



**ARTICLE**

## A Binomial Model Approach: Comparing the $R_0$ Values of SARS-CoV-2 rRT-PCR Data from Laboratories across Northern Cyprus

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### ABSTRACT

Northern Cyprus has implemented relatively strict measures in the battle against the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The measures were introduced at the beginning of the COVID-19 pandemic, in order to prevent the spread of the disease. One of these measures was the use of two separate real-time reverse transcription polymerase chain reaction (rRT-PCR) tests for SARS-CoV-2 referred to as the double screening procedure, which was adopted following the re-opening of the sea, air and land borders for passengers after the first lockdown. The rRT-PCR double screening procedure involved reporting a negative rRT-PCR test which was carried in 72 to 120 h before departure whilst presenting no known symptoms of the COVID-19 and performing a second rRT-PCR test at the point of arrival. This study compares the results of SARS-CoV-2 rRT-PCR tests performed on incoming flight passengers from the 1<sup>st</sup> July to 9<sup>th</sup> of September 2020 to Northern Cyprus. The rRT-PCR test results collected by the Near East University (NEU) DESAM COVID-19 laboratory were compared with the rRT-PCR test results collected by the Ministry of Health and/or private COVID-19 laboratories in Northern Cyprus. This comparative study was conducted using binomial distribution. In addition, by applying the Susceptible-Exposed-Infected-Removed (SEIR) model to Northern Cyprus, overall basic reproduction number ( $R_0$ ) value of the COVID-19 was analysed for the same time period to act as a threshold for this comparison. In both the statistical and SEIR mathematical model,  $R_0$  was calculated. It was assumed that, the more similar the  $R_0$  results of NEU DESAM COVID-19 laboratory and other laboratories were with the overall  $R_0$  value of Northern Cyprus, the more reliable the results would be. We calculated that the median  $R_0$  values of the NEU DESAM COVID-19 laboratory and other laboratories performing the SARS-CoV-2 rRT-PCR on air passengers during the studied period to be 0.96 and 1.29, respectively, compared to Northern Cyprus median  $R_0$  value which was 0.99. The rRT-PCR screening results from the NEU DESAM COVID-19 laboratory were closely aligned with the screening results of Northern Cyprus whereas the screening results reported by other laboratories were not in a fit with the regional pattern. This study also aimed to point out the importance of the rRT-PCR screening procedure



since asymptomatic positive SARS-CoV-2 cases entry to Northern Cyprus was inhibited and this prevented the spread of the disease within the population.

#### KEYWORDS

COVID-19; tests performed; basic reproduction number; statistical analysis; comparison

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## 1 Introduction

2019 novel coronavirus—later named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—first emerged in Wuhan, China in late December 2019. SARS-CoV-2 is the cause of coronavirus disease 2019 (COVID-19) and has spread outside China, leading to a major public health crisis worldwide [1]. World Health Organization (WHO) declared on the 11<sup>th</sup> March 2020 that SARS-CoV-2 had reached epidemiological characteristics to be announced as a pandemic [2].

Clinical presentation of COVID-19 may range from mild to severe symptoms. The symptoms may occur 2 to 14 days after being exposed to SARS-CoV-2. Frequently observed signs of COVID-19 include high fever, sore throat, dry cough, sneezing, muscle pain and fatigue. People who have underlying conditions such as diabetes, cancer, lung or heart diseases may develop more serious symptoms which could lead to death [3].

In addition, there are asymptomatic individuals who carry the SARS-CoV-2 but present no symptoms. These individuals have the ability spread the virus efficiently, and therefore are silent spreaders, making it a challenge to control the spread [4].

Transmission can occur either directly through inhaling infected droplets and aerosols from breathing, sneezing or coughing or through indirect transmission routes from fomites where the virus can enter the body through the mouth, nose, or eyes [5,6].

As of the 27<sup>th</sup> September 2020, statistical data published by the WHO stated that 32.7 million confirmed cases and 991,000 confirmed COVID-19 related deaths have occurred. The situation follows an increasing pattern in the Eastern Mediterranean region. According to the aforementioned data, a total of 2,340,215 SARS-CoV-2 confirmed cases and 60,345 COVID-19 related deaths had occurred in in the Eastern Mediterranean region since the start of the pandemic [7].

Cyprus is the third largest island located in the Eastern Mediterranean region. The population in Northern is approximately 375 000, majority of whom are Turkish Cypriots. The first case of SARS-CoV-2 in Northern Cyprus was identified on 9<sup>th</sup> March—a German female tourist (patient zero) who arrived on the island as part of a tour group. Soon after, everyone with close contact to patient zero, including fellow tour group members who arrived in the same flight were quarantined in three different hotels [8].

Consequently, strict measures were adopted starting from the 10<sup>th</sup> March 2020, such as the closure of schools.

By the 14<sup>th</sup> March 2020, travel restrictions were put in place such that only Northern Cyprus citizens were allowed to enter the country with an obligatory 14-day quarantine. In addition, gatherings in associations, unions and communal spaces as well as performing collective worship were prohibited. The hospitality sector was also closed [9]. Moreover, to promote isolation of the

individuals, a partial daytime curfew was imposed as of 23<sup>rd</sup> March 2020 during which people were only allowed to go to the market, pharmacy and petrol stations to maintain their essential needs (all other non-essential shops were closed in this period). At the beginning of April, a “full curfew” between 21:00 pm and 06:00 am was adopted as an additional precaution [10].

These strict measures, however were lifted shortly thereafter due to the deteriorating economic circumstances. On 29<sup>th</sup> April 2020 the partial daytime curfew was lifted, and the hospitality sector were allowed to re-open [11]. Schools re-opened on 1<sup>st</sup> September 2020 for the new academic year [12]. By the 1<sup>st</sup> of July, sea, air and land borders were re-established. With the opening of the borders, new regulations were established to prevent and control the spread of SARS-CoV-2. This included two separate real-time reverse transcription polymerase chain reaction (rRT-PCR) referred to as the double screening procedure for all individuals coming from abroad. According to this regulation, a negative rRT-PCR test conducted in 72 to 120 h prior to arrival as well as presenting no symptoms such as dry cough or fever were mandatory for passengers’ entry to Northern Cyprus. Upon arrival at the border, a second rRT-PCR test was performed on the spot and the passengers were allowed to enter Northern Cyprus only if this second test was also negative, otherwise they were quarantined [13].

The rRT-PCR is one of the diagnostic methods used to detect SARS-CoV-2 infection. This method qualitatively detects viral nucleic acid of SARS-CoV-2 from upper and lower respiratory specimens such as nasopharyngeal or oropharyngeal swabs obtained from individuals. The rRT-PCR test method is highly sensitive and is considered as the gold standard frontline test in the detection of SARS-CoV-2 infection [5].

Approximately 40% of all COVID-19 infections are estimated to be asymptomatic infections. SARS-CoV-2 can be detected in asymptomatic patients and the viral load can be similar to a symptomatic person [14–16]. In addition, after contracting SARS-CoV-2, it may take 3 to 5 days on average to be able to detect SARS-CoV-2 infection with rRT-PCR [17].

The two separate rRT-PCR screening test method was implemented with the aim of detecting individuals who had a SARS-CoV-2 infection which may have gone undetected in the first PCR test and in turn presented as SARS-CoV-2 negative. However, with the second rRT-PCR the result come out as SARS-CoV-2 positive for the same person. Thus, the double screening strategy enabled such cases to be identified and prevented the transmission of the virus to the local population. Hence, we propose that performing a double rRT-PCR procedure is instrumental in preventing SARS-CoV-2 transmission from imported cases to the local population.

Many innovative approaches have been established by combining physics and mathematical models to study infectious diseases and epidemiological dynamics. Such innovative approaches include the use of calculus in nearly all branches of sciences [18], the study of the role of liver by a new model of Caputo–Fabrizio fractional derivative with the exponential kernel [19], the use of hyperchaotic models for a biological snap oscillator [20] and many other [21,22].

With the rise of the COVID-19 pandemic, many attempts have been made to study and analyze the SARS-CoV-2 dynamics, such studies include studying the dynamical structures of the physical behavior of SARS-CoV-2 via a fractional natural decomposition method [23], the study of reported and unreported SARS-CoV-2 cases by Caputo derivative [24], a mathematical model to analyze local/global stability and diseases free/endemic equilibrium points of COVID-19 [25], other mathematical model called the Bats-Hosts-Reservoir-People coronavirus model to analyze the transmission of SARS-CoV-2 from reservoir to people [26] and hybrid analytical method

$q$ -HASTM for the accomplishment of numerical solutions of COVID-19 model with fractional operator [27].

Motivated by the aforementioned papers, this study aimed to calculate the basic reproduction number ( $R_0$ ) using a statistical model—the Binomial method for 1- Near East University (NEU) DESAM COVID-19 laboratory and 2- Northern Cyprus Ministry of Health laboratories and/or private laboratories located across Northern Cyprus, by solely using the SARS-CoV-2 positive cases detected by the double rRT-PCR screening procedure for air passengers from 1<sup>st</sup> July to 9<sup>th</sup> September 2020 (“the study period”). The  $R_0$  value for all SARS-CoV-2 cases (not limited to the air passengers) in Northern Cyprus was also, calculated by a mathematical model [Susceptible-Exposed-Infected-Removed (SEIR) model] as a baseline for the comparison of  $R_0$  values between the NEU DESAM COVID-19 laboratory and the other laboratories in relation to the overall SARS-CoV-2 transmission pattern observed in Northern Cyprus.  $R_0$  is the number of infected people from one infected individual. The calculated value of the  $R_0$  is important for understating the dynamics of the infectious diseases that is  $R_0 < 1$  implies that the disease is under control and will disappear eventually whereas if  $R_0 \geq 1$  it means the disease is not under control and it is spreading within the studied population.  $R_0$  value is also a crucial indicator to measure the effectiveness of the various precautions taken against the SARS-CoV-2 infection and provides key insights into the decision-making process with regards to the measures which need to be put in place for the duration of the pandemic.

## 2 Methods

### 2.1 Laboratory Data Collection

Upon arrival at the Northern Cyprus airport, all passengers which had SARS-CoV-2 rRT-PCR negative results were subjected to a second rRT-PCR test collected under sterile conditions by healthcare workers from the Northern Cyprus Ministry of Health. After collection of the combined nasopharyngeal and oropharyngeal swabs, samples were stored at 4°C and transported to dedicated laboratories for SARS-CoV-2 rRT-PCR testing. Until the rRT-PCR results were released, all passengers were obligated to self-isolate. If they didn't comply, legal action was initiated against them.

From 1<sup>st</sup> July to 9<sup>th</sup> September 2020, a total of 62 passengers were detected to be SARS-CoV-2 RNA positive by rRT-PCR screening in the NEU DESAM COVID-19 laboratory. Samples which arrived with cold chain to NEU DESAM COVID-19 laboratory was treated immediately and the results were released within 4 to 8 h. Between the 1<sup>st</sup> and 12<sup>th</sup> July 2020, the detection kit referred to as Bio-Speedy® (Bioeksen R&D Technologies Inc. COVID-19 rRT-PCR Detection Kit v2.0, Istanbul-Turkey) was used [28] and from the 13<sup>th</sup> of July to the 9<sup>th</sup> of September 2020, Diagnovital® (RTA Laboratories Inc., SARS-CoV-2 Real-Time PCR Kit v2.0 Istanbul-Turkey) [29] was used in the detection of SARS-CoV-2 from combined nasopharyngeal and oropharyngeal swab samples.

For both of the kits, a Q96 rRT-PCR device was used in routine screening. Results were analyzed independently by qualified molecular biologists and confirmed by an infectious disease specialist before releasing the results. In both used kits, positive results indicated the presence of SARS-CoV-2 RNA. Similarly, in the absence of SARS-CoV-2 RNA, samples were reported as negative. Upon detection of positive SARS-CoV-2 cases, three different confirmative steps were performed. These included repeating the combined nasopharyngeal and oropharyngeal swab, performing Diagnovital Magicprep Fast Extraction kit 2 and RNA isolation from the swab samples, Diagnovital RTA Viral RNA isolation Kit (Istanbul-Turkey) and screening these samples using an

Insta Q96 plus rRT-PCR (Mumbai, India) device as well as in a different device named Rotor-Gene-Q (Qiagen, Hilden, Germany). These three procedures on different rRT-PCR devices were used to ensure the reported results were reliable and to prevent reporting of false positive results. The obtained results were reported to the official Ministry of Health Pandemic Information System (<https://COVID-19.gov.ct.tr/>) using the barcoding system. If the results of the patients were positive, they were quarantined immediately for the prevention of further spread of the virus to the local population. This study was approved by the NEU scientific research Ethics Committee (YDU/2020/85-1213).

The other COVID-19 laboratories of the Ministry of Health and/or private laboratories found a total of 88 SARS-CoV-2 positive cases via rRT-PCR in Northern Cyprus from air passengers arriving on the island between the 1<sup>st</sup> July to 9<sup>th</sup> September 2020. Other COVID-19 laboratories are distributed across Northern Cyprus, performing SARS-CoV-2 rRT-PCR tests for the population as well as the passengers coming from abroad. The number of positive SARS-CoV-2 cases found in the study period for air passengers from these laboratories were obtained from the Northern Cyprus Ministry of Health official website [30].

## 2.2 Statistical Model

Present research has adopted statistical modelling that used statistical distributions. For this purpose, the statistical distributions, gamma, binomial and posterior were applied.

In this study, gamma distribution was used in the delay of reported cases in of SARS-CoV-2 obtained from NEU DESAM COVID-19 laboratory and other COVID-19 laboratories rRT-PCR results from air passengers in Northern Cyprus. Since some of the cases were reported the day after their diagnosis, gamma distribution was used in this study with the purpose of minimizing the error in the delay in reported cases to make sure accurate forecasting was made by using the initial data. The data used in the model was the number of reported cases of SARS-CoV-2 per day in the study period. It is important to start with minimized error data since starting with an error contained data will affect the future estimation. Therefore, in distribution, mean and standard deviation of reported cases were represented and distributed as follows:

$$\delta \sim \Gamma(\mu, \sigma) \quad (1)$$

where  $\delta$  denotes delay in reported cases,  $\mu$ , the mean of reported cases, and  $\sigma$ , the standard deviation of reported cases.

Binomial distribution is a random process that can result in two exact outcomes (success or failure). In this study, it was used for the assumption of cases, i.e., assuming the cases were distributed according to binomial distribution. Here, success was the positive SARS-CoV-2 cases and failure was the negative SARS-CoV-2 cases. This distribution can be used to predict the upcoming week's cases by using the previous week's cases. The formula is given below:

$$C_t \sim \text{Binom} \left( \int_0^{\infty} \Gamma(\mu, \sigma) I_{t-x}^r dx, r_{\mu} \right) \quad (2)$$

This formula is based on reported positive cases of SARS-CoV-2 within the 1<sup>st</sup> July to 9<sup>th</sup> of September 2020. Here,  $C_t$  is the number of cases at time  $t$ ,  $I_t^r$  is the reported number of cases at time  $t$ , and  $r_t$  denotes the ratio of cases to reported cases at time  $t$ .

In order to use posterior distribution, a prior distribution is needed as evidence. Here, the prior distribution is binomial distribution and the evidence is the assumption of predicted

SARS-CoV-2 cases obtained from the binomial distribution above. Posterior distribution was used to obtain daily  $R_0$  values for NEU DESAM COVID-19 and other laboratories of Northern Cyprus Ministry of Health and/or private laboratories. Basic reproduction number, denoted by  $R_0$ , is the number of infected individuals caused by a single infected person in a completely susceptible population. It is an efficient way to analyze the epidemic character of an infectious disease and also to analyze how effective taken precautions were against the spread of the SARS-CoV-2.  $R_0$  is a threshold such that when  $R_0 \geq 1$  an epidemic will occur, in other words, the infectious disease continues to spread within the population. On the other hand, when  $R_0 < 1$ , the disease is under control and the epidemic will eventually die out. So, to see the infectiousness of SARS-CoV-2 in Northern Cyprus, posterior distribution is used for daily  $R_0$  values for NEU DESAM COVID-19 and other laboratories with the formula given below:

$$\rho_t = \frac{FR}{r_t} \quad (3)$$

where  $\rho_t$  denotes  $R_0$  values at time  $t$ .  $FR$  denotes the future records of cases.

Using this approach, together with the predictions calculated from the gamma, binomial and posterior distributions,  $R_0$  values were found for each day from 1<sup>st</sup> July to 9<sup>th</sup> September 2020 for NEU DESAM COVID-19 laboratory and other laboratories performing SARS-CoV-2 rRT-PCR tests for air passengers arriving at Northern Cyprus.

Following this,  $R_0$  values were calculated separately with confidence intervals 2.5%, 50%, 97.5% using the statistical model- binomial method.

### 2.3 Susceptible-Exposed-Infected-Removed (SEIR) Model

By applying data and parameter values listed in [Tab. 1](#), to the Susceptible-Exposed-Infected-Removed (SEIR) model in [\[31\]](#), daily  $R_0$  values of Northern Cyprus were calculated for the period of the study. This allowed the comparison between the  $R_0$  values for NEU DESAM COVID-19 laboratory and other laboratories performing SARS-CoV-2 rRT-PCR tests for air passengers to the  $R_0$  value representing all of the diagnosed SARS-CoV-2 cases across Northern Cyprus. We assumed that the more accurate the results of NEU DESAM COVID-19 laboratory and other laboratories, the closer it will be to the  $R_0$  values of Northern Cyprus overall.

**Table 1:** Variables and parameters needed to calculate basic reproduction number ( $R_0$ ) for Northern Cyprus using the Susceptible-Exposed-Infected-Removed (SEIR) model [\[30,32\]](#)

Variable/Parameter	Description	Value
$\beta$	Transmission rate	0.5432
$\alpha_i, (i = 1, 2, 3)$	Disease induced death rates	0.045, 0.8, 0.037
$\theta_i, (i = 1, 2, 3, 4)$	Progression rates	0.4398, 0.0571, 0.0075, 0.0054
$\omega$	Hospitalization rate from $I_1$ class	0.000089
$\varphi$	Hospitalization rate from $I_2$ class	0.00098
$\delta_i, (i = 1, 2, 3, 4)$	Recovery rates	0.86, 0.94, 0.2, 0.96
$\tau_i, (i = 1, 2, 3, 4)$	Contact rate of each compartments $I_1, I_2, Q, H$ respectively to S	0.16, 0.45, 0.46, 0.056

Notes: ( $I_1$ : infected with SARS-CoV-2 presenting mild to moderate symptoms,  $I_2$ : infected with SARS-CoV-2 presenting severe symptoms,  $Q$ : quarantined individuals,  $H$ : hospitalized individuals, S: susceptible individuals).

### 3 Results

By using the binomial model outlined in the Methods section and daily SARS-CoV-2 cases from air passengers for a total of 71 days (from 1st July to 9th September 2020) taken from NEU DESAM COVID-19 laboratory and other laboratories of Northern Cyprus Ministry of Health and/or private laboratories,  $R_0$  values were calculated separately with confidence intervals of 2.5%, 50%, and 97.5% respectively. This is demonstrated in [Tab. 2](#).

**Table 2:** Comparison of median basic reproduction number ( $R_0$ ) values for COVID-19 rRT-PCR results obtained from air passengers to Northern Cyprus from NEU DESAM and other laboratories

From 1 <sup>st</sup> July to 9 <sup>th</sup> of September	Median of $R_0$ value with average CI with 2.5%	Median of $R_0$ value with average CI with 50%	Median of $R_0$ value with average CI with 97.5%
Near East University DESAM COVID-19 laboratory (min.–max.)	0.64 (0–1.92)	0.96 (0.04–3)	1.39 (0.2–4)
Other COVID-19 laboratories (min.–max.)	0.71 (0–1.94)	1.29 (0.05–4.08)	2.16 (0.26–7.42)

Note: (CI: Confidence Internal).

In the 2.5% confidence interval, the sample represents a small part of the population which makes it hard to generalize the results for the whole population. On the other hand, 97.5% confidence interval means the sample represents the whole population with 97.5% confidence interval. In this case, error in data will be ignored with a high percentage which affects future predictions negatively. In 50% confidence interval, the median taken from sample may include 50% error but at least 50% should contain the true value. Thus, 50% confidence interval gives the most reliable results compared to 2.5% and 97.5% confidence intervals. Therefore, in this study 50% confidence interval  $R_0$  values are considered to be the most reliable results.

In the  $R_0$  calculation for Northern Cyprus, all SARS-CoV-2 cases were taken from the Ministry of Health [33,34], and this was not limited to air passengers SARS-CoV-2 cases, it included the total number of SARS-CoV-2 diagnosed in the Northern Cyprus in the studied period of time. Then, estimations for the median of  $R_0$  values of NEU DESAM COVID-19 laboratory and other laboratories were compared with the median of  $R_0$  values of Northern Cyprus in the period of 1<sup>st</sup> July to 9<sup>th</sup> of September 2020 ([Tab. 3](#)).

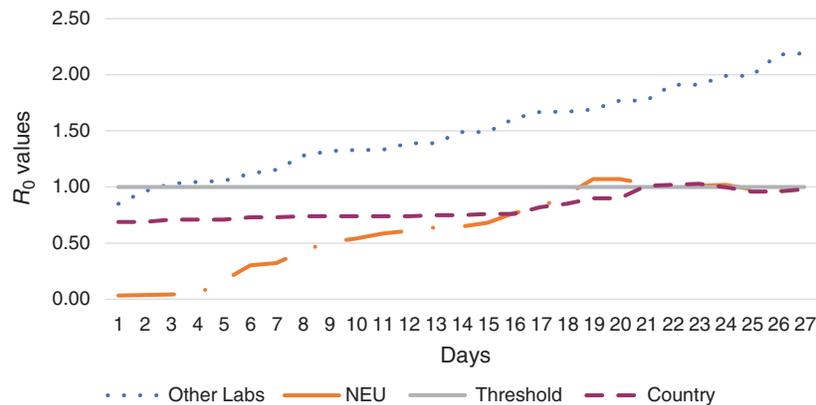
The comparison of  $R_0$  values of NEU DESAM COVID-19 laboratory and other COVID-19 laboratories, to the overall Northern Cyprus  $R_0$  value indicated that  $R_0$  values of NEU DESAM COVID-19 laboratory showed the same pattern with the  $R_0$  values of the Northern Cyprus. On the other hand,  $R_0$  values of other laboratories indicated a different pattern with higher  $R_0$  values when compared with NEU DESAM COVID-19 laboratory and Northern Cyprus  $R_0$  values. Whereas  $R_0$  values of NEU laboratory were very close with the  $R_0$  values of Northern Cyprus within the study time period. Hence, we conclude that estimations and data of NEU DESAM COVID-19 laboratory were consistent with the Northern Cyprus  $R_0$  values. This is demonstrated

in Fig. 1. The study also suggests that statistical modelling supports the mathematical modelling since the results were consistent.

**Table 3:** Comparison of median of basic reproduction number ( $R_0$ ) values of NEU DESAM COVID-19 and other laboratories with the median  $R_0$  value of Northern Cyprus [33,34]

From 1 <sup>st</sup> July to 9 <sup>th</sup> of September 2020	Near East University DESAM COVID-19 laboratory	Other COVID-19 laboratories	Northern Cyprus overall
Median value of $R_0$ with CI 50%	0.96 Total of positive SARS-CoV-2 cases 62	1.29 Total of positive SARS-CoV-2 cases 88	0.99 Total of positive SARS-CoV-2 cases 386 (not limited to air passengers)

Note: (CI:Confidence Internal).



**Figure 1:** Comparison of basic reproduction number ( $R_0$ ) values of NEU DESAM COVID-19 and other COVID-19 laboratories to Northern Cyprus  $R_0$  values

Comparison of basic reproduction number ( $R_0$ ) values calculated by binomial method for NEU DESAM COVID-19 and other laboratories air passengers’ rRT-PCR results to Northern Cyprus  $R_0$  value calculated by a mathematical model, for all diagnosed SARS-CoV-2 cases in the country were made. The analysis of  $R_0$  values were made for the period of 1<sup>st</sup> July to 9<sup>th</sup> of September 2020. The calculated  $R_0$  values for NEU DESAM COVID-19 and the Northern Cyprus  $R_0$  values denoted as ‘country’ in the figure indicated a very similar pattern. For most of the studied period, NEU DESAM COVID-19 and the Northern Cyprus  $R_0$  values were below 1, suggesting that the SARS-CoV-2 was under control in the studied period. However, the other laboratories performing rRT-PCR analysis for air passengers indicated a different pattern to NEU DESAM COVID-19 and the Northern Cyprus  $R_0$  values with  $R_0$  being above 1 for most of the studied period, suggesting that the SARS-CoV-2 was not under control in the country. While NEU

DESAM COVID-19 and the Northern Cyprus  $R_0$  values were consistent with each other, and other laboratories results were not in a fit.

#### 4 Discussions and Conclusions

By using the binomial model outlined in the Methods section and daily SARS-CoV-2 cases from air passengers for a total of 71 days (from 1<sup>st</sup> July to 9<sup>th</sup> September 2020) taken from NEU DESAM COVID-19 laboratory and other COVID-19 laboratories of Northern Cyprus Ministry of Health and/or private laboratories,  $R_0$  values were calculated separately with confidence intervals of 2.5%, 50%, and 97.5% respectively as demonstrated in Tab. 2. There are multiple active COVID-19 laboratories across Northern Cyprus that performs the COVID-19 rRT-PCR detection method.

Each COVID-19 laboratory uses different rRT-PCR kits, equipment, devices and employs staff of varying degrees of experience in the COVID-19 diagnosis procedure. In this research, all the steps carried in NEU DESAM COVID-19 laboratory and the COVID-19 diagnosis protocol were revealed. With this study, SARS-CoV-2 rRT-PCR results from air passengers to Northern Cyprus upon arrival (the second rRT-PCR test carried as a part the double screening procedure) were analyzed and the results obtained from NEU DESAM COVID-19 laboratory to other laboratories were compared using the binomial method. In order to carry out the comparison using the binomial method the  $R_0$  values were calculated solely using the positive SARS-CoV-2 cases in the period of from 1<sup>st</sup> July to 9<sup>th</sup> of September 2020.

The calculated  $R_0$  values in the study period for NEU DESAM COVID-19 laboratory and other laboratories were then compared separately with the overall  $R_0$  value of the Northern Cyprus for the same time period—calculated with the number of total SARS-CoV-2 cases and other parameters (Tab. 1) using SEIR model [31]. This comparison revealed that the median of  $R_0$  value (with 50% confidence interval) for NEU DESAM COVID-19 laboratory was 0.96 which was closer to the overall Northern Cyprus  $R_0$  median value of 0.99 (Tab. 3). With 71 days of median calculation of the  $R_0$  values, we found that, infection rates of COVID-19 evidenced by the  $R_0$  values in Northern Cyprus and the NEU DESAM COVID-19 laboratory were close enough such that, for the time period in question, the COVID-19 epidemic was under control (Fig. 1). Thus, based on these findings we suggest that the calculated estimations and the data of NEU DESAM COVID-19 laboratory were consistent with the overall Northern Cyprus  $R_0$  values.

However, data from other laboratories revealed a  $R_0$  median value of 1.29, suggesting that the COVID-19 epidemic was not under control (Tab. 3). The overall  $R_0$  values of other laboratories were above 1 while the  $R_0$  value of the country was below 1 for the most of the time period studied. This showed that the  $R_0$  pattern of other laboratories were not in a fit with the pattern of  $R_0$  values of the country (Fig. 1). We argue that this might be due to the number of false positive tests reported by the other laboratories, which led to a higher  $R_0$  value. False positive results can occur due to contaminations in the laboratories, mis-diagnosis by inexperienced staff, problems that can arise with the kits used or not confirming the positive results with SARS-CoV-2 RNA isolation. It is therefore critical that a properly trained specialist in this field analyses the results to avoid mis-diagnosis, and that the procedure is carried out at in well-equipped laboratory. NEU DESAM COVID-19 laboratory performed SARS-CoV-2 RNA isolation to ensure robust results and the results were analyzed by molecular biology experts and an infectious disease specialist before reporting a positive case of SARS-CoV-2. Also, the laboratory adopted a standardization of the kits and the procedure relatively quickly following the start of the rRT-PCR screening efforts. Hence, the results of this study suggest that the standardization of procedure in COVID-19

rRT-PCR screening is integral to producing more reliable test results. Moreover, we argue that performing COVID-19 rRT-PCR tests and analyses in well-equipped laboratories with well-trained scientists is another key factor in producing reliable test results.

It is also worthwhile to mention that, with the double rRT-PCR screening procedure in the given period of 71 days, 62 positive SARS-CoV-2 cases were identified in NEU DESAM COVID-19 laboratory and 88 in other laboratories across Northern Cyprus. This firmly suggested that performing the double rRT-PCR screening procedure for passengers is really important since it prevented the spread of the disease among the population by the asymptomatic positive SARS-CoV-2 individuals, also known as the silent spreaders.

This was an original study that used statistical distributions to construct a statistical model in infectious disease to analyze and find the dynamics of COVID-19. Statistical models are less frequently adapted to study infectious diseases compared to the mathematical modelling. One example of frequently used mathematical modelling is the SEIR model, which is commonly used to analyze infectious diseases such as SARS-CoV-2 and Human immunodeficiency virus, under conditions where data is present for the diseases [35]. However, mathematical modelling is a deterministic type of model which ignores randomness and variability. Generally, at each time point, it calculates a single estimation for new infections. In mathematical modelling, such as the SEIR model, neglect randomness and variability. In other words, single estimation is made and the results lack in uncertainty whereas in statistical modelling results are given in confidence intervals. Also, distributions in statistical modelling can give evidence about the future dynamics of an epidemic, to analyze whether the decisions made by the government and the public health interventions are efficient or not. Thus, evidence about these questions can be found in terms of probability [31].

Also, COVID-19 experts who are not familiar with statistical models can easily adopt the created binomial model and obtain  $R_0$  value estimations solely by using the SARS-CoV-2 cases. On the other hand, adopting mathematical models needs more parameters and data (birth rate, death rate, population number, etc.) and is harder to perform compared to statistical modelling. Binomial method can be used to analyze and predict the future dynamics of infectious diseases. SARS-CoV-2 data obtained from laboratories in Northern Cyprus were analyzed successfully using the binomial method and we have demonstrated that similar results were obtained to the SEIR model, suggesting that statistical models can support the mathematical models.

Further statistical studies can be conducted using the SARS-CoV-2 -cases or -related deaths for future predications rather than the sole analysis of  $R_0$  values. On the other hand, it is possible to apply fractional calculus to the gamma function in our model [36]. In the future studies, fractional approach could be also applied to the model to analyze and compare if similar results are obtained. With this study, we encourage the use of binomial method in the analysis and prediction of infectious disease epidemiology. In addition, there are many other alternative methods used to study SARS-CoV-2 dynamics which can also be used to develop control strategies to overcome the spread of the disease such as the numerical methods [37–39].

The main aim of this study was to compare the results of SARS-CoV-2 rRT-PCR results from different laboratories in Northern Cyprus and to point out the importance of the SARS-CoV-2 rRT-PCR double screening procedure to prevent the silent SARS-CoV-2 spreaders entering the country. As a result of the comparison, it was revealed that the SARS-CoV-2 RT-PCR results were dramatically different between the laboratories, revealing the need of standardized methods, techniques and kits to be implemented and used across all laboratories.

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