RNA genome size of 30.000 bases and a viral particle size between 70 and 90 nm. It is transmitted using large respiratory droplets, generated by coughing or sneezing, and from hands touching contaminated objects and surfaces [14]. In some cases, aerosol transmission is also possible by exposure to elevated aerosol concentrations within closed spaces [15]. Even in countries with higher hygiene standards, the health care systems, and not only in economic terms, are currently suffering and struggling from the COVID-19 pandemic. As a result of the pandemic, patients who suffer from other kind of illnesses and/or diseases not related to COVID-19, face limited access to health care services provided by hospitals in the framework of the public health care sector [16]-[21].

The present study aimed to study the patients that were admitted to Nikea General Hospital "Agios Panteleimon", Piraeus, Greece, a tertiary care hospital, which is not a referral center for COVID-19 and to investigate the potential correlation between hospitalization and RT-PCR for SARS-CoV-2 results with demographic characteristics, underlying diseases, travel history, symptoms, etiology for hospital admission and history of contact with confirmed cases. Moreover, we tried to examine a mathematical formula that might describe the correlation of the aforementioned parameters.

II. Materials and Methods

The population under study consisted of 1244 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, patients were asked about travel history, symptoms, contact with confirmed positive COVID-19 cases and underlying diseases. Data were collected between November 2020 and May 2021. RT-PCR for SARS-CoV-2 tests were performed on Cepheid Inc GeneXpert® Cepheid Inc, Sunnyvale, CA, USA. The test for the qualitative detection of SARS-CoV-2 (CE IVD) is based on cartridge technology, in which multiple regions of the viral genome are targeted. The test can rapidly detect the current coronavirus SARS-CoV-2 in as soon as approximately 50 minutes for positive results. For Quality Control of the assay, we used both Internal Controls, as well as External Controls (AccuPlex™ SARS-CoV-2 Reference Material 0505-0126, Milford, MA, USA).

Specimens were collected by doctors, stored in viral transport medium at room temperature (15-30 °C) and were transported within 15-30 minutes at the molecular laboratory, according to the WHO Laboratory Biosafety Guidance Related to the Coronavirus Disease 2019 [22]. RT-PCR for SARS-CoV-2 results were correlated to gender, patient age, travel history, contact with a confirmed case, rapid antigen test result, hospitalization, cough, fever, dyspnea, pneumonia, underlying disease, and etiology for laboratory testing using chi-square independence test. Patient hospitalization was also correlated with gender, travel history, contact with a confirmed case, cough, fever, dyspnea, pneumonia, underlying disease, and etiology for hospital admission, using chi-square independence test. Moreover, we developed a logistic regression model with hospitalization as the dependent variable and travel history, contact with a confirmed case, age, gender, fever, dyspnea, pneumonia, underlying disease, and RT-PCR for SARS-CoV-2 result as independent variables. We also developed a logistic regression model with RT-PCR for SARS-CoV-2 result as the dependent variable and all the explanatory variables as independent variables. Statistical analysis was performed using the statistical package "R". Categorical variables are presented as frequencies (N) and percentages (%). *p*-values < 0.05 were set as significant.

III. Results

Out of the 1244 patients, 696 (55,9 %) were male and 542 (43,6 %) were female. In 6 cases patient gender was not recorded in the referral form, due to administrative nonconformity. Patient age in males ranged from 10 to 94 years and in females from 8 to 98 years. Gender and distribution in the population under study is presented in Table I.

TABLE I: Gender and Age Distribution in the Population under Study

	Gender		Age		
	Frequency	Percent	Min	Max	Mean
Male	696	55,9%	10	94	65,6
Female	542	43,6%	8	98	70,6
Not recorded	6	0,5%			
Total	1244	100,0%			

Patients were asked if they had a recent travel history. 665 patients (53,3 %) did not have a recent travel history, while 10 patients (0,8 %) had a recent travel history and in these cases a detailed travel history with the chronology of symptoms was recorded. In 569 cases (45,7%) information about travel history was missing. 98 patients (7,9 %) had contact with a confirmed COVID-19 case and 375 patients (30,1 %) did not have contact with a confirmed COVID-19 case. 771 patients (62 %) did not know if they had such a contact. Among the patients under study in 157 cases (12,6 %) presence of underlying diseases was recorded, in 989 there were not underlying diseases and in 98 cases such information was not available, due to administrative reasons (these patients were admitted form mental health centers and nursing homes). Travel history of the population under study, contact with confirmed COVID-19 case and presence of underlying diseases are presented in Table II.

On admission to the hospital, patients were asked for previous rapid antigen test results. Such a result was available in 450 cases (36,2%). For the rest of the patients such information was not available, because the rapid antigen test was not required on a regular basis. Previous rapid antigen test results are presented in Table III.

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TABLE II: DISTRIBUTION OF TRAVEL HISTORY, CONTACT WITH CONFIRMED COVID-19 CASE AND PRESENCE OF UNDERLYING DISEASE IN THE POPULATION UNDER STUDY

	Travel history		Contact with confirmed Covid-19 case		Underlying disease	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Yes	10	0,8%	98	7,9%	157	12,6%
No	665	53,5%	375	30,1%	989	79,5%
Unknown	569	45,7%	771	62,0%	98	7,9%
Total	1244	100,0%	1244	100,0%	1244	100,0%

TABLE IV: DISTRIBUTION OF FEVER, DYSPNEA, COUGH AND RADIOLOGICALLY CONFIRMED PNEUMONIA ON ADMISSION AMONG THE POPULATION UNDER STUDY

	Fever		Dyspnea		Cough		Pneumonia	
	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
YES	320	25,7%	142	11,4%	50	4,0%	297	23,9%
NO	826	66,4%	1004	80,7%	1096	88,1%	849	68,2%
unknown	98	7,9%	98	7,9%	98	7,9%	98	7,9%
TOTAL	1244	100,0%	1244	100,0%	1244	100,0%	1244	100,0%

TABLE III: DISTRIBUTION OF RAPID ANTIGEN TEST RESULTS IN THE POPULATION UNDER STUDY

Rapid antigen test	Frequency	Percent
Positive	174	14,0%
Weak positive	4	0,3%
Negative	272	21,9%
Not available	794	63,8%
Total	1244	100,0%

On admission to the hospital, the following patient symptoms were recorded: fever, dyspnea, cough, and pneumonia confirmed by radiography. Their distribution is presented in Table IV.

We performed a RT-PCR for SARS-CoV-2 test for all the patients. Etiology for hospital admission, as recorded in the referral note, is presented in Table V.

TABLE V: DISTRIBUTION OF ETIOLOGY FOR VIRAL LOAD DETECTION

Etiology	Frequency	Percent
Digestive disease	15	1,2%
Fever	7	0,6%
Cough and/or dyspnea and/or fever	387	31,1%
Cough and/or dyspnea and/or fever combined with other non respiratory symptoms	6	0,5%
Cough and/or dyspnea and/or fever with combined with other respiratory symptoms	23	1,8%
Preoperative examination	96	7,7%
Pneumonia	13	1,0%
Hospitalization in icu	13	1,0%
Admission from other hospital/ nursing home	27	2,2%
Acute respiratory disease	283	22,7%
Underlying disease	130	10,5%
Orthopaedic/multiple injuries/ neurologic symptoms	146	11,7%
Admission from prison, refugee camp, mental health center	98	7,9%
Total	1244	100,0%

RT-PCR for SARS-CoV-2 test was performed for all patients. The majority of RT- PCR for SARS-CoV-2 tests were performed in nasopharyngeal specimens. Invalid test results were recorded on 16 cases and are attributed to inappropriate sample quality. Specimen origin and RT-PCR for SARS-CoV-2 results are presented in Tables VI and VII.

Out of the patients under study, 608 (48,9%) were not hospitalized while 294 (23,6%) remained for a few hours in a day care ward for follow-up and then they were discharged. 337 patients (27,1%) were hospitalized and 5 (0,4%) were admitted to the ICU. Patient hospitalization is presented in Table VIII.

TABLE VI: SPECIMEN ORIGIN IN THE POPULATION UDER STUDY

Specimen origin	Frequency	Percent
Nasopharyngeal	1232	99,0%
Oropharyngeal	4	0,3%
Tracheal aspirate	7	0,6%
Sputum	1	0,1%
Total	1244	100,0%

TABLE VII: RT-PCR FOR SARS-COV-2 RESULTS IN THE POPULATION UDER STUDY

RT- PCR for SARS-CoV-2	Frequency	Percent
Viral load present	369	29,7%
Viral load absent	859	69,1%
Invalid result	16	1,2%
Total	1244	100,0%

TABLE VIII: HOSPITALIZATION OF THE POPULATION UNDER STUDY

Hospitalization	Frequency	Percent
Yes	337	27,1%
Yes in ICU	5	0,4%
No	608	48,9%
Day care ward and discharge	294	23,6%
Total	1244	100,0%

We performed a chi-square test of independence to observe if the RT-PCR for SARS-CoV-2 result is correlated with any of the following paramters: gender, travel history, contact with a confirmed case, rapid antigen test result, hospitalization, cough, fever, dyspnea, pneumonia, underlying disease, and etiology for hospital admission. The results are presented in Table IX.

TABLE IX: CHI-SQUARE TEST OF INDEPENDENCE FOR RT-PCR FOR SARS-COV-2 RESULT

	RT-PCR for sars-cov-2 result			
	X-squared	Df	P-value	Correlation
Gender	1.6608	1	0.1975	No
Travel history	0.34611	1	0.5563	No
Contact with confirmed case	98.47	1	< 2.2e-16	Yes
Hospitalization	97.494	2	0.007637	Yes
Cough	2.3629	1	0.1243	No
Fever	2.58	1	0.1082	No
Dyspnea	0.6296	1	0.4275	No
Pneumonia	1.0731	1	3002	No
Rapid antigen test result	392.66	2	< 2.2e-16	Yes
Underlying disease	1.0	1	0.1863	No
Etiology for hospital admission	117,8	11	< 2.2e-16	Yes

We performed a chi-square of independence test to observe if hospitalization is correlated with any of the following parameters: gender, travel history, contact with a confirmed case, cough, fever, dyspnea, pneumonia, underlying disease, and etiology for hospital admission. The results are presented in Table X.

TABLE X: CHI-SQUARE OF INDEPENDENCE TEST FOR HOSPITALIZATION

	Hospitalization			
	X-squared	DF	P-value	Correlation
Gender	3.2468	1	0.07156	No
Travel history	42.954	3	2,52e-06	Yes
Contact with confirmed case	1.3941	1	0.2377	No
Cough	25.911	1	3,58e-04	Yes
Fever	54.966	1	1,23e-10	Yes
Dyspnea	18.071	1	2,13e-02	Yes
Pneumonia	52.833	1	3,63e-10	Yes
Underlying disease	2.1349	1	0.144	No
Etiology for hospital admission	198.45	11	< 2.2e-16	Yes

A. Logistic Regression for Hospitalization

A logistic regression model was fitted, with response variable the hospitalization (yes, no) and explanatory variables: travel history, contact with a confirmed COVID-19 case, RT-PCR for SARS-CoV-2 test output, gender, age, cough, fever, dyspnea, pneumonia, and underlying diseases. Etiology for hospital admission due to administrative requirements, such as preoperative examination, were not included. Note that "yes in intensive care" (for hospitalization) was considered “yes” for the logistic analysis. Also, a person may have multiple occurrences of the reasons present, i.e., could have cough and fever and dyspnea, for example. Each of the reasons considered is having 0,1 for 0:No and 1:Yes. Travel history, contact with a confirmed COVID-19 case, gender and age were not proven to be significant in explaining the variability for hospitalization. Also, the cough was not significant in explaining the variability in hospitalization. The estimated model was the following:

$$\text{logit}(p)=-2.22 - 0.47\times(x1) + 1.18\times(x2) + 0.93\times(x3) - 0.49\times(x4) + 0.47\times(x5)$$

x1 is a positive result for PCR, x2 is the absence of fever, x3 is the absence of dyspnea, x4 is the absence of pneumonia and x5 is the absence of underlying diseases.

Where p is the probability of a hospitalization (Pr(Y=1)). According to the estimated coefficients, we can note the following:

- exp(-0.47)=0.63 is the odds ratio for the probability of hospitalization given that RT-PCR for SARS-CoV-2 is positive compared to the odds given that RT-PCR for SARS-CoV-2 is negative. In other words, a case with a positive RT-PCR test result has 37% reduced odds of hospitalization compared to the corresponding odds of hospitalization for a case that does not have a positive RT-PCR test result.
- exp(1.18)=3.25 is the odds ratio for the probability of hospitalization. The case does not have fever compared to the corresponding odd of hospitalization when a case has a fever. In other words, a case that is not having a fever has 225% increased odds of hospitalization compared to the corresponding odd for hospitalization for a case that is having a fever.
- exp(0.93)=2.53 is the odds ratio of hospitalization given that the case does not have dyspnea compared to the odd of hospitalization when the case has dyspnea. In other words, a case not having dyspnea has 153% increased odds of hospitalization compared to the corresponding odd of hospitalization for a case with this symptom.
- exp(-0.49)=0.61 is the odds ratio of the probability of hospitalization given that a patient is not having pneumonia, compared to the odd of hospitalization under the presence of pneumonia. In other words, when a case does not have pneumonia, it has a 39% reduced odd for hospitalization compared to the corresponding odd under the presence of pneumonia.
- exp(0.47)=1.60 is the odds ratio for the probability of hospitalization given that the patient is not having an underlying disease compared to the odd of hospitalization when the patient has an underlying disease.

TABLE XI: LOGISTIC REGRESSION MODEL STATISTICS

Coefficients:	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-2,2175	0,5027	-4,411	1,03E-05
RT-PCR (pos)	-0,4723	0,168	-2,812	0,004928
Fever (no)	1,1819	0,2105	5,615	1,97E-08
Dyspnea (no)	0,9336	0,2757	3,387	0,000708
Pneumonia (no)	-0,4943	0,184	-2,686	0,007222
Underlying disease (no)	0,4769	0,2273	2,098	0,035913

B. Logistic Regression for the RT-PCR for SARS-CoV-2 Test Result Output (1= positive, 0=negative)

We run a logistic regression with all the explanatory variables. Only the contact with a confirmed COVID-19 case proved to be significant in explaining the variability in the output of the RT-PCR for SARS-CoV-2 test. Specifically, the estimated model has the form:

$$\text{logit}(p)=1.58 - 2.57\times(x1)$$

where x1 is the absence of contact with a confirmed COVID-19 case, according to the x1 estimated coefficient, exp(-2.57)=0.077 is the odds ratio of a positive RT-PCR for SARS-CoV-2 test given that the case has none COVID-19 confirmed contact as compared to the odd of a positive RT-PCR for SARS-CoV-2 when the patient had a COVID-19 confirmed contact. In other words, a patient who had not been in contact with a COVID-19 confirmed case had 92% reduced odds of a positive RT-PCR for SARS-CoV-2 test as compared to the corresponding odd of a positive RT-PCR for SARS-CoV-2 for a patient that was in contact with a confirmed COVID-19 case.

Deviance Residuals:
Min 1Q Median 3Q Max
-1.8819 -0.7972 -0.7972 0.6109 1.6131
Coefficients:
Estimate Std. Error z value Pr(>|z|)
(Intercept) 1.5841 0.2744 5.772 7.83e-09 ***

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IV. Discussion

The rapid spreading of the new COVID-19 disease pandemic due to infection by SARS-CoV-2 increased the need for early detection of viral load and early diagnosis, that is crucial for disease treatment and infection control [23]-[25]. Viral load detection assays represent the so-called "gold standard" for the control of the disease, together with the chest CT imaging and the serological IgM-IgG antibody testing [26]-[30]. In the present study we examined the suspected COVID-19 cases admitted in a tertiary care hospital and we correlated their demographic and clinical characteristics with viral load results and hospitalization. Moreover, we tried to estimate a mathematical relation that describes the correlation of these parameters by means of logistic regression. The patient sample of our study included 1244 patients, both males (55,9%) and females (43,6%), aged between 8 and 98 years. In our study we did not observe any correlation between patient gender or age with hospitalization and RT-PCR for SARS-CoV-2 results. On admission to the hospital, patients were asked for travel history, contact with a confirmed case, previous rapid antigen test result if available, symptoms (such as cough, fever, dyspena) and underlying diseases. Moreover, CT was performed in order to radiologically confirm pneumonia. Travel history to high-risk regions is posing a difficult challenge for epidemic prevention and control [23]. Given the COVID-19 situation, the Greek government had issued entry restrictions and quarantine measures for travellers. In our study 10 patients (0,8%) had a travel histoty and 665 (53,5%) declared that they had no travel history. Chi-square independence test showed significant correlation of travel history with hospitalization. Contact with confirmed case is also posing a difficult challenge for epidemic prevention and control. Socializing and modern transportation have made personal movements and contact more rapid and have contributed to the virus transmission speed [24]. Moreover, high percentages of asymptomatic infections have been reported in the literature, which constitute a considerable risk of COVID-19 transmission [25], [26]. In our study 98 (7,9%) patients confirmed contact with a positive COVID-19 case, while 375 (30,1%) declared that they had no such contact. However, 771 (62,0%) patients did not know if they had such a contact, since a large percentage of affected patients are asymptomatic. Chi-square independence test showed no significant correlation between contact with a confirmed case and hospitalization or RT-PCR for SARS-CoV-2 results. Underlying diseases might be risk factors for poor prognosis in patients with COVID-19 infection. Current knowledge has shown that death rate is high in people with chronic underlying diseases [27], [28]. In our study, 989 patients (79,5%) had no underlying diseases, while 12,6% had an underlying disease, such as hypertension, cardiovascular diseases, diabetes mellitus, malignancy, and chronic kidney disease. Chi-square independence test showed no significant correlation between underlying disease and hospitalization or RT-PCR for SARS-CoV-2 results. Symptoms such as fever, cough, dyspnea, decreased oxygen saturation or lung auscultation findings, are the most characteristic information available in order to rule out COVID-19 disease, or select patients for further diagnostic testing [29], [30]. In our study we examined cough, fecer, dyspnea and radiologicallyconfirmed pneumonia among the patients under study. We observed a significant correlation between all four parameters and hospitalization. We did not observe correlation between any of these parameters and RT-PCR for SARS-CoV-2 results. The rapid antigen test for the detection of SARS-CoV-2 has been widely applied for patient screening. It is a qualitative test based on a rapid chromatographic immunoassay [31]. Rapid antigen test is highly specific, but its sensitivity is acceptable with higher viral laods. It is suitable in cases where a short-term evaluation of infectivity is required, or in POCT settings [32]. In our study patients on admission were asked if they had a precvious rapid antigen test result. Such a result was available for 450 patients (36,2%). We observed significant correlation between rapid antigen test result and RT-PCR for SARS-CoV-2 results. Etiology for hospital admission and laboratory testing by means of viral load detection with RT-PCR for SARS-CoV-2, included patient symptoms and their severity, underlying disease, as well as administrative protocols, such as preoperative testing for asymptomatic patients. An appropriate specimen is of utmost importance in the detection of viral load [33], [34]. In our study viral load detection was performed in nasopharyngeal swabs (99%), as well as in oropharyngeal swabs, tracheal aspirates and sputum. These specimen types from the lower respiratory tract are the recommended ones for viral load detection. Presence of viral load was detected in 29,7% of the patients. Such positivity rates are also described in the literature, concerning tertiary care institutions in other countries [30], [35], [36]. In the present study we tried to estimate a mathematical formula that describes the correlation of hospitalization and RT-PCR for SARS-CoV-2 result with the parameters under study, by means of logistic regression. The mathematical modeling of epidemics has been the object of a vast number of studies since the past century. Many models for COVID-19 infection are presented in the literature, which contribute to predict the number of cases and fatalities of this pandemic, or correlate symptoms with disease outcomes [37], [38]. The fitted logistic regression model with hospitalization as the response variable, showed that a viral load presence, absence of fever, absence of dyspnea, absence os pneumonia and underlying disease are tied to reduced odds of hospitalization. The fitted logistic regression model with RT-PCR for SARS-CoV-2 result as the response variable, showed that contact with a confirmed COVID-19 case appears to be the only coefficient with a statistically important effect on the test result. This study has some limitations; first due to the heavy workload of the hospital on duty days, many referral forms had missing data and consecuently 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. Third, all symptoms were recorded by the physicians at initial presentation of the patient, without any updates for symptoms in subsequent time.

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