TURKISH REPUBLIC OF NORTHERN CYPRUS
NEAR EAST UNIVERSITY
INSTITUTE OF GRADUATE STUDIES

COVID-19: NORTHERN CYPRUS AS A GOOD MODEL TO PREVENT SPREAD OF THE DISEASE

NAZIFE SULTANOGLU

PhD THESIS

MEDICAL MICROBIOLOGY AND CLINICAL MICROBIOLOGY DEPARTMENT

ADVISOR
Prof. Dr. TAMER SANLIDAG
CO-ADVISOR
Prof. Dr. MURAT SAYAN

NICOSIA, 2021

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The Directorate of Institute of Graduate Studies,

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Director of Institute of Graduate Studies

DECLARATION

I hereby declare that the work in this thesis entitled "**COVID-19: NORTHERN CYRUS AS A GOOD MODEL TO PREVENT SPREAD OF THE DISEASE**" is the product of my own research efforts undertaken under the supervision of Prof. Dr. Tamer Sanlidag and Prof. Dr. Murat Sayan. No part of this thesis was previously presented for another degree or diploma in any university elsewhere, and all information in this document has been obtained and presented in accordance with academic ethical conduct and rules. All materials and results that are not original to this work have been duly acknowledged, fully cited and referenced.

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Date:

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The title earned from this thesis and years of hard work is gifted to my angel grandmother "Fatma Sultan", Fatma Sultanoglu.

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LIST OF ABBREVIATIONS

SEIR: Susceptible-Exposed-Infected-Recovered model

WHO: World Health Organization

$\boldsymbol{R_0}$**:** Basic reproduction number

CoVs: Coronaviruses

MERS-CoV: Middle East Respiratory Syndrome Coronavirus

SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

2019-nCoV: 2019 novel coronavirus

COVID-19: Coronavirus disease 2019

rRT-PCR: real-time reverse transcription polymerase chain reaction

CI: Confidence interval

$\boldsymbol{S}$**:** Susceptible

$\boldsymbol{E}$: Exposed

$\boldsymbol{Q}$**:** Quarantined

$\boldsymbol{I_1}$**:** Infected 1, SARS-CoV-2 infected and indicating mild to moderate symptoms

$\boldsymbol{I_2}$**:** Infected 2, SARS-CoV-2 infected and indicating severe symptoms

$\boldsymbol{H}$**:** Hospitalized individuals due to the SARS-CoV-2 infection

$\boldsymbol{R}$**:** Removed, recovered individuals after the SARS-CoV-2 infection

ABSTRACT

Nazife Sultanoglu. COVID-19: Northern Cyprus as a good model to prevent spread of the disease. Near East University, Institute of Graduate Studies, Medical Microbiology and Clinical Microbiology Program, PhD Thesis, Nicosia, 2021

Currently the world is going through the COVID-19 pandemic, with the official announcement made by the World Health Organization (WHO) in mid-March 2020. Northern Cyprus, located in the Eastern Mediterranean has also been affected by the pandemic. Many new and innovative approaches have been developed in order to study the behavior of COVID-19 within a given population. One of the approaches involves the use of mathematical modelling in order to study and analyze the dynamics of COVID-19. Susceptible-Exposed-Infected-Recovered model (SEIR) model is fundamental to all mathematical modeling in epidemiology. A particular model was designed using the SEIR model and implemented in Northern Cyprus to calculate the basic reproduction number (R_0). R_0 is the average number of infected individuals generated by one infected person within a population where all individuals are susceptible to infection. The value of the R_0 is the threshold within the model, in which if the $R_0 \geq 1$, the disease in question is in epidemic character within the studied population. On the other hand, when $R_0 < 1$, the disease is not in epidemic character and will eventually die out within the population. In addition, R_0 value is really valuable to evaluate the efficacy of the health-related policies adopted by the governing authorities. With the identification of patient zero on March 9th 2020 in Northern Cyprus, researchers at Near East University (NEU) DESAM began to calculate the R_0 on a daily basis and reported the results to the relevant authorities. According to the SARS-CoV-2 statistics as of 15th April 2021, the R_0 value of Northern Cyprus was 2.86, indicating that the disease has an epidemic character. As part of this project, all the results obtained for Northern Cyprus as well the adopted precautions are explained. In addition, practices, awareness and attitudes of Northern Cyprus residents toward the SARS-CoV-2 outbreak was investigated via an online survey. The results of the survey indicated that the awareness levels among the residents were high and practices were followed diligently during the pandemic period.

This type of vigilance played a significant role in shaping the dynamics of COVID-19 in the country. Moreover, the SARS-CoV-2 real time polymerase chain reaction tests' data obtained from air passengers visiting Northern Cyprus from 1st July to 9th of September 2020 were used to calculate R_0 for NEU DESAM COVID-19 laboratory and other laboratories in Northern Cyprus via a statistical model - binomial method. The resulting R_0 values for NEU DESAM were compared with the values of Northern Cyprus Ministry of Health and/or other laboratories. To act as a threshold to this comparison Northern Cyprus R_0 results was calculated using the SEIR model for the same period in question. It was assumed that the more the R_0 results of binomial were similar to the Northern Cyprus R_0, the more reliable the results would be. It was observed that NEU DESAM COVID-19 laboratory results (median R_0 0.98) were consistent with the Northern Cyprus R_0 (median R_0 0.99). Whereas, other laboratories' R_0 value pattern (median R_0 1.25) was inconsistent with both Northern Cyprus and NEU DESAM R_0 patterns. These findings indicated that NEU DESAM COVID-19 laboratory data was more reliable when compared to the data of other laboratories. Since similar results were obtained, we deduced that the SEIR model supported the binomial method.

Keywords: COVID-19, basic reproduction number, Northern Cyprus, mathematical model, statistical model, online survey

ÖZET

Nazife Sultanoglu. Kuzey Kıbrıs Türk Cumhuriyeti: COVID-19 salgınının yayılmasını önlemede iyi bir model. Yakın Doğu Üniversitesi, Sağlık Bilimleri Enstitüsü, Tıbbi Mikrobiyoloji ve Klinik Mikrobiyoloji Programı, Doktora Tezi, Lefkoşa, 2021

Dünya Sağlık Örgütü (DSÖ)'nün 2020 Mart ayı ortalarında yaptığı açıklamayla resmiyet kazanan COVID-19 salgını bir yılı aşkın bir süredir dünyayı etkisi altına almıştır. Doğu Akdeniz'de yer alan Kuzey Kıbrıs Türk Cumhuriyeti (KKTC) de pandemiden etkilenen ülkelerden biri olmuştur. COVID-19'un belirli bir popülasyondaki davranışını incelemek için birçok yeni ve yaratıcı yaklaşım geliştirilmiştir. Bu yaklaşımlardan biri, COVID-19'un dinamiklerini incelemek ve analiz etmek için matematiksel modellemenin kullanılmasıdır. Susceptible-Exposed-Infected-Recovered (SEIR) modeli, epidemiyoloji alanındaki tüm matematiksel modellemelerin temelidir. SEIR modeli kullanılarak özel bir model tasarlanmış ve temel üreme sayısını (R_0) hesaplamak için KKTC de uygulanmıştır. R_0, tüm bireylerin bulaş riskine açık olduğu bir nüfus içinde, enfekte olan bir kişinin virüsü bulaştıracağı ortalama insan sayısıdır. R_0 değeri model içinde bir eşiktir, eğer $R_0 \geq 1$ ise, incelenen popülasyondaki hastalık epidemik karakterdedir. Öte yandan, $R_0 < 1$ olduğu zaman, hastalık epidemik karakterde değildir ve giderek nüfus içinde yok olacaktır. Bunun yanında, R_0 değeri yöneticiler tarafından benimsenen sağlık politikalarının ne derece etkin olduğunu değerlendirmek açısından oldukça önemlidir. 9 Mart 2020'de KKTC'de ilk SARS-CoV-2 tanısı tespit edilmiştir. Bu tarihten itibaren, Yakın Doğu Üniversitesi (YDÜ) DESAM araştırmacıları günlük olarak R_0 değerini hesaplayarak sonuçları ilgili makamlara bildirmiştir. 15 Nisan 2021 tarihli SARS-CoV-2 verilerine göre KKTC'nin R_0 değeri 2,86 olarak hesaplanmış, hastalığın salgın karakterinde olduğu ortaya konulmuştur. Bu proje kapsamında KKTC için elde edilen tüm sonuçlar ve alınan önlemler anlatılmaktadır. Buna ek olarak, çevrimiçi anket yoluyla KKTC'de ikamet edenlerin SARS-CoV-2 salgınına yönelik uygulamaları, farkındalıkları ve tutumları sorgulanmıştır. Anketin sonuçları, pandemi döneminde farkındalık seviyesinin yüksek olduğunu ve uygulamalara titizlikle uyulduğunu ortaya koyarak, bu ihtiyatlı tavrın ülkedeki COVID-19 dinamiklerinde önemli bir rol

oynadığını göstermiştir. Ayrıca, 1 Temmuz - 9 Eylül 2020 tarihleri arasında KKTC'yi ziyaret eden hava yolu yolcularından elde edilen SARS-CoV-2 gerçek zamanlı polimeraz zincir reaksiyon testi verileri istatistiksel bir model olan binom yöntemi ile YDÜ DESAM COVID-19 laboratuvarı ve KKTC'deki diğer laboratuvarlar için R_0 değerinin hesaplanmasında kullanılmıştır. YDÜ DESAM için elde edilen R_0 değerleri KKTC Sağlık Bakanlığı ve/veya diğer laboratuvarlar ile karşılaştırılmıştır. Bu karşılaştırmada KKTC R_0 sonuçları eşik olarak kabul edilmiş ve SEIR modeli kullanılarak söz konusu zaman aralığı için hesaplanmıştır. Binom modelinin R_0 sonuçları ne kadar çok KKTC R_0 sonuçlarına benzerse, sonuçların o kadar güvenilir olacağı varsayılmıştır. YDÜ DESAM COVID-19 laboratuvarının sonuçları (ortanca R_0 0,98) KKTC R_0 (ortanca R_0 0,99) değeri ile uyumluyken, diğer laboratuvarların R_0 değerinin (ortanca R_0 1,25) uyumsuz olduğu gözlemlenmiştir. Bu bulgular, YDÜ DESAM COVID-19 laboratuvar verilerinin diğer laboratuvarlara göre daha güvenilir olduğunu göstermiştir. Benzer sonuçlar elde edildiğinden, SEIR modelinin binom yöntemlerini desteklediği sonucuna varılmıştır.

Anahtar kelimeler:

COVID-19, temel üreme sayısı, Kuzey Kıbrıs Türk Cumhuriyeti, matematiksel model, istatistiksel model, çevrimiçi anket

SECTION ONE: INTRODUCTION

1.1. Aims and Scope

Mathematical modelling has always had a significant place in the field of health sciences, especially in the study and analysis of infectious diseases. With the prevalence of various infectious diseases worldwide and more recently, with the emergence of COVID-19 pandemic, its application to public health research has increased significantly. By using mathematical methods, it is possible to study what is likely to happen in the future, to analyze the current situation of any given disease such as its epidemic character, as well as to monitor how well the adopted measures have worked to prevent the spread of the disease; the interventions such as vaccination, mask use, social distancing rules, quarantining etc.

The aim of this study was to use a mathematical model to analyze the dynamics of the COVID-19 outbreak shortly after the identification of the first positive SARS-CoV-2 case in Northern Cyprus. Susceptible-Exposed-Infected-Recovered model (SEIR), which is one of the fundamental methods of mathematical analysis and was applied to the SARS-CoV-2 case numbers in Northern Cyprus to calculate the basic reproduction number (R_0) on a daily basis. Calculation of the R_0 allowed the analysis of the epidemic character of the SARS-CoV-2 as well as monitoring the spread of the disease in conjunction with the intervention measures to prevent the spread of the disease. The calculation of the R_0 was presented to government authorities and the precautions were taken in accordance with R_0 values. Moreover, a statistical binomial method was used to calculate R_0 value for air passengers visiting Northern Cyprus who were diagnosed as SARS-CoV-2 positive and the results were compared with the SEIR model. Data obtained from NEU DESAM COVID-19 laboratory and from Northern Cyprus Ministry of Health and/or other laboratories were used.

1.2 General Information

1.2.1. Coronaviruses

Coronaviruses (CoVs) were first identified in the 1960s as a human pathogen Coronaviruses are large, 27–32 kb enveloped, positive-stranded RNA viruses, with club-like spike proteins which project from the surface resembling a crown-like appearance hence named the 'coronavirus' ('corona' being the Latin word for crown) (European Centre for Disease Prevention and Control 2021; Sharma et al. 2020).

CoVs viruses are found in the order of Nidovirales which includes Arteriviridae, Roniviridae, Mesoniviridae and Coronavirinae, families. The coronavirinae family subdivides into two subfamilies consisting of Coronaviridae and Torovirinae families. Coronaviridae further divides into four genera on their basis of phylogenetic clustering - the alpha, beta, delta and gamma coronaviruses.

Currently, seven known Coronaviridae CoVs can infect humans. Amongst these seven CoVs, four (HCoV-OC43, HCoV-HKU1, HCoV-229 and HCoV-NL63) of them can lead to mild to moderate seasonal respiratory tract disease. The other three have emerged recently (in the last 20 years) and can cause more severe to fatal respiratory tract infections: these are Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and SARS-CoV-2, which emerged in 2002, 2012, and 2019 respectively (Figure 1.1. - demonstration of the Human coronavirus Coronaviridae family taxonomy) (European Centre for Disease Prevention and Control 2021; Fehr and Perlman 2015; Synowiec et al. 2021).

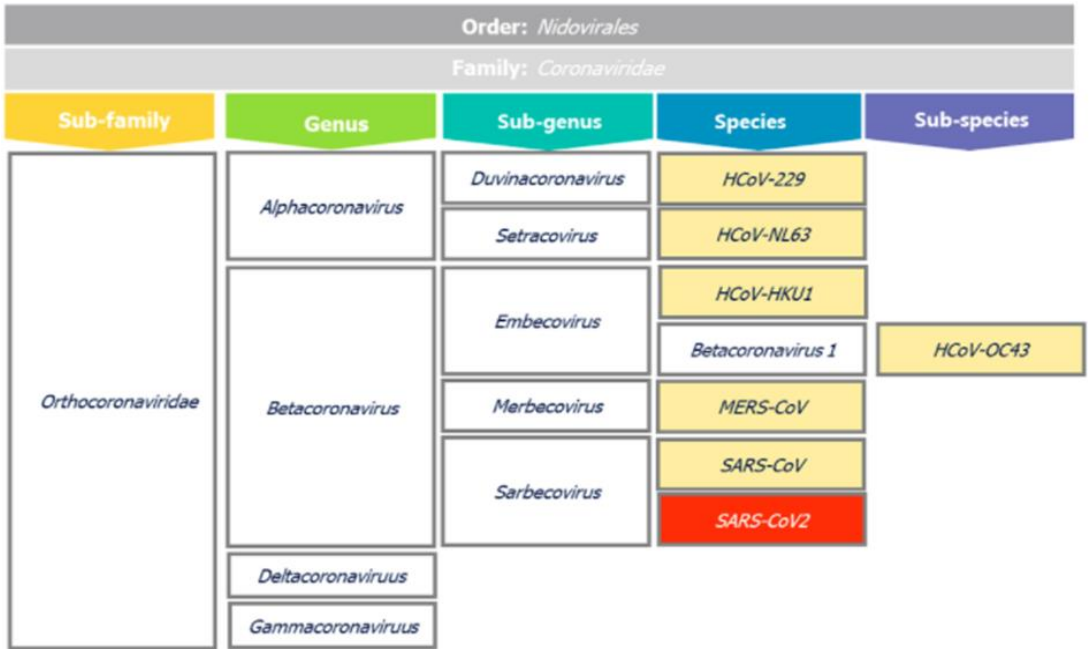


Figure 1.1. Taxonomy of human Coronaviruses (CoVs) Coronaviridae family.
The coronaviruses belong to the Nidovirales order which consists of four family groups. One of these families are the Coronaviridae which further subdivides into the sub-families of Coronaviridae and Torovirinae. Coronaviridae further subdivides into 4 genera - the alpha, beta, delta and gamma coronaviruses, and seven known species under these genera are known to be pathogenic to humans. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is one of these species which emerged in 2019 and led to a pandemic. This figure is adapted from (European Centre for Disease Prevention and Control 2021).

The more the virus circulates within the population the more likely it is to mutate. When one or more mutations take place a 'variant' of the original virus emerges (Sanjuán et al. 2010; WHO 2021c). CoVs are known with their high mutation and recombination rates (Lau and Chan 2015). Due to the known error frequency of RNA polymerases in the replication process, several point mutations are expected to take place within the 30 kb RNA genome On the other hand, in the RNA recombination process small or large deletions at the sites of recombination can occur leading to production of mutant viruses (Holmes 1999). Depending on where the mutations occur within the genetic material of the virus, the virus might gain the ability to cause infections, develop resistance to the available treatments, or become more transmissible. Thus, the high mutation rates render the treatment efficiency and development of vaccines to be difficult (Sanjuán et al. 2010; WHO 2021c).

The above mentioned features also enable CoVs to cross between species and adapt to a new host. Thus, they are referred to as the zoonotic viruses, meaning that transmission between animals and people is possible. SARS-CoV, MERS-CoV and SARS-CoV-2 all transferred to humans from infected civet cats, dromedary camels, and probably from horseshoe bats with an undetermined intermediate host respectively (Konda et al. 2020; WHO 2021a).

SARS-CoV which emerged in Guangdong province, China in 2002 accounted for approximately 8,000 confirmed cases with a 9.6% fatality rate. Although human to human transmission was efficient the epidemic cleared out in May 2004 as a result of the precautions taken as well as the seasonal nature of the virus. No new SARS-CoV-2 cases have been reported since then.

Ten years later, MERS-CoV emerged in Saudi Arabia and South Korea causing outbreaks. MERS-CoV is a virus that transferred to humans from infected dromedary camels. It is transmitted between animals and people, and it is contractible through direct or indirect contact with infected animals. Human to human transmission which required close and prolonged contact accounted for half of the cases approximately 2400 confirmed cases occurred with a fatality rate of 34% (Synowiec et al. 2021). From the 29th of January to 13th of February 2019, 39 cases of MERS-CoV have been reported and four MERS-CoV related deaths have occurred (WHO 2019).

In late December, 2019 a novel coronavirus which has not been previously identified in humans emerged in Hubei province, China (Synowiec et al. 2021).

1.2.2. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

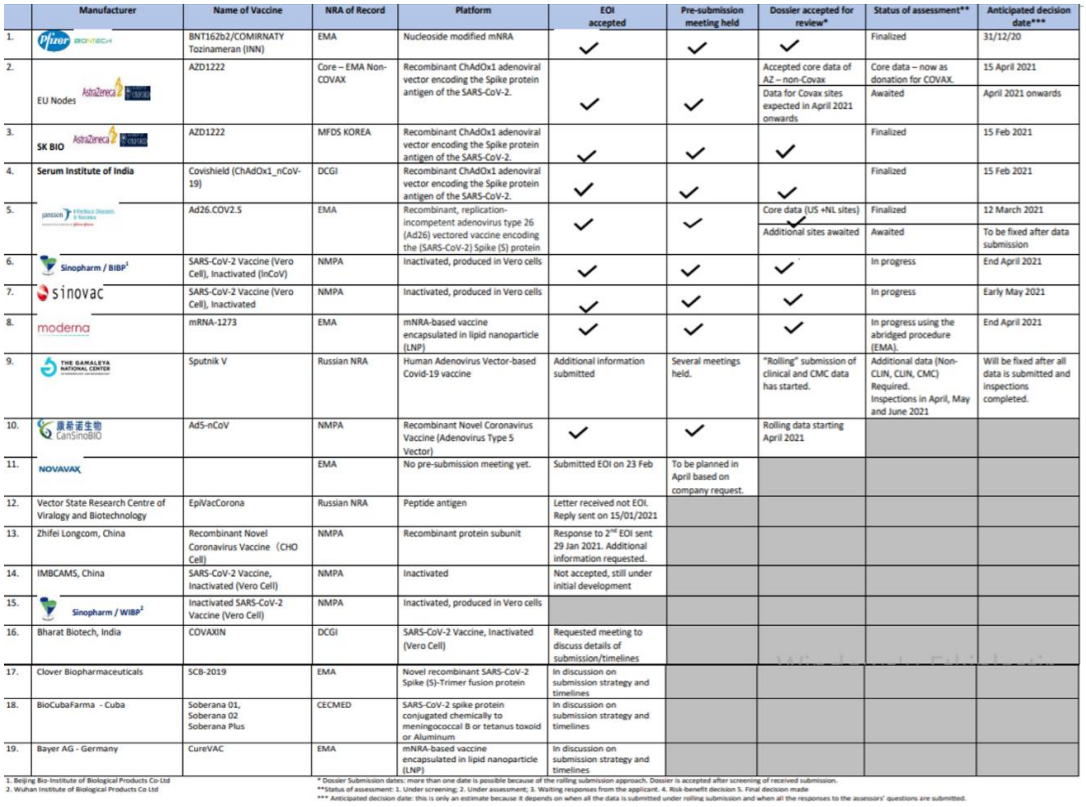
In late December 2019, a group of people in Wuhan, Hubei Province, China were diagnosed with pneumonia-like illness whose causative pathogen was identified soon after to be novel enveloped RNA betacoronavirus firstly named as the 2019 novel coronavirus (2019-nCoV). Later the 2019-nCoV was re-named as the SARS-CoV-2 by the International Committee on Virus Taxonomy due to the phylogenetic similarity to the previously isolated SARS-CoV in 2002 (Castagnoli et al. 2020). The disease caused by SARS-CoV-2 was named as ‘coronavirus disease 2019’ (COVID-19) in February 2020 by the World Health Organization (WHO) (Sharma et al. 2020).

SARS-CoV-2 emerged in early December 2019 in China, just before the Chinese New Year holiday period, during which a massive population movement occurs every year between rural and urban areas. This played a significant role in spreading the SARS-CoV-2 epidemic globally. Shortly after the infection spread to other countries and continents. On 11th March 2020, WHO announced that SARS-CoV-2 was characterized as a pandemic.

The SARS-CoV-2 pandemic continues to be a major public health problem more than a year after its emergence. Worldwide circulation of the virus among the global population over this long period of time has resulted in variants of the original SARS-CoV-2 to develop. These variants which emerged in the fall of 2020 majorly are: B.1.1.7, B.1.351, and P.1. The B.1.1.7 variant emerged in the United Kingdom and soon after its emergence it was detected in many other countries including the USA. It is suggested that the death rate of the B.1.1.7 variant is higher than the other known variants of the SARS-CoV-2. Independently of the B.1.1.7 variant, a second variant named B.1.351 emerged in South Africa, and other countries also reported cases attributed to this variant. Another known variant of SARS-CoV-2 is P.1 which emerged in Brazil, and soon after its discovery it was detected in other countries including the USA (CDC 2021).

Meanwhile, the vaccine developments against the SARS-CoV-2 continue rapidly. According to WHO vaccine development data, it is reported that at least seven different vaccines have been distributed to various countries and more than 200 additional vaccines are in development. Amongst the 200, 60 are in clinical development (WHO 2021b).

Pfizer/BioNTech vaccine was the first vaccine to receive the emergency validation from WHO since the beginning of the pandemic. Other available vaccines in use are demonstrated in Figure 1.2. (WHO 2020d).



	Manufacturer	Name of Vaccine	NRA of Record	Platform	EOI accepted	Pre-submission meeting held	Dossier accepted for review*	Status of assessment**	Anticipated decision date***
1.	Pfizer BIONTECH	BNT162b2/COMIRNATY Tozinameran (INN)	EMA	Nucleoside modified mNRA	✓	✓	✓	Finalized	31/12/20
2.	EU Nodes AstraZeneca	AZD1222	Core – EMA Non-COVAX	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	Accepted core data of AZ – non-Covax Data for Covax sites expected in April 2021 onwards	Core data – now as donation for COVAX. Awaited	15 April 2021 April 2021 onwards
3.	SK BIO AstraZeneca	AZD1222	MFDS KOREA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	15 Feb 2021
4.	Serum Institute of India	Covishield (ChAdOx1_nCoV-19)	DCGI	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	✓	✓	✓	Finalized	15 Feb 2021
5.	janssen	Ad26.COV2.S	EMA	Recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein	✓	✓	Core data (US +NL sites) ✓ Additional sites awaited	Finalized Awaited	12 March 2021 To be fixed after data submission
6.	Sinopharm / BIBP[1]	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV)	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	In progress	End April 2021
7.	sinovac	SARS-CoV-2 Vaccine (Vero Cell), Inactivated	NMPA	Inactivated, produced in Vero cells	✓	✓	✓	In progress	Early May 2021
8.	moderna	mRNA-1273	EMA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	✓	✓	✓	In progress using the abridged procedure (EMA).	End April 2021
9.	THE GAMALEYA NATIONAL CENTER	Sputnik V	Russian NRA	Human Adenovirus Vector-based Covid-19 vaccine	Additional information submitted	Several meetings held.	"Rolling" submission of clinical and CMC data has started.	Additional data (Non-CLIN, CLIN, CMC) Required. Inspections in April, May and June 2021	Will be fixed after all data is submitted and inspections completed.
10.	康希诺生物 CanSinoBIO	Ad5-nCoV	NMPA	Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)	✓	✓	Rolling data starting April 2021		
11.	NOVAVAX		EMA	No pre-submission meeting yet.	Submitted EOI on 23 Feb	To be planned in April based on company request.			
12.	Vector State Research Centre of Virology and Biotechnology	EpiVacCorona	Russian NRA	Peptide antigen	Letter received not EOI. Reply sent on 15/01/2021				
13.	Zhifei Longcom, China	Recombinant Novel Coronavirus Vaccine (CHO Cell)	NMPA	Recombinant protein subunit	Response to 2nd EOI sent 29 Jan 2021. Additional information requested.				
14.	IMBCAMS, China	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	NMPA	Inactivated	Not accepted, still under initial development				
15.	Sinopharm / WIBP[2]	Inactivated SARS-CoV-2 Vaccine (Vero Cell)	NMPA	Inactivated, produced in Vero cells					
16.	Bharat Biotech, India	COVAXIN	DCGI	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	Requested meeting to discuss details of submission/timelines				
17.	Clover Biopharmaceuticals	SCB-2019	EMA	Novel recombinant SARS-CoV-2 Spike (S)-Trimer fusion protein	In discussion on submission strategy and timelines				
18.	BioCubaFarma - Cuba	Soberana 01, Soberana 02 Soberana Plus	CECMED	SARS-CoV-2 spike protein conjugated chemically to meningococcal B or tetanus toxoid or Aluminum	In discussion on submission strategy and timelines				
19.	Bayer AG - Germany	CureVAC	EMA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	In discussion on submission strategy and timelines				

1. Beijing Bio-Institute of Biological Products Co Ltd
2. Wuhan Institute of Biological Products Co Ltd

* Dossier Submission dates: more than one date is possible because of the rolling submission approach. Dossier is accepted after screening of received submission.
**Status of assessment: 1. Under screening, 2. Under assessment, 3. Waiting responses from the applicant. 4. Risk-benefit decision 5. Final decision made
*** Anticipated decision date: this is only an estimate because it depends on when all the data is submitted under rolling submission and when all the responses to the assessors' questions are submitted.

Figure 1.2. Status of COVID-19 Vaccines.

One of the diagnostic methods used to detect SARS-CoV-2 infection is the real-time reverse transcription polymerase chain reaction (rRT-PCR). By using the rRT-PCR method, viral nucleic acid of SARS-CoV-2 can be qualitatively detected efficiently from the samples obtained from nasopharyngeal or oropharyngeal swabs. To date, due its specificity, this test is considered as the gold standard in detection of SARS-CoV-2 infection (Rao, Agarwal, and Batura 2020).

1.2.3 General status of the current COVID-19 pandemic world wide

The first patient admission of SARS-CoV-2 positive case was reported on 12th of December 2019 and the first SARS-CoV-2 related death occurred in early January 2020 in China. Subsequently, by mid-January 2021 travel-related cases began reaching the United States, Thailand, South Korea, France, and Japan. By the end of January 2020, the spread of the virus has already reached South-East Asia, Canada, Europe, Western Pacific, USA and Eastern Mediterranean countries (Sanyaolu et al. 2021).

According to WHO statistics data as of 15th of April 2021, 137.866.311 confirmed cases of SARS-COV-2 have been reported and 2.965.707 COVID-19 related deaths occurred globally. COVID-19 cases' distribution by regions can be visualized in Figure 1.3. (WHO 2021d).

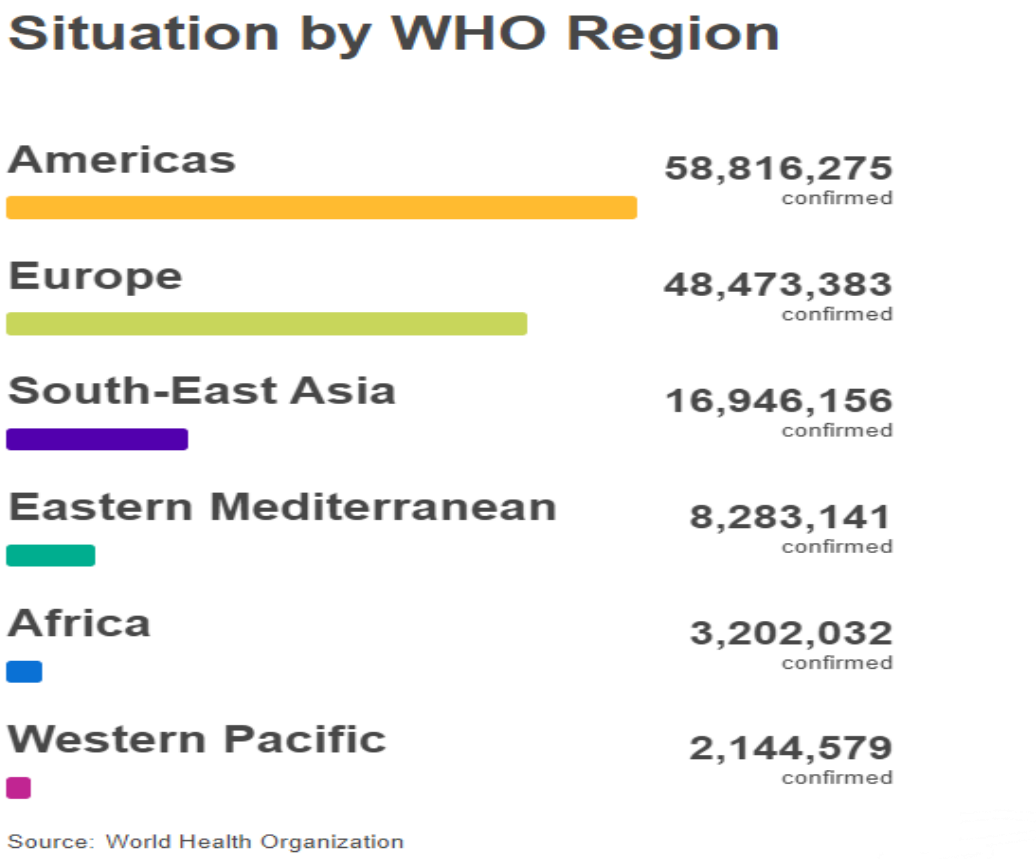


Figure 1.3. SARS-CoV-2 confirmed cases distribution worldwide.

As it can be seen from the figure, from WHO statistics data as of 15th of April 2021, the United States takes the first place for the number of positive SARS-CoV-2 cases. This is followed by the European, South East Asian, Eastern Mediterranean, African and Western Pacific countries (WHO 2021d).

To combat the spread of the virus, a total of 734.121.870 vaccine doses have been administered worldwide as of 15th of April 2021 (WHO 2021d). Seychelles, Israel, United Arab Emirates, Chile, Bahrain, Bhutan, UK, USA, Maldives and San Marino are the top 10 countries that have the highest vaccine rates in relation to their

population. Figure 1.4. demonstrates the doses of vaccine administered per 100 people among the populations of different countries (The New York Times 2021).

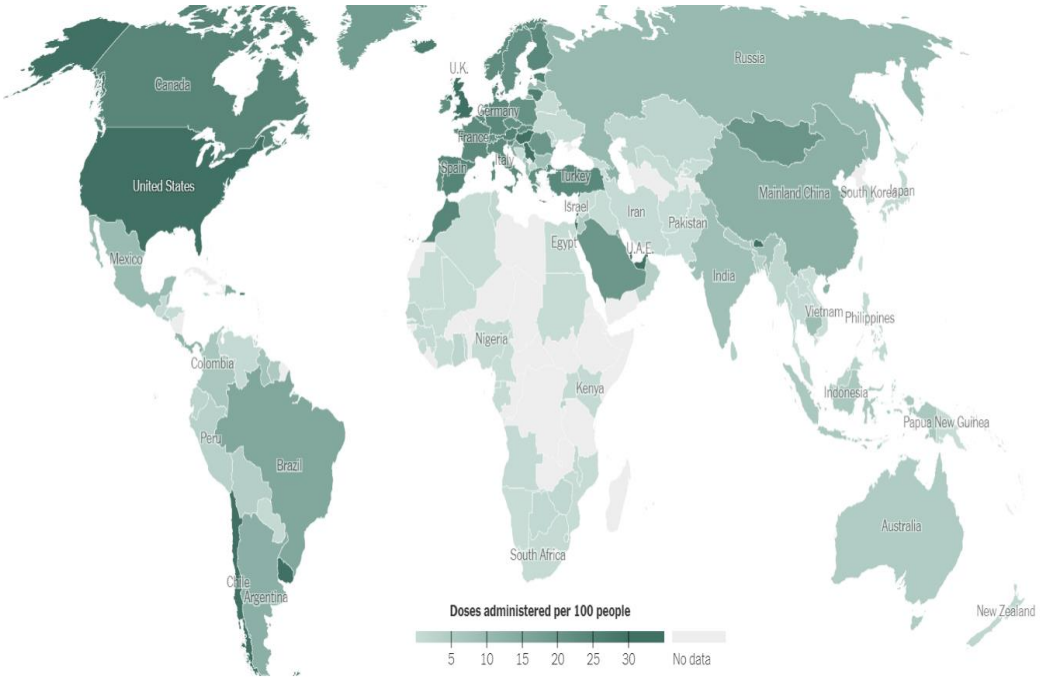


Figure 1.4. Doses of vaccine administered per 100 people in the population of different countries.

1.2.4 General status of the current COVID-19 pandemic in Northern Cyprus

It was thought that the first case of SARS-CoV-2 in Northern Cyprus was identified on 9th of March in a female German tourist who came to visit Northern Cyprus with a tour group on 8th of March 2020. On 9th March the German tourist (65) was hospitalized with high fever and diagnosed as SARS-CoV-2 positive (patient zero) (Sultanoglu et al., 2020).

However, a study has later proven that the first case of SARS-CoV-2 was not the aforementioned German tourist, but a 17-year-old male Northern Cyprus citizen from Famagusta (Baddal et al. 2021)

As of 15th of April 2021, statistics for Northern Cyprus show that, since the identification of patient zero, a total of 862 270 tests have been conducted, revealing a 5337 positive SARS-CoV-2 cases and 28 COVID-19 related deaths (Figure 5).

In Northern Cyprus, the population is approximately 375 000, majority of whom are Turkish Cypriots. Fifteen percent of the population have been successfully vaccinated with two doses against SARS-CoV-2 infection and the rest of the population is waiting to be vaccinated when the country is supplied with more vaccines (TRNC Ministry of Health 2020c)

Figure 1.5. COVID-19 Chart for Northern Cyprus for 15th of April 2021

1.2.5. General status of the current COVID-19 pandemic in the Southern part of Cyprus

When compared on a population level, the overall picture of the COVID-19 pandemic is similar in the Southern part of the Cyprus where Greek Cypriots live in majority with a population of approximately 875 900 (REPUBLIC OF CYPRUS MINISTRY OF FINANCE 2018).

The first COVID-19 cases in the Southern part of Cyprus were detected on 9th of March 2020. These were two people with recent travel history, from Italy and the United Kingdom (Quattrocchi et al. 2020).

As of 8th of April 2021, statistics for the Southern part of Cyprus show that since the identification of the first SARS-CoV-2 case a total of 49 988 confirmed SARS-CoV-2 cases has been identified in which 268 COVID-19 related deaths occurred. It is reported that 6.0% of the population have been vaccinated with two doses against SARS-CoV-2 infection (Statistics 2021).

1.2.6 What is the Mathematical Model and why is it used?

Mathematical modeling is a multidisciplinary field that can bridge the study of mathematics and health sciences to address scientific hypotheses, and solve related questions. When applied to the surveillance data of any infectious disease, mathematical modeling becomes an important tool to study the dynamics of infectious diseases. In this way, the size of the epidemic in the studied population can be revealed and the appropriate levels of intervention could be applied to control the spread of the disease. Moreover, the mathematical model can be applied to the surveillance data after the intervention has been introduced to assess the efficacy of disease-control policy (Grassly and Fraser 2008; Zaman et al. 2017).

Many infectious diseases have been studied with a mathematical model such as the HIV, Hepatitis B, influenza etc (Hincal et al. 2019; Kanyiri, Mark, and Luboobi 2018; Zhao, Xu, and Lu 2000). Mathematical modeling can also be used to carry out simulation analysis in order to predict what is likely to happen in future for the disease in question.

With the rise of the SARS-CoV-2 pandemic, mathematical models were one of the most prominent tools to study and analyze the dynamics of the SARS-CoV-2.

Susceptible-Exposed-Infected-Recovered model - referred to as the SEIR, is one of the fundamental mathematical models applied to the infectious diseases data to analyze the dynamics of the diseases as well as the epidemiology.

By applying the surveillance data of any infectious disease to the SEIR model, basic reproduction number denoted as the R_0 can be calculated. R_0 is the number of

infected people from one infected individual (Figure 1.6.). R_0 is the threshold within the mathematical model such that when $R_0 < 1$, the disease is under control and will disappear eventually within the population. On the other hand, when $R_0 \geq 1$ the disease is not under control, will continue to spread it is at an epidemic character within the studied population.

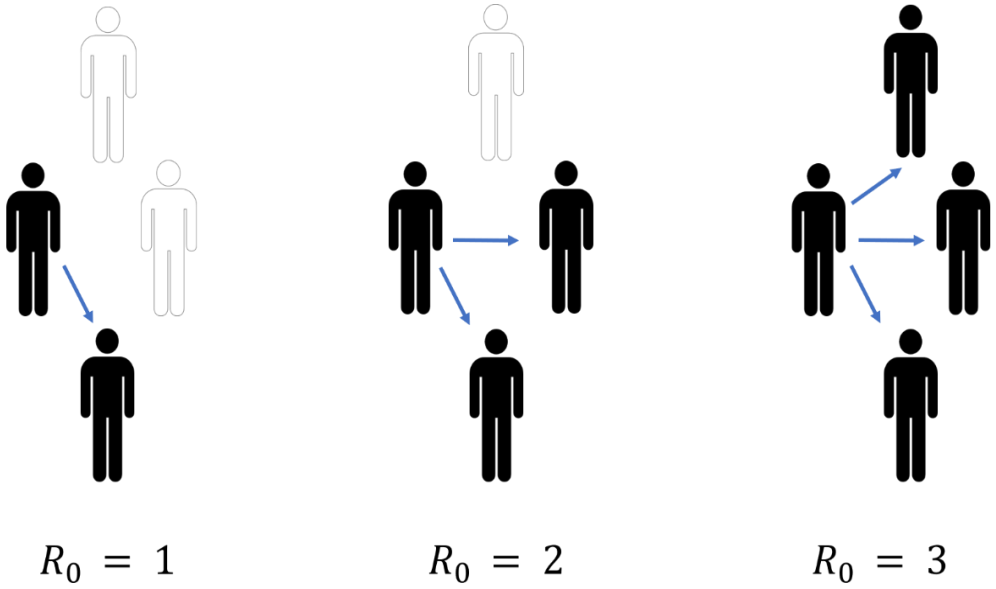


Figure 1.6. The representation of the basic reproduction number.
Basic reproduction number referred to as R_0 and it is the number of infected people from one infected individual. The value of R_0 is important in determining the dynamics of the studied infectious disease. The calculated R_0 value from the mathematical model, after the integration of the parameters needed, if the value is equal to 1 or above 1, the disease is in epidemic character and continues to spread within the population. Whereas, when the R_0 is below one, the disease within the studied population will die out eventually and it's not in epidemic character.

1.2.7. Statistical model - the Binomial method

Besides aforementioned mathematical models, there are also statistical models employed in studying the epidemiology of infectious diseases. An example of a statistical model that can be used to study and analyze infectious disease dynamics is the binomial method. The use of binomial methods is not widely adopted compared to the SEIR model. However, when compared to SEIR model it requires fewer number of parameters for the calculation of R_0. In the SEIR model, calculation of R_0 value requires the parameters of transmission rate, disease induced death rate, progression

rate, birth rate, death rate and population number of the studied region. Whereas when calculating the R_0 value for only one parameter such as the number of positive cases of an infectious disease is sufficient to obtain R_0 value.

As a part of this study, we have compared R_0 values calculated via a mathematical model - SEIR, to a statistical model - binomial method.

1.2.8. The use of Online Surveys

Qualitative analysis provided by an online survey conducted at the early stages of April 2020, in the first lockdown during this pandemic period in Northern Cyprus complemented the results obtained via mathematical modelling. During the pandemic period, conventional survey methods were not feasible. Thus, surveys conducted on online platforms have become an important tool for COVID-19 research (Hlatshwako et al. 2021). Many online research surveys have been conducted to measure the overall knowledge of the population as well as to investigate a variety of subjects in relation to COVID-19. The survey subjects included: perceptions during infectious disease outbreaks, knowledge, attitudes, and practices towards COVID-19 and psychological impact of COVID-19 (Geldsetzer 2020; Tee et al. 2020; Zhong et al. 2020). The results of the online surveys are important for public health policies since when reported to relevant authorities' new regulations can be set in accordance with the survey results conducted within the population.

SECTION TWO: MATERIALS AND METHODS

2.1. Mathematical Model of Northern Cyprus

Near East University (NEU) DESAM Mathematical group has designed a model which was adopted from Umar et al. (accepted yet unpublished manuscript: Bulletin of the Karaganda University - Mathematics-2021, *Transmission Dynamics and Control Strategies of COVID-19: A Modelling Study*, Umar T. Mustapha, Evren Hincal, Abdullahi Yusuf, Sania Qureshi, Tamer Sanlidag, Salisu M. Muhammad, Bilgen Kaymakamzade, and Nezihal Gokbulut) to study and analyze the dynamics of SARS-CoV-2 in Northern Cyprus. The model consists of seven compartments as follows:

$$I_1, I_2, Q, H, S, E, R$$

- Susceptible (S): all individuals within the population is considered as susceptible to get the disease
- Exposed (E): people who are likely to be exposed to SARS-CoV-2
- Quarantined (Q): quarantined individuals due to possible SARS-CoV-2 exposure
- Infected 1 (I_1,): SARS-CoV-2 infected and indicating mild to moderate symptoms
- Infected 2 (I_2,): SARS-CoV-2 infected and indicating severe symptoms
- Hospitalized (H): hospitalized individuals due to the SARS-CoV-2 infection
- Removed (R): recovered individuals after the SARS-CoV-2 infection

A simplified version of the model, devised by Near East University DESAM Mathematical team, is demonstrated in Figure 2.1.

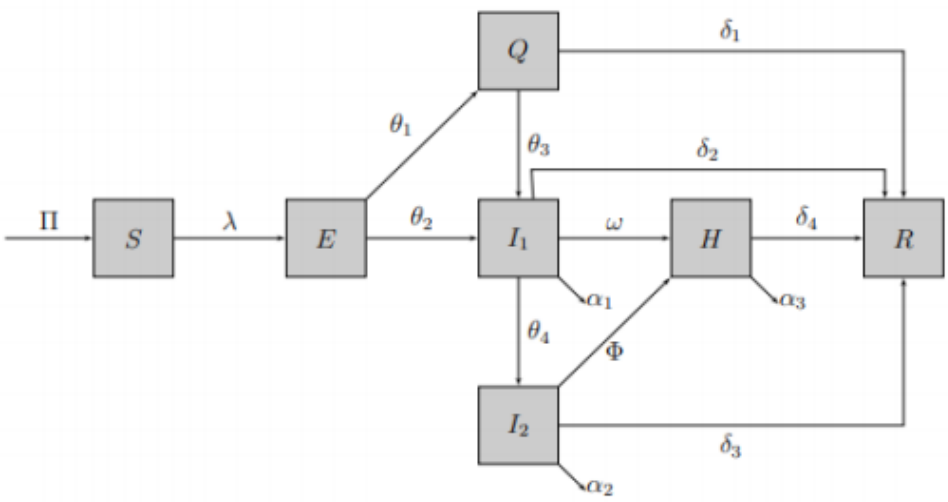


Figure 2. 1. Compartments of the Mathematical model of Northern Cyprus.
The simplified version of the mathematical model is demonstrated consisting of the seven compartments. These seven compartments are indicated as I_1, I_2, Q, H, S, E, R with the meaning of susceptible, exposed, quarantined, infected with SARS-COV-2 indicating mild to moderate symptoms, infected with SARS-CoV-2 indicating severe symptoms, hospitalized individuals due to SARS-CoV-2 infection and recovered individuals from the infection; respectively. The data demonstrated in Table 1.1 was used and input into the devised model to calculate the basic reproduction number.

Table 1.1. The parameters and variables needed for Northern Cyprus to calculate basic reproduction number

Parameter	Meaning	Value
β	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
ω	Hospitalization rate from I_1 class	0.000089
φ	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 compartment I_1, I_2, Q, H respectively to S	0.16, 0.45, 0.46, 0.056

All the values for parameters needed to calculate the basic reproduction number (R_0) were obtained from the Northern Cyprus state planning official website (TRNC State Planning Organization 2020). The meaning of each parameter is described. (I_1: people infected with SARS-CoV-2 showing mild to moderate symptoms, I_2: people infected with SARS-CoV-2 showing severe symptoms, Q: quarantined individuals due to possible exposure of the virus, H: hospitalized individuals due to SARS-CoV-2 infection and S: susceptible individuals - all individuals living in the same population are considered as susceptible contracting the SARS-CoV-2)

2.2 An online survey among Northern Cyprus residents about COVID-19

An online survey was designed and conducted between 7th and 17th of April 2020 during the partial curfew to analyze the practices, awareness and attitudes towards the SARS-CoV-2 in Northern Cyprus. The survey was on demographics (5 questions), awareness (7 questions), practices (6 questions) and attitudes towards the SARS-CoV-2 outbreak (3 questions) with a total of 21 questions. This study was conducted on Northern Cyprus residents only. This sole criterion was clearly conveyed to the

participants at the beginning of the survey with the statement 'please contribute to the survey only if you are a Northern Cyprus resident'. Since the survey was open to 'residents', non-Northern Cyprus citizens who are residing in the North were also welcome to participate. The survey was conducted in Turkish as the main language of the country, and only through online medium. These factors posed some limitations to this study since the survey questions were only available to speakers of Turkish who had technological devices. The collected data was analyzed using the SPSS Statistic, Version 24.0. Near East University Ethics Committee (YDU/2020/78-1041) approved the study (supplement document 1).

2.3 Comparing R_0 values for SARS-CoV-2 rRT-PCR Data from Laboratories Across Northern Cyprus

2.3.1. Laboratory data collection

Between 1st July to 9th September 2020 a total of 62 air passengers screened in the NEU DESAM COVID-19 laboratory were diagnosed to be SAR-CoV-2 positive. During this period, according to the Northern Cyprus Ministry of Health regulations, passengers from air, sea and land border were allowed to enter Northern Cyprus upon presenting two separate SARS-CoV-2 rRT-PCR tests. This was referred to as the double screening procedure which involved performing a rRT-PCR test 72 to 120 hours prior to departure and also immediately upon arrival at the border. Until the results of the second rRT-PCR test were released, passengers were obligated to self-isolate themselves, otherwise legal action was taken against them. From 1st to 12th July 2020, the rRT-PCR detection kit referred to as Bio-Speedy® (Bioeksen R&D Technologies Inc. COVID-19 rRT-PCR Detection Kit v2.0, Istanbul-Turkey) was used (Biospeedy 2020). Whereas, from 13th July to the 9th of September 2020, Diagnovital® (RTA Laboratories Inc, SARS-CoV-2 Real-Time PCR Kit v2.0 Istanbul-Turkey) (Diagnovital 2020) was used in the NEU DESAM COVID laboratory to detect SARS-CoV-2 . In both of the kits, combined nasopharyngeal and oropharyngeal swab samples were used. In the detection of a positive SARS-CoV-2 sample, three different confirmative steps were applied. Firstly, the rRT-PCR test from the previously combined nasopharyngeal and oropharyngeal swab was repeated. Secondly, an isolation test from the swab sample was performed using Diagnovital Magicprep Fast Exraction kit 2 and RNA Diagnovital RTA Viral RNA isolation Kit

(Istanbul-Turkey). Thirdly, these samples were screened in two different devices namely an Insta Q96 plus Mumbai, India rRT-PCR device and Rotor-Gene-Q (Qiagen, Hilden, Germany).

During the same time period, 88 SARS-CoV-2 positive cases from the air passengers were detected by Northern Cyprus Ministry of Health laboratories and/or private laboratories. This information was tracked on the Northern Ministry of Health for the 71-day period since reporting of such cases is mandatory.

2.3.2 Binomial Method

A statistical model of binomial method was used to calculate the R_0 values for SARS-CoV-2 positive cases obtained from NEU DESAM COVID-19 laboratory and Ministry of Health and/or private laboratories performing SARS-CoV-2 rRT-PCR tests in the studied period of time for air passengers upon arrival in Northern Cyprus. In order to calculate the R_0 values, only the number of positive SARS-CoV-2 cases were used.

The statistical distributions used in the binomial method were gamma, binomial and posterior. Some of the SARS-CoV-2 positive cases were reported the day after their diagnosis. In order to minimize the error in the delay in reported cases gamma distribution was implemented. Thus, this ensured accurate forecasting by using the initial data. In gamma distribution, mean and standard deviation of reported SARS-CoV-2 cases were represented as follows:

$$\delta \sim \Gamma(\mu, \sigma) \tag{1}$$

Here, δ referred to as delay in the reported SARS-CoV-2 cases. On the other hand, μ, is the mean and σ is the standard deviation of reported cases.

Binomial distribution which is a random process leads into two exact outcomes: success or failure. For the purpose of this study, the binomial distribution was the assumption of cases, where success corresponds to the positive SARS-CoV-2 cases, and failure corresponds to the negative SARS-CoV-2 cases. By using this distribution, represented as below, upcoming week's SARS-CoV-2 cases were determined by using the previous week's cases.

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

The reported positive cases of SARS-CoV-2 in the days between 1st July to 9th of

September 2020 were input into this formula. Here, the number of cases is denoted as C_t 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 was required as evidence. Here, the prior distribution was the binomial distribution and the evidence was 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. To see the infectiousness of SARS-CoV-2 in Northern Cyprus, posterior distribution was used for daily R_0 values for NEU DESAM COVID-19 and other laboratories with the formula given below.

$$\rho_t = \frac{FR}{r_t} \tag{3}$$

Where ρ_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 1st July to 9th 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. To act as a threshold to the R_0 obtained from binomial method, Northern Cyprus R_0 values were calculated using the previously mentioned SEIR model, with the input of all SARS-CoV-2 cases diagnosed during the above time period. Total of 386 positive SARS-CoV-2 cases diagnosed in that time period as well as the variables described in the Table 1.1 was used to calculate the R_0 for Northern Cyprus. Near East University Ethics Committee (YDU/2020/85-1213) approved this study (supplement document 2.).

SECTION THREE: RESULTS

3.1. Basic reproduction number calculated for Northern Cyprus on a daily basis

With the announcement of the patient zero by Northern Cyprus Ministry of Health, the mathematical modeling group of the NEU COVID-19 DESAM Research Institute adapted the model devised by Umar et al. (accepted manuscript: Bulletin of the Karaganda University - Mathematics-2021, *Transmission Dynamics and Control Strategies of COVID-19: A Modelling Study*, Umar T. Mustapha, Evren Hincal, Abdullahi Yusuf, Sania Qureshi, Tamer Sanlidag, Salisu M. Muhammad, Bilgen Kaymakamzade, and Nezihal Gokbulut) and calculated the R_0 for each day for Northern Cyprus as shown in Figure 3.1.

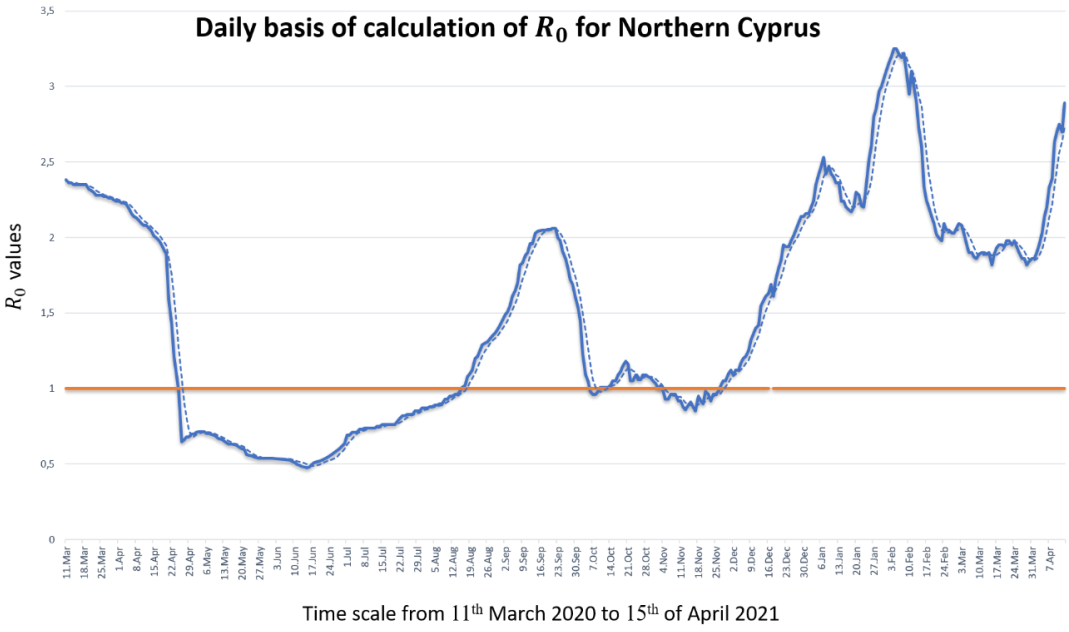


Figure 3. 1. Basic reproduction number (R_0) pattern for Northern Cyprus.
The figure demonstrates the basic reproduction number (R_0) pattern calculated for Northern Cyprus using a mathematical model for the period of 11th of March 2020 to 15th April 2021. The R_0 fluctuated throughout the pandemic in correlation with the measures taken.

Soon after the identification of patient zero, strict measures and regulations were introduced throughout Northern Cyprus to prevent the spread of the virus. These strict measures and regulations included:

- Closure of schools and universities on 10th of March
- Implementation of travel restrictions on 14th of March, which allowed only Northern Cyprus citizens to enter the country with a mandatory, 14-day self-isolation at home.
- On 23rd of March a partial day time curfew was adopted in which people were only allowed to leave their homes for essential needs such as market and pharmacy visits, and from 31st March 2021 onwards a full curfew between 09.00pm to 06.00am was announced.

As mentioned above, these measures were adopted after 9th March. A report summarizing the COVID-19 epidemic in Northern Cyprus, entitled '**Current situation of COVID-19 in northern Cyprus**' was written and published in one of the WHO journals - Eastern Mediterranean Health Journal. Soon after its publication, the report reached number one among the most read reports in the Journal in 2021. This report is also the first publication by WHO that used the term 'northern Cyprus'. This is significant since the territory is unrecognized by other countries except Turkey (Eastern Mediterranean Health Journal 2021; Sultanoglu et al. 2020) (supplement documents 3 and 4).

By using the model, between 11th of March and 24th of April 2020, the calculated R_0 value fluctuated between 2.38 and 1. The change of the R_0 values are easily observed on Figure 3.1., in tandem with the implementation of new regulations. During this period, with the detection of the first case of SARS-CoV-2, schools were closed on March 10th 2020 followed by the closure of borders on March 14th 2020. Additionally, cultural and artistic events were canceled and places of worship were prohibited. In addition, a partial curfew was declared on March 23rd 2020. With these measures taken, the epidemic was brought under control in a short period of time, within approximately one and a half months. Also, no new SARS-CoV-2 cases were diagnosed between April 17th and July 1th 2020 in Northern Cyprus. Between April 25th and August 15th 2020, the calculated R_0 value fluctuated as 0.48-0.98. During this

period, the partial curfew ended on April 29th and in addition, borders were reopened on July 1th 2020. With the opening of the country's borders, the virus was reintroduced to the country and transmission rates started to increase. As of August 16th 2020, the R_0 value was 1 and above ($R_0 \geq 1$). In the first weeks of September 2020, the R_0 value increased up to 2.1. With the additional measures taken, the epidemic was brought under control in November 2020. However, during the first weeks of December, the epidemic started to take off rapidly, and the R_0 value increased to 2.60 on December 30th 2020. The rise in the R_0 continued after this time reaching a peak value of 2.47 on 6th of January 2021. Following this increase, fluctuations around 2.30 occurred, followed by a rise with the value of R_0 reaching 3.25 on 4th February 2021. Then a steep decreasing trend occurred following the fluctuation in 1.95 in mid-March 2021. Following this, R_0 value showed a dramatic increasing pattern which started on 3rd April with 1.95 and reaching 2.89 by 15th April 2021 (Figure 3.1.).

The mathematical modeling group of the NEU COVID-19 DESAM Research Institute monitored this process on a daily basis, reported it to decision makers in the country at certain intervals and shared it with the public. As a result, the measures taken throughout the course of the epidemic have been updated.

3.2 Practices, Awareness and Attitudes of Northern Cyprus residents towards SARS-CoV-2 outbreak

The survey consisted of 21 questions and was completed by 738 Northern Cyprus residents in the days between via online platforms. The social-demographic characteristics of the survey participants are presented in Table 3.1. Majority of the participants were (30.6%) (226) between the ages of 31 and 40, female (67.3%) (497), with an education status of Bachelor's degree (38.8%) (286), Northern Cyprus citizen (90.0%) (664) and from Nicosia 53.7% (396).

Table 3.1. Socio-demographic characteristics of the participants

	n	%
Age		
30 age and below	193	26.2
31-40 age	226	30.6
41-50 age	142	19.2
51-60 age	119	16.1
61 age and above	58	7.9
Gender		
Female	497	67.3
Male	241	32.7
Education status		
Primary school	48	6.5
High School	188	25.5
Bachelor degree	286	38.8
Post graduate degree	141	19.1
PhD	75	10.2
Citizenship		
Northern Cyprus citizen	664	90.0
Other	74	10.0
Districts		
Nicosia	396	53.7
Famagusta	103	14.0
Kyrenia	169	22.9
Guzelyurt	32	4.3
Iskele	22	3.0
Lefke	16	2.1

The questions studying the awareness of Northern Cyprus residents on COVID-19 were as follows. The 76.8% (567) stated that they first heard of COVID-19 on social networks and followed information, developments and measures about COVID-19 on Facebook (87.0 %) (642) amongst the other social networks. Social media page of Northern Cyprus Ministry of Health (Facebook, Instagram) was the most followed page (69.1%) (510) when compared with the social media pages of Local news agencies (Facebook, Instagram) (48.1%) (355), Social media page of Northern Cyprus Prime Ministry Directorate of crisis communication (36.3%) (268) and Anonymous social media (i.e. Facebook, Instagram) group(s) etc. 15.0% (111). When the awareness of the adopted measures was questioned, it was revealed that 80.0% (590) were aware that only essential services were open; all other shops, entertainment

centers etc. were closed. Moreover, 78.3% (578) were aware that only Northern Cyprus citizens with an obligatory 14-day quarantine were allowed to come from abroad. 56.8% percent were aware that there was no access between the districts and 60.6% knew that no gatherings were allowed in clubhouses and public worship was prohibited. Only 12% (1.6%) indicated that they were not aware of the aforementioned precautions.

At the same time, most common symptoms of COVID-19, mode of SARS-CoV-2 transmission and COVID-19 characteristics were examined. Most of the participants were aware of the symptoms, mode of transmission and the characteristics of the diseases such that 96.3 % (711) were conscious of the symptoms of high fever, dyspnea and dry cough, 96.2% (710) stated they knew that they could contract the disease via Sneeze and/or cough from a COVID-19 infected person and 93.9% (693) knew when close contact with an infected person or touching the mouth, nose or eyes after contact with contaminated objects, they could contract the virus. Only 0.4% (3) participants were unaware of the above stated transmission routes of SARS-CoV-2. On the other hand, when the knowledge of COVID-19 characteristics was examined among the participants it was revealed that 96.8% (714) had the knowledge of the severe effects COVID-19 had on the elderly, people with weak immune systems and chronic diseases; 92.6% (683) knew the incubation period of the virus and 41.5% (306) knew the COVID-19 agent was SARS-CoV-2 (Table 3.2.).

Table 3.2. Awareness of Participants on COVID-19

	n	**%**
Where they first heard about COVID-19		
Social Networks	567	76.8
Radio/TV/Newspaper	149	20.2
Friends/Relatives	22	3.0
Where the follow information, developments and measures about the COVID-19 Outbreak		
Facebook	642	87.0
TV channels	489	66.3
SMS by Northern Cyprus government	170	23.0
Newspapers	159	21.5
Twitter	84	11.4
YouTube	62	8.4
Official Authorities	30	4.1
Radio	67	9.1

Table 3.3. Awareness of Participants on COVID-19 (Continuation)

	n	%
Social Networks for COVID-19 Developments		
Social media pages of the Northern Cyprus Ministry of Health (Facebook, Instagram)	510	69.1
Local news page(s) on social media (Facebook, Instagram)	355	48.1
Social media page of Northern Cyprus Prime Ministry Directorate of crisis communication	268	36.3
Anonymous social media (i.e. Facebook, Instagram) group(s) etc.	111	15.0
None	28	3.8
Previous Information on the measures and precautions taken in Northern Cyprus for the COVID-19 pandemic		
All shops, establishments, casinos, night clubs, bet offices, entertainment centers etc. will be closed other than services that provide basic needs in the private sector like pharmacies, petrol stations and supermarkets	590	80.0
14-day quarantine for Northern Cyprus citizens if they come from abroad	578	78.3
Administrative leave for all public officers other than police, fire department, health, civil aviation, financial matters etc.	524	71.0
No access between districts in Northern Cyprus	419	56.8
No gatherings at associations and clubhouses, or public worship	447	60.6
None	12	1.6
Most common symptoms of COVID-19		
High fever	711	96.3
Dyspnea	643	87.1
Dry cough	636	86.2
Mode of SARS-CoV-2 Transmission		
Sneeze and/or cough from a COVID-19 infected person	710	96.2
Close contact with an infected person	700	94.9
Touching the mouth, nose or eyes after contact with contaminated objects	693	93.9
No idea	3	0.4
COVID-19 characteristics		
Severe effect on elderly, people with weak immune systems and chronic diseases	714	96.8
Incubation period between 2-14 days	683	92.6
COVID-19 agent is called SARS-CoV-2	306	41.5
Low mortality rate	189	25.6

Another point of the survey was to investigate the participants' personal practices with regards to COVID-19 pandemic: for example, to what extent they follow the hygiene rules of washing hands, proper house cleaning, or following the curfew rules when outdoors. Generally, the participants were observed to follow the various

hygiene and preventative measures against COVID-19: 96.9% (715) washed their hands frequently with water and soap for at least 20 seconds, 95.5% stated that they washed their hands after toilet use, 93.0% (686) indicated that they open windows to let fresh air into the house, 78.9% (582) only left the house during the studied period for supermarket and pharmacy visits. When outdoors 75.3% (556) declared that they wear a mask and 85.5% (631) stated that they do not enter the house with their shoes on when coming from outside. (Table 3.3)

Table 3.4. Practices of Participants regarding COVID-19

	n	**%**
Hygiene rules during the COVID-19 pandemic		
I frequently wash my hands with water and soap for at least 20 seconds	715	96.9
I avoid hugging, hand-shaking and kissing	692	93.8
When water and soap are not available, I use antiseptic hand gel or cologne	672	91.1
I use disposable tissues when coughing and sneezing or I sneeze and cough into my elbow if there is no paper tissue	650	88.1
When the wash hands with water and soap		
After using the toilet	705	95.5
Before preparing food	684	92.7
Before eating	673	91.2
After wiping my nose, coughing or sneezing	645	87.4
After contact with animal feed or animals	434	58.8
Sometimes wash my hands for less than 20 seconds	205	27.8
Issues related to domestic and surface cleanliness during the COVID-19 pandemic		
I often let fresh air in from windows	686	93.0
I clean the most touched surfaces (door knob, sockets etc.) with bleach or alcohol-based cleaning agents	621	84.2
I clean cell phones, tablets and computer keyboards with alcohol-based disinfectants or cologne	578	78.3
No cleaning	9	1.2
Following the curfew rules in Northern Cyprus		
I go to the supermarket and pharmacy	582	78.9
I go to the bank	103	14.0
I do not leave the house	150	20.3
I go to the park	3	0.4
Precautions taken when outdoors		
I wear a mask even without symptoms	556	75.3
I do not touch my mouth, nose or eyes	627	85.0

Table 3.5. Practices of Participants regarding COVID-19 (Continuation)		
	n	**%**
I wear gloves	535	72.5
I wear a mask if I have symptoms (i.e., cough, sneeze)	81	11.0
I do not take any precautions	2	0.3
Precautions when returning home from outside during the COVID-19 pandemic		
I do not enter the house with my shoes on	631	85.5
I immediately wash my hands with water and soap for at least 20 seconds	699	94.7
I wash my clothes	540	73.2
I take a shower	462	62.6
I enter the house after disinfecting my shoes	141	19.1

Besides the practices and knowledge against the COVID-19 pandemic, attitudes of the participants about the current COVID-19 pandemic were questioned. Upon this investigation, 41.3% revealed that measures taken by the government were sufficient whereas, 58.7% stated that it was insufficient. 96.9% believed that increasing the awareness of the disease within the population is important to prevent the spread of the virus. Lastly, the question 'Do you believe that Northern Cyprus will win the fight against the COVID-19?' was asked to the participants to reveal their overall attitudes toward the COVID-19 pandemic in Northern Cyprus. Upon this question it was shown that most of the participants of 83.2% (614) believed that Northern Cyprus would win the fight against COVID-19 (Table 3.4.) (Supplement document 5).

Table 3.6. Attitudes of the Participants towards COVID-19

	n	**%**
Sufficiency of the Measures taken against COVID-19		
Sufficient	305	41.3
Not sufficient	433	58.7
Is the awareness of COVID-19 in Northern Cyprus important in preventing the spread of the virus?		
Yes	715	96.9
No	23	3.1
Do you believe that Northern Cyprus will win the fight against COVID-19?		
Yes	614	83.2
No	124	16.8

3.3 The calculation of R_0 values using SARS-CoV-2 rRT-PCR Data from Laboratories Across Northern Cyprus via Binomial Method

With the Binomial method outlined in Methods section 2.3.3 R_0 values were calculated separately with confidence intervals of 2.5%, 50%, and 97.5% for data from NEU DESAM COVID-19 laboratory, and data from Northern Cyprus Ministry of Health and/or private laboratories obtained from 1st July to 9th September 2020 for rRT-PCR positive results arriving as air passengers (Table 3.5.). In the studied period 62 and 88 air passengers with the double screening rRT-PCR were detected in NEU DESAM and other laboratories respectively.

Table 3.7. Median basic reproduction number (R_0)values in confidence intervals of 2.5%, 50%, and 97.5% for COVID-19 rRT-PCR results obtained from NEU DESAM and other laboratories for air passengers to Northern Cyprus

From 1st July to 9th 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)

(CI:Confidence Interval)

In the context of this study, 50% confidence interval was considered to represent the most reliable results since it was representing the majority of data obtained at least with 50% of data containing the true value. Whereas, in the 2.5% confidence interval, only small part of the population was represented which made it difficult for generalizing the outcomes. On the other hand, 97.5% confidence interval ignored any possible errors with a high percentage that was interfering with the future predictions negatively. Thus 50% confidence interval result was considered as the most reliable. In Figure 3.2. and 3.3. normal distribution of the data used in the Ministry of Health

and/or private COVID-19 laboratories and NEU DESAM COVID-19 laboratory are indicated, demonstrating that most of the data used were in 50% representing the real situation of the pandemic.

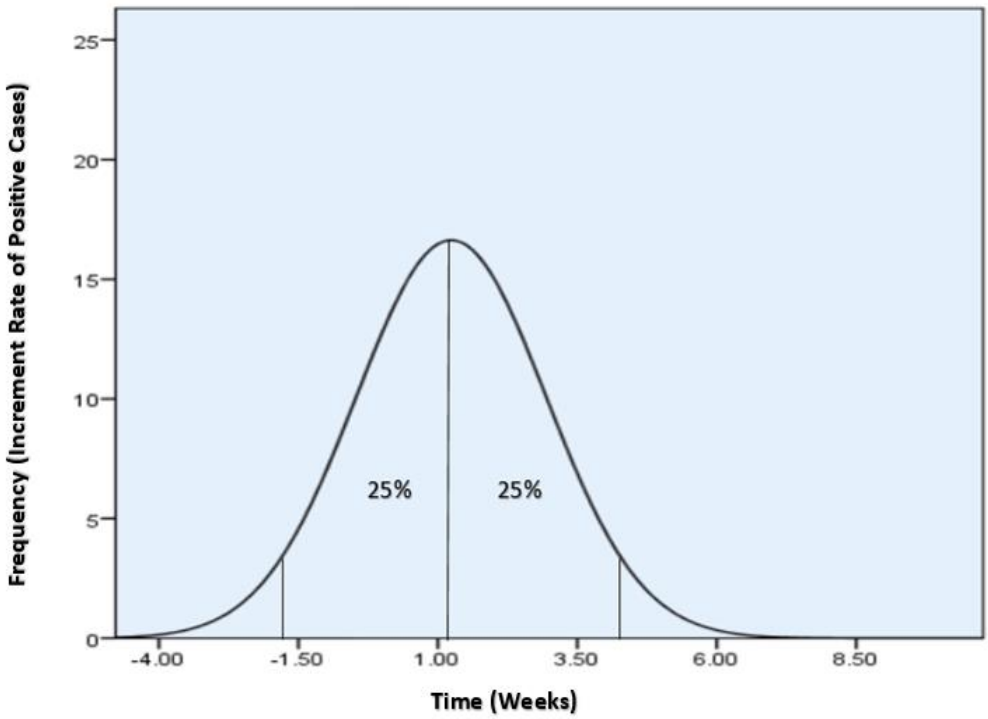


Figure 3.2. Normal distribution for Ministry of Health and/or private COVID-19 laboratories diagnosing positive SARS-CoV-2 cases for air passengers in the study period of 9 weeks. The normal distribution of the SARS-CoV-2 positive cases identified among air passengers from 1st July to 9th September 2020 in Northern Cyprus Ministry of Health and/or private laboratories diagnosed by real-time reverse transcription polymerase chain reaction (rRT-PCR) are given. Figure was generated using the SPSS Version 24.

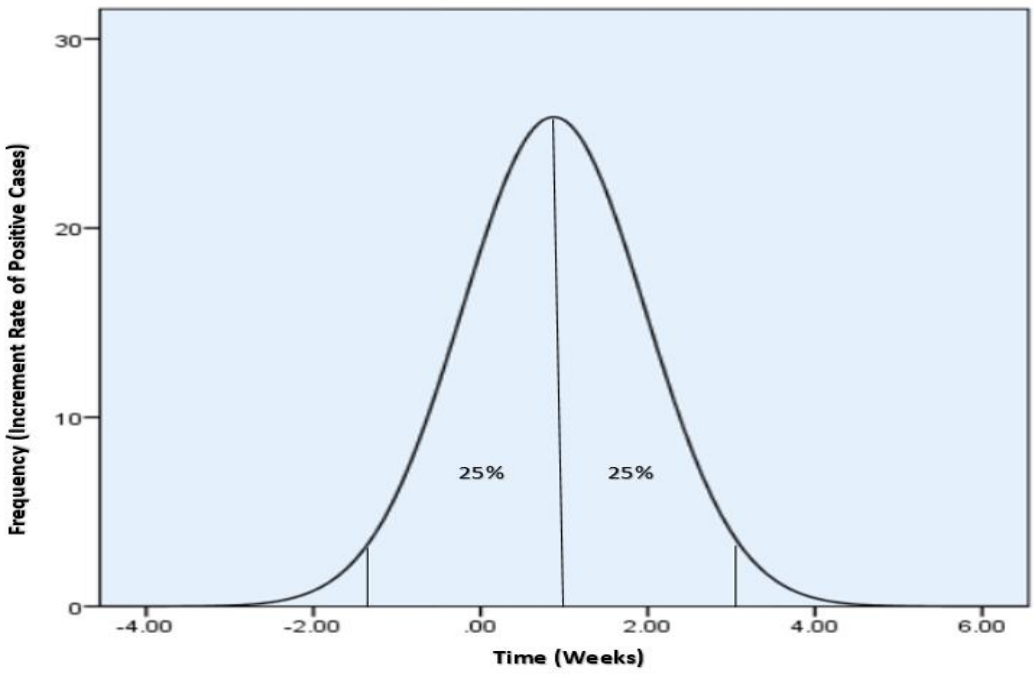


Figure 3.3. Normal distribution for NEU DESAM COVID-19 laboratory diagnosing positive SARS-CoV-2 cases for air passengers in the study period of 9 weeks. The normal distribution of the SARS-CoV-2 positive cases identified among air passengers from 1st July to 9th September 2020 in NEU DESAM COVID-19 laboratory diagnosed by real-time reverse transcription polymerase chain reaction (rRT-PCR) are given. Figure was generated using the SPSS Version 24.

To act as a threshold, R_0 values for air passengers in NEU DESAM and other laboratories in the studied period were calculated using binomial model. R_0 value of the Northern Cyprus with all diagnosed SARS-CoV-2 cases in the same period were calculated using the previously mentioned SEIR model in section 3.1. The same parameters previously in Table 1.1. were applied with the only change being the number of SARS-CoV-2 positive which was 386 for Northern Cyprus for the studied period. The comparison of median R_0 values for NEU DESAM and for other laboratories are indicated in Table 3.6. It was revealed that with this comparison, the median value of R_0 for NEU DESAM COVID-19 (0.96) was much similar with the overall R_0 value for Northern Cyprus (0.99). Whereas, in other laboratories R_0 value (1.29) was not in a range with either that of Northern Cyprus nor that of NEU DESAM.

Table 3.8. NEU DESAM COVID-19 and other laboratories Comparison with median basic reproduction number (R_0) values of the median R_0 value of Northern Cyprus

From 1st July to 9th 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)

(TRNC Ministry of Health 2020a, 2020b)

(CI:Confidence Interval)

Moreover, the daily basis of R_0 values were also plotted for NEU DESAM and other laboratories (using air passengers' data), and for Northern Cyprus R_0 (using all diagnosed SARS-CoV-2) in the studied period, which is shown in Figure 3.4. Here, the overall Northern Cyprus R_0 value indicated a very similar pattern to the R_0 values of NEU DESAM COVID-19 laboratory. In comparison, other laboratories showed a different pattern - higher R_0 values than those of Northern Cyprus and NEU DESAM COVID-19 laboratory. We assumed that the more similar the R_0 results of Northern Cyprus to the result of NEU DESAM and other laboratories are, the more reliable the results will be. This assumption was made since the Northern Cyprus R_0 results represented the whole SARS-CoV-2 distribution of the country. Thus, we concluded that NEU DESAM COVID-19 laboratory's estimations and real data were more reliable since it was consistent with the overall Northern Cyprus R_0 values. In addition, this firmly implied that statistical modelling supports the mathematical modelling because the results were consistent (supplement document 6.)

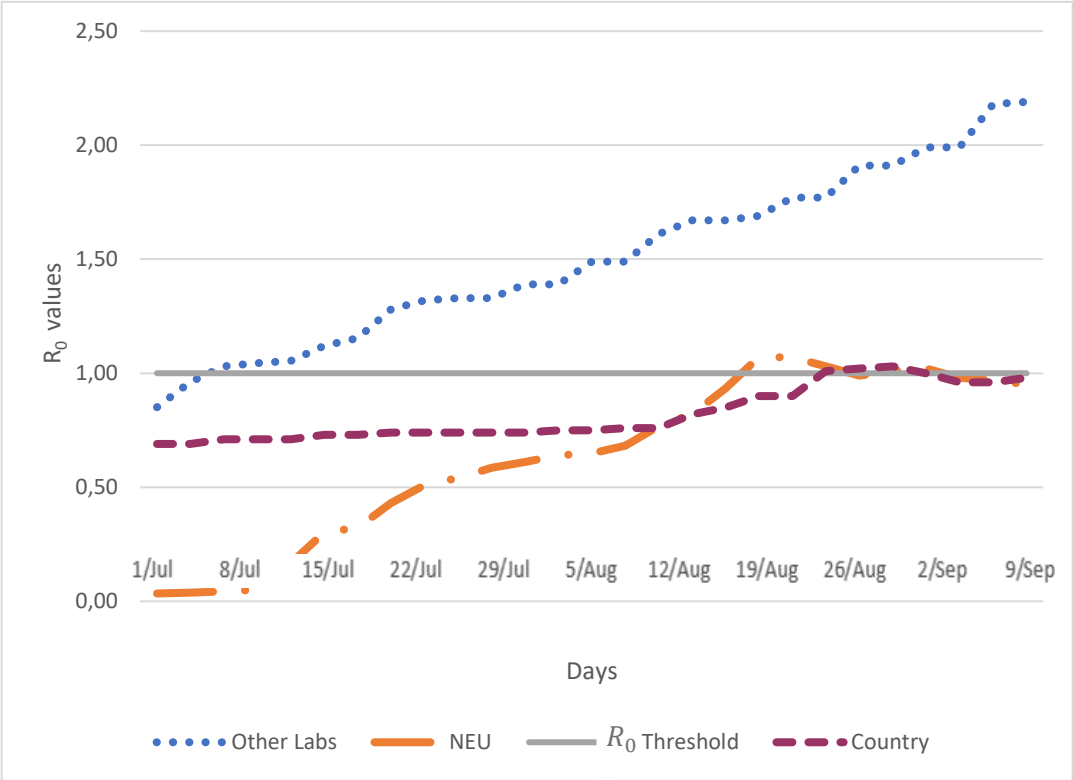


Figure 3.4. Daily basis Comparison of basic reproduction number (R_0) values of NEU DESAM COVID-19 and other laboratories to Northern Cyprus R_0 values.

Basic reproduction number (R_0) for NEU DESAM and other laboratories based on the SARS-CoV-2 positive cases among air passengers were calculated using the binomial method. Whereas, Northern Cyprus R_0 value was calculated using the mathematical model based on all diagnosed SARS-CoV-2 cases in that period. It was assumed that the more consistent the results obtained via binomial method are with the mathematical model of Northern Cyprus the more reliable the results will be. The comparison revealed that the NEU DESAM COVID laboratory R_0 values were consistent with those of Northern Cyprus whereas other laboratories' R_0 results were not consistent. For majority of the studied period, NEU DESAM COVID-19 and Northern Cyprus R_0 values were below 1, suggesting that SARS-CoV-2 was under control. However, other laboratories performing rRT-PCR analysis for air passengers indicated R_0 values above 1 for most of the studied period, suggesting that SARS-CoV-2 was not under control in the country.

SECTION FOUR: DISCUSSION

4.1. From the first positive case of SARS-CoV-2 on 9th March 2020 to current situation as of 15th of April 2021

Northern Cyprus government took precautions the day after the first positive case of SARS-CoV-2 was diagnosed on 9th of March 2020. With the announcement of the first patient, NEU DESAM COVID-19 mathematical team implemented a mathematical model adapted for Northern Cyprus and calculated the R_0 value on a daily basis. The R_0 value fluctuated in accordance with the alternating regulations. This was easily tracked by the R_0 value demonstrated in Figure 3.1.

The team has worked and is still working actively through the COVID-19 pandemic period and reporting these results to relevant authorities in the government as well as sharing them periodically with the public. The R_0 values were the key determinant in setting of the new regulations for public health. It would not be wrong to say that the NEU DESAM COVID-19 team was the invisible hero of the medical science board of the Northern Cyprus government.

According to the currently available data up until 15th April 2021, Northern Cyprus R_0value was calculated to be 2.89. This means that on average, one infected SARS-CoV-2 person in Northern Cyprus may infect at least 3 individuals on average. In addition, since the R_0 value is above one, the SARS-CoV-2 infection in Northern Cyprus is in epidemic character.

4.2. Revealing of online survey results conducted among Northern Cyprus residents to relevant authorities

Many online surveys have been carried out worldwide to study and collect data of different aspects of COVID-19 within the studied population. Also, with the start of pandemic, we observed a lot of surveys on online platforms implemented for Northern Cyprus. Our survey was one of the first conducted and in terms of its subject remit around ‘Awareness, practices and attitudes’ it is the first online survey that was successfully peer reviewed and published.

The online research survey conducted from 7th to 17th April 2020 with a total of 738 participants revealed that majority of the Northern Cyprus residents were aware of the precautions, had high knowledge of the characteristics of COVID-19 and had a positive attitude towards the battle against COVID-19. As result of the survey, it was concluded that Facebook (87.0%) (642) was the most used social media channel in terms of following the news on COVID-19 in Northern Cyprus. Moreover, majority of the participants were following the suggested practices during the pandemic such as washing hands, wearing masks and avoiding physical contact.

The result of the study indicated the importance of residents' knowledge and practices towards the SARS-CoV-2 outbreak is critical in the prevention of the spread of the virus. In addition, authorities began to announce more information on online platforms since most of the participants followed social media compared to other channels such as TV, newspaper or the radio.

4.3. The binomial approach: Comparing the R_0 values across Northern Cyprus

In addition to SEIR mathematical model, a statistical model called binomial method was implemented to calculate R_0 for Northern Cyprus. In this study, only SARS-CoV-2 positive cases among air passengers were used in the nine-week period (1st July to 9th September 2020). This study was conducted using laboratory results and tests performed in NEU DESAM laboratory and allowed the comparison of other laboratories performing rRT-PCR for air passengers in the same period. Also, to act as threshold to this comparison aforementioned SEIR model was used to calculate the R_0 value for Northern Cyprus. It was assumed that the more the results of the binomial method were similar to the SEIR model, the more reliable the results would be.

As a result of this study, as depicted in Figure 3.4., the pattern of NEU DESAM R_0 values based on SARS-CoV-2 cases among air passengers were in a very similar pattern with Northern Cyprus R_0. This implied that the results of NEU DESAM were consistent with those of Northern Cyprus even when just using the air passengers' data and no other groups. However, other laboratories' rRT-PCR R_0 results were out of pattern when compared to NEU DESAM as well as Northern Cyprus R_0 results. We were able to interpret the results as follows: The higher value of R_0 obtained from other laboratories might be due to the reported number of false positive SARS-CoV-2

cases. The number of false positive cases can be explained by a variety of problems such as inexperienced staff mis-diagnosing the cases, contaminations in the laboratories, not confirming the positive results with SARS-CoV-2 RNA isolation and the problems associated with the kits used.

We argue that it is very critical to train specialists in this field in order to analyze the results efficiently and thus, to avoid mis-diagnosis. Moreover, it is equally vital to carry out screening and diagnosis in well-equipped laboratories.

In accordance with these results, it was suggested that the consistency of R_0 values of NEU DESAM COVID-19 laboratory with those of Northern Cyprus were owing to the state-of-the-art equipment as well as the rigorous protocol followed in the laboratory. The protocol included performing SARS-CoV-2 RNA isolation to ensure accurate diagnosis of SARS-CoV2 cases and the results were analyzed by molecular biology experts and an infectious disease specialist.

This study suggested that standardization of procedure in COVID-19 rRT-PCR screening is needed. In addition, the study pointed out the importance of the double screening procedure since in the studied period of 71 days, 62 and 88 positive SARS-CoV-2 cases were identified in NEU DESAM COVID-19 laboratory and in other laboratories across Northern Cyprus; respectively.

Present research was unique in many ways as mentioned above but it is also one of the rare studies that have used mathematical model as well as a statistical model to calculate and compare R_0 results. The results obtained from the binomial method was consistent with the mathematical model. Hence, for future studies binomial method can be adapted easily as it is a very intuitive option for studying the dynamics of infectious diseases. In this study, only positive SARS-CoV-2 cases diagnosed were used to calculate the R_0 values. Whereas in a mathematical model many other parameters are required such as the population numbers, birth and death rates, transmission rate and so on.

SECTION FIVE: CONCLUSION

Considering the population of Northern Cyprus, SARS-CoV-2 cases and related death rates are relatively low. Although, the Northern Cyprus government is not recognized politically except by Turkey and has very limited resources, we believe that Northern Cyprus has been a 'good model' compared to other countries in the battle against COVID-19 pandemic. As of 15th April 2021, a total of 862 270 SARS-CoV-2 tests have been conducted, revealing 5337 positive SARS-CoV-2 cases and 28 COVID-19 related deaths. With the designated mathematical adapted for Northern Cyprus, R_0 value calculated to be 2.89 which indicated that the COVID-19 outbreak is in epidemic character within the country. For future avenues of possible research, incorporating different SARS-CoV-2 variants into the model could be done as further analysis to visualize dynamics of the virus.

In conclusion, various factors such as lack of a well-equipped public transport infrastructure, relatively high vaccination rates (approximately 15% of the population received their two doses), high education levels as well as high socioeconomic status among the population have all played a significant role in shaping the dynamics of COVID-19 in Northern Cyprus.

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APPENDIX

Supplement document 1 - Ethics Committee approval YDU/2020/78-1041

YAKIN DOĞU ÜNİVERSİTESİ
BİLİMSEL ARAŞTIRMALAR ETİK KURULU

ARAŞTIRMA PROJESİ DEĞERLENDİRME RAPORU

Toplantı Tarihi : 23.04.2020

Toplantı No : 2020/78

Proje No :1041

Yakın Doğu Üniversitesi Tıp Fakültesi öğretim üyelerinden Prof. Dr. Tamer Şanlıdağ'ın sorumlu araştırmacısı olduğu, YDU/2020/78-1041 proje numaralı ve **"Yeni Koronavirüs Salgınıyla İlgili Kuzey Kıbrıs Türk Cumhuriyeti Halkının Farkındalığı"** başlıklı proje önerisi kurulumuzca online toplantıda değerlendirilmiş olup, etik olarak uygun bulunmuştur.

Prof. Dr. Rüştü Onur

Yakın Doğu Üniversitesi

Bilimsel Araştırmalar Etik Kurulu Başkanı

Supplement document 2 - Ethics Committee approval YDU/2020/85-1213

YAKIN DOĞU ÜNİVERSİTESİ
BİLİMSEL ARAŞTIRMALAR ETİK KURULU

ARAŞTIRMA PROJESİ DEĞERLENDİRME RAPORU

Toplantı Tarihi : 26.11.2020

Toplantı No : 2020/85

Proje No :1213

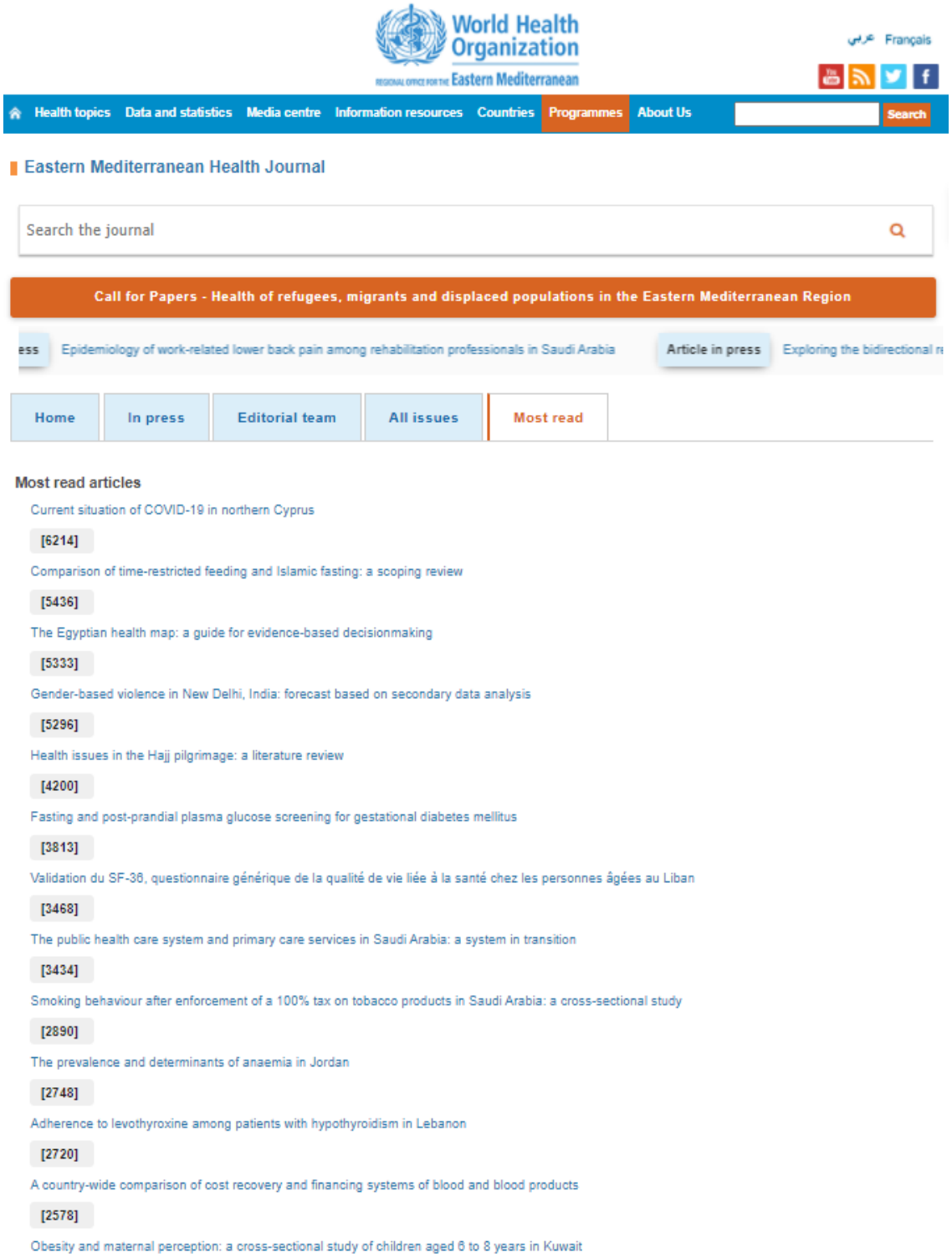
Yakın Doğu Üniversitesi DESAM Enstitüsü öğretim üyelerinden Prof. Dr. Tamer Şanlıdağ'ın sorumlu araştırmacısı olduğu, YDU/2020/85-1213 proje numaralı ve **"Comparison of Near East University DESAM COVID-19 laboratory rRT-PCRresults from air passengers to other laboratories by Binomial method"** başlıklı proje önerisi kurulumuzca online toplantıda değerlendirilmiş olup, etik olarak uygun bulunmuştur.

Prof. Dr. Rüştü Onur

Yakın Doğu Üniversitesi

Bilimsel Araştırmalar Etik Kurulu Başkanı

Supplement document 3 - Eastern Mediterranean Journal Most Read on 18.04.21



Supplement document 4 - Current situation of COVID-19 in northern Cyprus

Current situation of COVID-19 in northern Cyprus

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Abstract

Background: The public health burden of the novel coronavirus disease 2019 (COVID-19) is expected to increase and urgent strict measures by decision-makers is critical for the containment of the novel coronavirus (SARS-CoV-2) outbreak worldwide.

Aims: This study aimed to give a real-time analysis of COVID-19 presence in northern Cyprus.

Methods: All official SARS-CoV-2 positive cases were tracked and reported in terms of the origin, nationality, and transmission routes. Preventive measures taken after the first reported case were analyzed for their effectiveness as control strategies.

Results: The index case of SARS-CoV-2 in northern Cyprus was identified as a female German tourist. First local case had travel history from the United Kingdom after which local transmission occurred. Rapid and strict containment measures have currently delayed a peak in observed cases.

Conclusions: Rapid implementation of social-distancing measures, good hygiene measures and travel/gathering bans in northern Cyprus has been effective in controlling the outbreak.

Keywords: SARS-CoV-2, COVID-19, Cyprus, surveillance, control measures

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Introduction

As of 11 March 2020, the World Health Organization (WHO) announced that the global spread of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) had become unstoppable and reached the required epidemiological characteristics to be declared as a pandemic (1). As of 4 May 2020, it has been confirmed that 3 435 894 people have been infected with SARS-CoV-2, out of which 239 604 deaths have occurred. Without a doubt, one of the most affected countries has been China where the pandemic emerged in Wuhan, one of the largest cities in Hubei province, and from there spread throughout the country, with 84 400 confirmed cases of SARS-CoV-2 and 4643 deaths. However, it appears that China has recently started to take control of the SARS-CoV-2 outbreak, with a declining trend of SARS-Co-V-2 cases, but the number of cases of SARS-CoV-2 continues to rise in other countries. According to the WHO Coronavirus Disease 2019 (COVID-19) Situation Report on 4 May 2020, 206 299 confirmed cases and 7971 deaths had occurred in the Eastern Mediterranean Region (2). Cyprus is the third largest island in the Mediterranean with a population of approximately 375 000 in the north, the majority of whom are Turkish Cypriots (3,4).

Methods

All official SARS-CoV-2 positive cases were tracked and reported in terms of the origin, nationality, and transmission routes. Preventive measures taken after the first reported case were analyzed for their effectiveness as control strategies.

Results

The first case of SARS-CoV-2 was identified as a female German tourist on 9 March 2020, who had arrived in northern Cyprus on 8 March 2020. As a result, people who were found to have had close contact with, or tourists who had travelled on the same plane as the first patient, were exposed to SARS-CoV-2 and were quarantined in three different hotels. Shortly after the identification of the first positive case of SARS-CoV-2, precautions were enacted in northern Cyprus, which continue to be amended for the benefit of the local population (5-7). Below are the important precautions taken by the Council of Ministers with regard to the current SARS-CoV-2 outbreak in northern Cyprus to prevent further transmission. The Decisions of the Council of Ministers announced that:

- All civil workers in the public sector except for police, fire brigade, civil aviation, finance, and health workers are considered on administrative leave.
- In the private sector, all shops including casinos, nightclubs, betting offices, entertainment centres, etc., except for businesses that provide services within the

framework of meeting basic needs such as pharmacies, gas stations, bakeries, and markets, are closed.

- Only northern Cyprus citizens and persons who have legal permission to reside in the country can enter northern Cyprus through sea, air and land border gates; entries to northern Cyprus by all other country citizens are banned.
- Regardless of which country they come from, northern Cyprus citizens and legal residents who enter the country through sea, air and land gates will be monitored and quarantined at home for 14 days. For those who do not comply with this requirement, legal action will be initiated under the Communicable Diseases Law No. 45/2018.
- Gathering in associations, unions, locales and performing collective worship are banned.
- To encourage citizens to remain in their homes, a full curfew from 21.00 to 6.00 hours is in force.
- Northern Cyprus citizens studying abroad were repatriated using charter flights, and students were quarantined for 14 days in hotels. After the 14-day quarantine period, all quarantined individuals were screened using a rapid antibody detection test. Individuals with a negative rapid test result were required to self-isolate in their homes for a further 7 days. Those with a positive rapid test result went through further confirmatory screening by polymerase chain reaction (PCR) test. These individuals were sent home if they had a negative PCR result and asked to self-isolate in their homes for a further 7 days, or were quarantined further in the case of a positive PCR result.
- After the identification of the first SARS-CoV-2 cases in Karpasia, 3 villages in Karpasia are quarantined (full curfew) and only controlled entry and exit are allowed in these villages (correct as of 27 March 2020)
- Mandatory use of face masks in public areas has been implemented by the government since 24 April 2020 (8-13).

In addition, Burhan Nalbantoglu State Hospital located in Nicosia has been fully transformed into a pandemic hospital, except for dialysis and oncology departments. Health workers will work in shifts for two weeks and will be accommodated in hotels and dormitories so as not to expose their families to the risk of infection (14).

Moreover, the 1102 Call Centre, as well as three mobile telephone numbers, were announced by the Ministry of Health as SARS-CoV-2 reporting lines. The 1102 number can be reached immediately from both landline phones and GSM operators, with more call operators commissioned to work in the call centre, where 5 calls can be taken at the same time and 10 people can be put on hold. The system has been designed to respond to callers in both Turkish and English. All citizens will be able to reach the call centre 24 hours a day, 7 days a week (15).

Although all precautions were taken rapidly, the number of SARS-CoV-2 cases identified in northern Cyprus has increased after the identification of the first case and the situation as of 4 May 2020 is summarized in Table 1. The number of cases per day after the first case (index case) was detected between 9 March 2020 and 4 May 2020 are shown in Figure 1. An increasing trend was observed after the first case was diagnosed. However, since the precautions were taken on time, the identified cases were from the same group of German tourists, since it is likely that transmission occurred in between them before the precautions were taken.

Conclusion

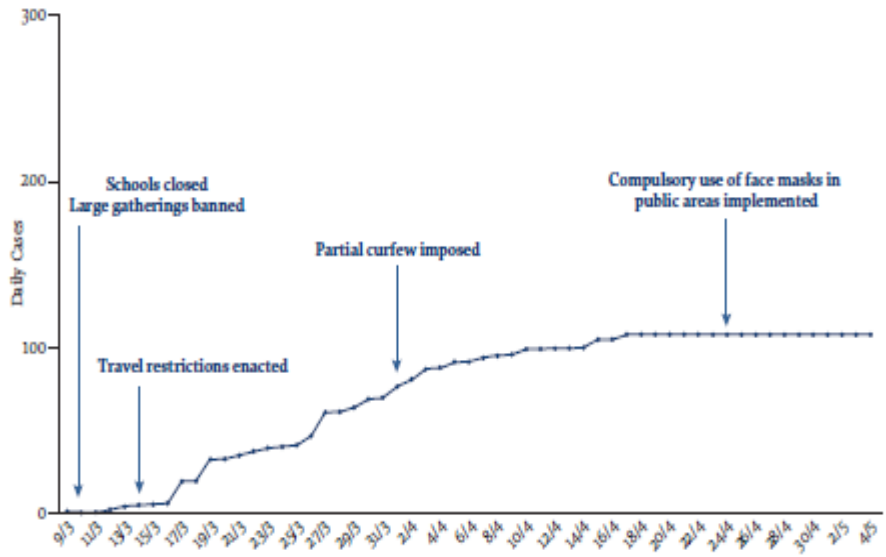
It is believed that as a result of the precautions that were implemented rapidly, the transmission from the German tourist group to the northern Cyprus population was prevented. No new COVID-19 cases have been detected in the country since 17 April 2020. The first SARS-CoV-2 cases involving northern Cyprus citizens had either travelled from the United Kingdom or had close contact with people who had arrived from the United Kingdom, while other cases were linked to a bus driver who had transported the German tourist group. This suggests that SARS-CoV-2 entered northern Cyprus through imported cases from Germany and the United Kingdom (9,16–20). The clinical presentations at illness onset of the COVID-19 patients diagnosed in northern Cyprus were mild to severe fever, fatigue and headache (19).

As of 4 May 2020, only four COVID-19 related deaths have occurred in northern Cyprus. First patient was a 73-year-old German citizen who had chronic obstructive pulmonary disease and hypertension and was hospitalized on 20 March 2020, and subsequently transferred to an intensive care unit on 25 March 2020.

Table 1 **SARS-CoV-2 cases identified in the northern Cyprus from 9 March to 4 May 2020 (25,26)**

Total number of tests performed in northern Cyprus:	15 428
Total number of positive cases:	108
Nationality:	Northern Cyprus citizens: 76 German citizens: 31 Turkmenistan citizen: 1
Discharged patients:	29 (German citizens) 1 (Turkmenistan citizen) 73 (Northern Cyprus citizens)
Ongoing treatment:	1 Northern Cyprus citizen
Covid-19 related deaths:	2 German citizens 2 northern Cyprus citizens

Figure 1 **COVID-19 surveillance in northern Cyprus between 9 March and 4 May 2020**



On 28 March, it was announced that this patient had died due to COVID-19-related respiratory failure and multiple organ failure.

The second patient was a German tourist, an 83-year-old female patient who also had diabetes and hypertension, and was hospitalized on 20 March 2020. She was taken into the intensive care unit on 24 March, 2020 and the death occurred on 1 April 2020. Apart from these 2 deaths, two Turkish Cypriot citizens also died due to COVID-19 - a 74-year-old male who had hypertension, diabetes and ischemic heart disease co-morbidities, and a 54-year-old male who had an underlying diabetic condition (5–7,21–24). Recently, 29 German citizens aged 65 and over from the original tourist group were discharged and sent back safely to their country. As of 4 May 2020, 103 patients have completed their treatment and recovered, with only one patient currently under treatment for COVID-19. There are no patients in the intensive care unit.

We firmly believe that northern Cyprus represents a 'good model' for other countries in the world with regard to dealing with the current COVID-19 pandemic. These stated precautions, as well as good hygiene practice, could also be used in other countries to control the further transmission of SARS-CoV-2. In addition to the precautions taken, official TV channels, universities and associations are continually sharing informative videos and information to increase awareness of the current outbreak and the role of each individual in northern Cyprus in preventing further transmission.

Funding: None.

Competing interests: None declared.

Situation actuelle de la COVID-19 dans la partie nord de Chypre

Résumé

Contexte : La charge de morbidité de la maladie à nouveau coronavirus 2019 (COVID-19) devrait augmenter. De ce fait, des mesures strictes et urgentes prises par les décideurs sont essentielles pour endiguer la flambée épidémique de nouveau coronavirus (SARS-CoV-2) dans le monde.

Objectifs : La présente étude visait à fournir une analyse en temps réel de la présence de la COVID-19 dans le nord de Chypre.

Méthodes : Tous les cas positifs officiels au SARS-CoV-2 ont été suivis et signalés en termes d'origine, de nationalité et de voies de transmission. Les mesures préventives prises après le premier cas notifié ont été analysées pour établir leur efficacité en tant que stratégies de lutte.

Résultats : Le cas indicateur de SARS-CoV-2 dans la partie nord de Chypre a été identifié comme étant une touriste allemande. Le premier cas local avait des antécédents de voyage en provenance du Royaume-Uni, ce qui a ensuite entraîné une transmission locale. Des mesures de confinement rapides et strictes ont actuellement retardé un pic dans le nombre des cas observés.

Conclusions : La mise en œuvre rapide de mesures de distanciation sociale, de bonnes mesures d'hygiène et l'interdiction de voyages/rassemblements dans la partie nord de Chypre ont été efficaces pour endiguer la flambée.

الحالة الراهنة لكوفيد-19 في شمال قبرص

نظيف سلطانوجلو، بوكت بادال، كايا سوار، تامر ساتليداج

الخلاصة

الخلفية: من المتوقع أن يزداد العبء الصحي العام لمرض فيروس كورونا المستجد 2019 (كوفيد-19)، ومن المهم أن يتخذ صانعو القرارات تدابير صارمة وعاجلة لاحتواء فاشية الفيروس التاجي المستجد (فيروس كورونا سارس- ٢) في جميع أنحاء العالم.

الأهداف: هدفت هذه الدراسة إلى تقديم تحليل آني لوجود فيروس كوفيد-19 في شمال قبرص.

طرق البحث: تُتبعت جميع الحالات الإيجابية لفيروس كورونا سارس-2 الرسمية وأُبلغ عنها من حيث المنشأ والجنسية وطرق انتقال العدوى للمصابين. وحُللت التدابير الوقائية المتخذة بعد الإبلاغ عن الحالة الأولى من حيث فعاليتها كاستراتيجيات للمكافحة.

النتائج: حُددت الحالة الدالة لمتلازمة «فيروس كورونا سارس-2» في شمال قبرص وكانت لسائحة ألمانية. وكان لأول حالة محلية تاريخ سفر إلى المملكة المتحدة وبعدها حدثت العدوى محليًا. وقد أدت تدابير الاحتواء الصارمة والسريعة في الوقت الآني إلى تأخير حدوث الذروة في الحالات المُلاحَظة.

الاستنتاجات: إن التنفيذ السريع لتدابير التباعد الاجتماعي (البدني) وتدابير النظافة الصحية الجيدة وحظر السفر والتجمع في شمال قبرص كان فعالًا في مكافحة فاشية المرض.

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Supplement document 5 - Awareness, Practices, and Attitudes Toward the SARS-CoV-2 Outbreak Among Northern Cyprus Residents: A Descriptive Research Study Using an Online Survey

RESEARCH ARTICLE / ARAŞTIRMA

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Awareness, Practices, and Attitudes Toward the SARS-CoV-2 Outbreak Among Northern Cyprus Residents: A Descriptive Research Study Using an Online Survey

Kuzey Kıbrıs Türk Cumhuriyeti'nde İkamet Edenlerin SARS-CoV-2 Salgınına Yönelik Farkındalığı, Uygulamaları ve Tutumları: Çevrimiçi Bir Anket Kullanılarak Çalışılmıştır

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Abstract

Introduction: Severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) has become a global health issue that was declared as a pandemic on March 11, 2020. The Eastern Mediterranean region, which includes the island of Cyprus, is one of the affected regions. This study aimed to analyse the awareness, practices, and attitudes towards the SARS-CoV-2 outbreak among Northern Cyprus residents during the period of a partial lockdown from April 7 to 17, 2020 through the online platform.
Materials and Methods: A descriptive research study using the online survey method was completed by Northern Cyprus residents anonymously. An online questionnaire was designed consisting of 21 questions focused on demographics (five questions), awareness (seven questions), practices (six questions), and attitudes toward the SARS-CoV-2 outbreak (three questions) and was completed by 738 Northern Cyprus residents. Statistical Package for Social Sciences Statistics, Version 24.0 was used in the statistical analysis.
Results: Facebook was the most often used platform for following news and information with regard to the SARS-CoV-2 outbreak. Additionally, most of the participants had good attitudes toward the SARS-CoV-2 outbreak, believing that Northern Cyprus would win the battle against the virus.
Conclusion: Once again, it was proven that online platforms, specifically Facebook, were the most used sources for following the news related to SARS-CoV-2. This strongly suggests that, in order to prevent dissemination of incorrect information, reliable authorities, such as the Ministry of Health, should publish information on online platforms to reach more people with correct information.
Keywords: SARS-CoV-2 outbreak, Northern Cyprus, online platform, awareness, practices

Öz

Giriş: Şiddetli akut solunum sendromu Koronavirüs-2 (SARS-CoV-2), 11 Mart 2020'de pandemi olarak ilan edilen küresel bir sağlık sorunu haline gelmiştir. Şüphesiz, Akdenizin doğusunda yer alan Kıbrıs adası da etkilenen bölgelerden biri olmuştur. Bu çalışma, 7-17 Nisan 2020 arasındaki kısmi sokağa çıkma yasağı ilan edilen dönemde Kuzey Kıbrıs Türk Cumhuriyeti'nde (KKTC) ikamet eden kişiler arasında SARS-CoV-2 salgınına yönelik farkındalığı, uygulamaları ve tutumları çevrimiçi platform aracılığıyla analiz etmeyi amaçlamıştır.
Gereç ve Yöntem: Kuzey Kıbrıs Türk Cumhuriyeti'nde ikamet edenler üzerinde çevrimiçi anket yöntemi kullanılarak tanımlayıcı bir araştırma gerçekleştirildi. Tasarlanan çevrimiçi anket, demografi (beş soru), farkındalık (yedi soru), uygulamalar (altı soru) ve SARS-CoV-2 salgınına yönelik tutumlara (üç soru) odaklanan 21 sorudan oluşuyordu. Çevrimiçi anket, KKTC'de ikamet eden 738 kişi tarafından tamamlandı. İstatistiksel analizde Statistical Package for Social Sciences 24.0 programı kullanıldı.
Bulgular: Facebook, SARS-CoV-2 salgını ile ilgili haber ve bilgileri takip etmek için en çok kullanılan platform oldu. Ek olarak, katılımcıların çoğu, KKTC'nin virüse karşı savaşı kazanacağına inanarak SARS-CoV-2 salgınına karşı iyi bir tutum içerisinde olduğunu belirttiler.

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Öz

Sonuç: SARS-CoV-2 ile ilgili haberleri takip etmek için en çok kullanılan platformun başta Facebook olmak üzere çevrimiçi platformlar olduğu bir kez daha kanıtlandı. SARS-CoV-2 hakkında topluma yayılabilecek yanlış bilgileri önlemek adına Sağlık Bakanlığı gibi güvenilir kaynakların daha fazla kişiye doğru bilgilerle ulaşmak için çevrimiçi platformlarda bilgi yayınlamaları gerektiğini önemle göstermektedir.
Anahtar Kelimeler: SARS-CoV-2 salgını, Kuzey Kıbrıs Türk Cumhuriyeti, çevrimiçi platform, farkındalık, uygulamalar

Introduction

The causative agent of coronavirus disease-2019 (COVID-19) is a new strain of coronavirus not previously identified in humans, which was later identified as Severe Acute Respiratory Syndrome Coronavirus-2 (now abbreviated SARS-CoV-2). SARS-CoV-2 was first detected in the city of Wuhan, Hubei Province, China in December 2019[1-3]. Shortly thereafter, SARS-CoV-2 emerged as a global pandemic, officially declared by the World Health Organization on March 11, 2020, and has since become a significant global health problem[4].

Although the SARS-CoV-2 outbreak first emerged in China, with effective control measures, the country has successfully managed the outbreak. However, SARS-CoV-2 infections continue to arise elsewhere in the world. In the Eastern Mediterranean region, 1.903,547 cases and 50,466 deaths had been reported as of August 30, 2020[5]. Cyprus is an island located in the Eastern Mediterranean region. The residents of the island mainly consist of Turkish Cypriots living on the Northern part of the island and Greek Cypriots living on the southern part of the island, with populations of approximately 375,000 and 875,900, respectively[6,7].

This study aimed to analyse the awareness, practices, and attitudes toward the SARS-CoV-2 outbreak among residents of Northern Cyprus. Up to February 6, 2021, 2722 confirmed cases and 15 COVID-19 related deaths had occurred in Northern Cyprus. Patient zero was first identified on March 9, 2020 among a German tourist group, and Northern Cyprus immediately started to take precautions against SARS-CoV-2 transmission soon after the identification of this patient. The precautions taken against the SARS-CoV-2 outbreak in Northern Cyprus from March 10 to June 1, 2020 can be summarized as follow: all forms of collective worship were banned; all workers in the public sector were placed on administrative leave, with the exception of police, fire brigade, civil aviation, finance, and health workers; all shops and entertainment centers were closed, and only pharmacies, gas stations, bakeries, and markets remained open; all schools and universities were closed; only Northern Cyprus citizens were allowed to enter the country, and these people were quarantined for 14 days in designated locations provided by the government; and a partial daytime curfew was announced on March 23, 2020, under which people were only allowed to leave home to maintain their essential needs (market and pharmacy). Full curfew from 21:00 h to 06:00 h was also imposed to ensure that people were staying in their homes. These precautions were taken as soon as patient zero was identified[8-11].

On June 1, 2020, some of the precautions started to be relaxed, such as the re-opening of entertainment locales; schools; and air, land, and sea borders to the country, and normalization of life in Northern Cyprus began. A total of 108 cases were reported in the days between March 9 and June 30 and from April 17, 2020 to June 30, 2020 no SARS-COV-2 cases was reported in Northern Cyprus, meaning that the strict measures taken had worked successfully to prevent the spread of the disease.

However, with the opening of land, air, and sea borders to Northern Cyprus, from July 1 to September 11, 2020, the number of newly-diagnosed SARS-CoV-2 cases started to rise, reaching a total of 541 cases. This indicates that public awareness regarding good hygiene practices has undoubtedly played a significant role in preventing further transmission of SARS-CoV-2 in Northern Cyprus, and the recent increase was due to imported cases. All the precautions taken against the SARS-CoV-2 outbreak and the COVID-19 situation in the country, such as how many tests have been performed and how many COVID-19 cases or deaths have occurred each day are announced on the official website and Facebook site of the Northern Cyprus Ministry of Health[12,13].

Materials and Methods

Study Design

This was a descriptive research study using the online survey method implemented in the period of partial lockdown from April 7 to 17, 2020 on Northern Cyprus residents. An online questionnaire was designed and consisted of 21 questions: five were about demographics, seven were related to awareness, six refered to practices implemented against SARS-CoV-2, and three were about attitudes toward the SARS-CoV-2 outbreak among Northern Cyprus residents. The survey questions were prepared in Turkish, as this is the mother tongue of Turkish Cypriots living in Cyprus. There were some limitations to this study, for example, the survey could only be filled out by participants who had internet access and technological devices

such as a smartphone or computer. Also, the form was in Turkish; thus, only people who could read and write Turkish were able to participate. Results were obtained via the internet, which was a major source of selection bias. No consent form was required because the study did not include any clinical trials. The results of the study were obtained via an online survey, which was based on the principle of voluntary participation.

Statistical Analysis

SPSS Statistics, Version 24.0 (Armonk, NY: IBM Corp. Released 2016) was used in the statistical analysis of the research data, and frequency analysis was performed to identify the participants' socio-demographic characteristics as well as their awareness, practices, and attitudes toward the COVID-19 pandemic. The Pearson chi-square test and Fisher's exact test were both performed to compare participants' attitudes toward SARS-CoV-2 according to their socio-demographic characteristics. Differences were considered significant at $p<0.05$. The study was approved by the Near East University Ethical Committee (YDU/2020/78-1041).

Results

Socio-demographic Characteristics

A total of 738 participants completed the survey, of which 497 (67.3%) were female and 241 (32.7%) were male. All the participants were assumed to be Northern Cyprus residents, since it was clearly mentioned in the beginning of the survey that "only Northern Cyprus residents should complete the survey". Six hundred sixty-four (90%) of the participant stated that they were Northern Cyprus citizens, whereas 74 (10%) of participants were not Northern Cyprus citizen but residents of the Northern Cyprus. Among the participating individuals, 26.2% were aged 30 or below, 30.6% were in the 31-40 -year age group, 19.2% were 41-50, 16.1% were 51-60, and 7.9% were aged 61 or above. Furthermore, 25.5% had a high school education, 38.8% were undergraduates, 19.1% were postgraduates, and 10.2% had a PhD. Fifty-four percent resided in Nicosia, 14.0% in Famagusta, and 23.0% in Kyrenia. The participants were distributed by occupation as follows: 14.0% freelance worker, 10.4% teacher, 9.1% housewife, 8.9% retired, 8.8% government official, 8.3% academician/research assistant, 6.6% health worker, and 33.9% stated other occupations on various subjects.

Awareness of Participants Toward COVID-19

Participants' awareness of COVID-19 is reported in Table 1. When asked where they first heard about the SARS-CoV-2 pandemic in Northern Cyprus, 76.9% of participants responded "via social networks", and 20.2% "via radio/TV/newspaper". Among the participants, 87.0% followed news, developments, and measures about the COVID-19 pandemic on Facebook, 66.3% on television, 23.4% on SMS messages sent by the government, and 11.4% on Twitter. With regard to social media, 69.1% of participants followed the accounts of the Northern Cyprus Ministry of Health (Facebook, Instagram), 48.1% followed those of local newspapers (Facebook, Instagram), 36.3% followed those of the Northern Cyprus Prime Ministry's Office Directorate of Crisis Communication, and 15.0% followed anonymous social media (Facebook, Instagram etc.) group(s) and other similar pages. Among the participants, 80.0% reported hearing that "all shops, establishments, casinos, night clubs, betting offices, entertainment centers etc. would be closed other than services that provide for basic needs in the private sector, such as pharmacies, petrol stations, and supermarkets", 78.3% heard that there would be a "14-day quarantine for Northern Cyprus citizens if they come from abroad", 71.0% heard that "there will be administrative leave for all public officers other than police, fire department, health, civil aviation, financial matters etc.," 56.8% heard that there would be "no access between districts in Northern Cyprus", and 60.6% said they heard that there would be "no gatherings at associations, clubhouses, or places of public worship". Furthermore, 96.3% of participants indicated that the most common symptoms of COVID-19 are fever, while 87.1% said dyspnea, and 86.2% said dry cough. In terms of COVID-19 transmission, 96.2% of participants indicated that SARS-CoV-2 is transmitted via the sneeze and/or cough of a COVID-19 infected person, 94.9% said from close contact with an infected person, and 94.0% said via touching the mouth, nose, or eyes after contact with infected objects. In all, 96.8% of participants noted that COVID-19 "severely affects the elderly and people with weak immune systems and chronic diseases", 92.6% stated that "its incubation period is between 2 and 14 days", 41.5% said that the agent of "COVID-19 is called SARS-CoV-2", and 25.6% indicated that it has a "low mortality rate".

Practices During the COVID-19 Pandemic Among Residents of Northern Cyprus

The general practices related to SARS-CoV-2 adopted by the participants are reported in Table 2. According to the survey, 96.9% of participants wash their hands with water and soap for at least 20 seconds to prevent the spread of the COVID-19; 93.8% avoid hugging, hand-shaking, and kissing; 91.1% use antiseptic hand gel or cologne when they have no access to soap and water; and 88.1% use disposable tissues when coughing and sneezing or they sneeze and cough into their elbow if there is no paper tissue. In terms of when participants wash their hands; 85.5% wash their hands after using the toilet, 92.7% wash them before preparing food, 91.2% wash them before eating, 87.4% wash them after wiping their nose, coughing, or sneezing, and 58.8% wash them after contact with animal feed or animals. Among the participants, 93.0% said they often let fresh air in through windows for house and surface cleanliness,

Table 1. Participants' awareness of Coronavirus disease-2019

Where they first heard about COVID-19	**n**	**%**
Social Networks	567	76.8
Radio/TV/Newspaper	149	20.2
Friends/Relatives	22	3.0
Where to follow information, developments, and measures about the COVID-19 outbreak		
Facebook	642	87.0
TV channels	489	66.3
SMS by Northern Cyprus government	170	23.0
Newspapers	159	21.5
Twitter	84	11.4
YouTube	62	8.4
Official authorities	30	4.1
Radio	67	9.1
Social networks for COVID-19 developments		
Social media pages of the Northern Cyprus Ministry of Health (Facebook, Instagram)	510	69.1
Local news page(s) on social media (Facebook, Instagram)	355	48.1
Social media page of Northern Cyprus Prime Ministry Directorate of crisis communication	268	36.3
Anonymous social media (i.e., Facebook, Instagram) group(s) etc.	111	15.0
None	28	3.8
Previous Information on the measures and precautions taken in Northern Cyprus for the COVID-19 pandemic		
All shops, establishments, casinos, night clubs, bet offices, entertainment centers etc. will be closed other than services that provide basic needs in the private sector like pharmacies, petrol stations, and supermarkets	590	80.0
14-day quarantine for Northern Cyprus citizens if they come from abroad	578	78.3
Administrative leave for all public officers other than police, fire department, health, civil aviation, financial matters etc.	524	71.0
No access between districts in Northern Cyprus	419	56.8
No gatherings at associations and clubhouses, or public worship	447	60.6
None	12	1.63
Most common symptoms of COVID-19		
High fever	711	96.3
Dyspnea	643	87.1
Dry cough	636	86.2
Mode of SARS-CoV-2 transmission		
Sneeze and/or cough from a COVID-19 infected person	710	96.2
Close contact with an infected person	700	94.9
Touching the mouth, nose or eyes after contact with infected objects	693	93.9
No idea	3	0.4
COVID-19 characteristics		
Severe effect on elderly, people with weak immune systems and chronic diseases	714	96.8
Incubation period between 2-14 days	683	92.6
COVID-19 agent is called SARS-CoV-2	306	41.5
Low mortality rate	189	25.6

SARS-CoV-2: Severe acute respiratory syndrome Coronavirus-2, COVID-19: Coronavirus disease-2019

Table 2. Participants' practices regarding Coronavirus disease-2019

Hygiene rules during the COVID-19 pandemic	n	%
I frequently wash my hands with water and soap for at least 20 seconds	715	96.9
I avoid hugging, hand-shaking, and kissing	692	93.8
When water and soap are not available, I use antiseptic hand gel or cologne	672	91.1
I use disposable tissues when coughing and sneezing or I sneeze and cough into my elbow if there is no paper tissue	650	88.1
When to wash hands with water and soap		
After using the toilet	705	95.5
Before preparing food	684	92.7
Before eating	673	91.2
After wiping my nose, coughing or sneezing	645	87.4
After contact with animal feed or animals	434	58.8
Sometimes wash my hands for less than 20 seconds	205	27.8
Issues related to in house and surface cleanliness during the COVID-19 pandemic		
I often let fresh air in from windows	686	93.0
I clean the most touched surfaces (door knob, sockets etc.) with bleach or alcohol-based cleaning agents	621	84.2
I clean cell phones, tablets, and computer keyboards with alcohol-based disinfectants or cologne	578	78.3
No cleaning	9	1.2
Following the curfew rules in Northern Cyprus		
I go to the supermarket and pharmacy	582	78.9
I go to the bank	103	14.0
I do not leave the house	150	20.3
I go to the park	3	0.4
Precautions taken when outdoors		
I wear a mask even without symptoms	556	75.3
I do not touch my mouth, nose or eyes	627	85.0
I keep at least one-meter social distance	697	94.4
I wear gloves	535	72.5
I wear a mask if I have symptoms (i.e., cough, sneeze)	81	11.0
I do not take any precautions	2	0.3
Precautions when returning home from outside during the COVID-19 pandemic		
I do not enter the house with my shoes	631	85.5
I immediately wash my hands with water and soap for at least 20 seconds	699	94.7
I wash my clothes	540	73.2
I take a shower	462	62.6
I enter the house after disinfecting my shoes	141	19.1

COVID-19: Coronavirus disease-2019

84.4% said they clean most touched surfaces (door knobs, light switches, etc.) with bleach or alcohol-based cleaning agents, and 78.3% clean cell phones, tablets, and computer keyboards with alcohol-based disinfectants or cologne.

With regard to meeting their needs, 78.9% said they go to the supermarket and pharmacy, 14.0% go to the bank, and 20.3% do not leave the house. Survey participants revealed that once outdoors the following precautions were taken; With respect to wearing masks, it was found that 75.3% of participants wear a mask even without symptoms, 85.0% do not touch their mouth, nose, or eyes, 94.5% keep at least a 1-m social distance, and 72.5% wear gloves. With regard to the precautions taken during the COVID-19 pandemic when they return home after being outside, 85.5% do not enter the house with shoes, 94.7% immediately wash their hands with soap and water for at least 20 seconds, 73.2% wash their clothes, 62.6% take a shower, and 19.1% enter the house only after disinfecting their shoes.

Attitudes of Participants Toward the COVID-19 Pandemic

A majority of the participants agreed that increasing awareness of the SARS-CoV-2 in Northern Cyprus is important to prevent the spread of the disease (96.9%), and 83.2% believed that Northern Cyprus would win the fight against SARS-CoV-2, whereas only 41.3% participant stated that the measures taken against the SARS-CoV-2 outbreak in Northern Cyprus were sufficient (Table 3).

Moreover, Table 4 presents the chi-square test results for the participants and their socio-demographic characteristics regarding whether they find the COVID-19 measures sufficient. There was a statistically significant difference between age groups regarding their opinions on the sufficiency of the current COVID-19 measures. A higher proportion of participants in the 41-50 and 51-60 age groups found the current COVID-19 measures sufficient, when compared with all other age groups

Table 3. Participants' attitudes toward Coronavirus disease-2019

Sufficiency of the measures taken against COVID-19	n	%
Sufficient	305	41.3
Not sufficient	433	58.7
Is the awareness of COVID-19 in Northern Cyprus important in preventing the spread of disease?		
Yes	715	96.9
No	23	3.1
Do you believe that Northern Cyprus will win the fight against the COVID-19?		
Yes	614	83.2
No	124	16.8

COVID-19: Coronavirus disease-2019

Supplement document 6 - 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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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 hours 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 1st July to 9th 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 prevented the spread of the disease within the population.

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

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 (Young et al. 2020). World Health Organization (WHO) declared on the 11th March 2020 that SARS-CoV-2 had reached epidemiological characteristics to be announced as a pandemic (WHO 2020c).

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 (Ali and Alharbi 2020).

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 (Long et al. 2020).

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 (Rao et al. 2020; WHO 2020a).

As of the 27th 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 (WHO 2020b).

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 9th 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 (Sultanoglu et al. 2020).

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

By the 14th 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 (detaykibris 2020). Moreover, to promote isolation of the individuals, a partial

daytime curfew was imposed as of 23rd 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 (kibrisadahaber 2020).

These strict measures, however were lifted shortly thereafter due to the deteriorating economic circumstances. On 29th April 2020 the partial daytime curfew was lifted, and the hospitality sector were allowed to re-open (AA 2020). Schools re-opened on 1st September 2020 for the new academic year (Gündem Kıbrıs 2020). By the 1st 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 hours 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 (Sozcu 2020).

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 (Rao et al. 2020).

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 (ECDC 2020; Lavezzo et al. 2020; Oran and Topol 2020). 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 (Kucirka et al. 2020).

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 (Baleanu, Ghanbari, et al. 2020), the study of the role of liver by a new model of Caputo–Fabrizio fractional derivative with the exponential kernel (Baleanu, Jajarmi, et al. 2020), the use of hyperchaotic models for a biological snap oscillator (Sajjadi et al. 2020) and many other (Abdullaev 2020; Al-Refai 2020).

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 (Gao, Veeresha, Prakasha, et al. 2020), the study of reported and unreported SARS-CoV-2 cases by Caputo derivative (Gao, Veeresha, Baskonus, et al. 2020), a mathematical model to analyze local/global stability and diseases free/endemic equilibrium points of COVID-19 (Akgül et al. 2021), other mathematical model called the Bats-Hosts-Reservoir-People coronavirus model to analyze the transmission of SARS-CoV-2 from reservoir to people (Gao, Baskonus, and Shi 2020) and hybrid analytical method *q*-HASTM for the accomplishment of numerical solutions of COVID-19 model with fractional operator (Yadav et al. 2021).

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 1st July to 9th 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 1st July to 9th 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 hours. Between the 1st and 12th 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 (Biospeedy 2020) and from the 13th of July to the 9th of September

2020, Diagnovital® (RTA Laboratories Inc, SARS-CoV-2 Real-Time PCR Kit v2.0 Istanbul-Turkey) (Diagnovital 2020) 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://covid19.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 1st July to 9th 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 (TRNC Ministry of Health 2020c).

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:

$$\delta \sim \Gamma(\mu, \sigma) \tag{1}$$

Where δ denotes delay in reported cases, μ, the mean of reported cases, and σ, 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.

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

This formula is based on reported positive cases of SARS-CoV-2 within the 1st July to 9th 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 ρ_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 1st July to 9th 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.

2.1 Susceptible-Exposed-Infected-Removed (SEIR) model

By applying data and parameter values listed in Table 1, to the Susceptible-Exposed-Infected-Removed (SEIR) model in (Hincal, Kaymakamzade, and Gokbulut 2020), 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

Variable/Parameter	Description	Value
β	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
ω	Hospitalization rate from I_1class	0.000089
φ	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

(TRNC Ministry of Health 2020c; TRNC State Planning Organization 2020)

(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 Table 2.

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.

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 1st July to 9th 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)

(CI: Confidence Internal)

In the R_0 calculation for Northern Cyprus, all SARS-CoV-2 cases were taken from the Ministry of Health (TRNC Ministry of Health 2020a, 2020b), 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 1st July to 9th of September 2020 (Table 3).

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

From 1st July to 9th 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)

(TRNC Ministry of Health 2020a, 2020b)

(CI:Confidence Internal)

The comparison of R_0 values of NEU DESAM COVID-19 laboratory and other 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 Figure 1. The study also suggests that statistical modelling supports the mathematical modelling since the results were consistent.

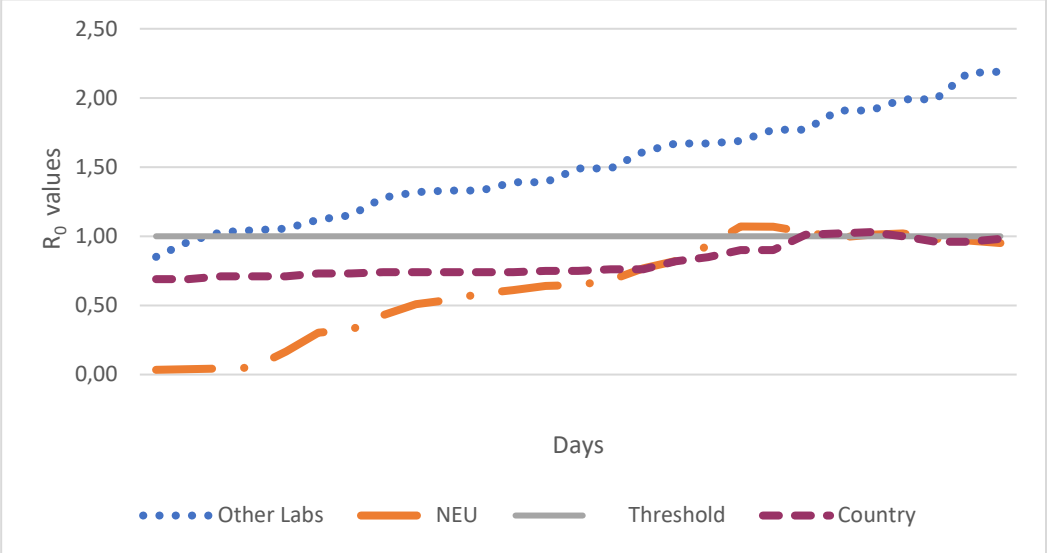

Figure 1: Comparison of basic reproduction number (R_0) values of NEU DESAM COVID-19 and other laboratories to Northern Cyprus R_0 values

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 1st July to 9th 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 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 as demonstrated in Table 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 1st July to 9th 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 (Table 1) using SEIR model (Hincal et al. 2020). 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 (Table 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 (Figure 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 (Table 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 (Figure 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 asymptotic 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 (Brown and Ozanne 2019). 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 (Hincal et al. 2020).

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 (Kalia and Keith 1990). 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

(Jajarmi and Baleanu 2020, 2021; Mohammadi et al. 2017).

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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Published Articles

Ergoren, Mahmut Cerkez, Stefano Paolacci, Elena Manara, Astrit Dautaj, Kristjana Dhuli, Kyrylo Anpilogov, Giorgio Camilleri, Huseyin Kaya Suer, Murat Sayan, Gulten Tuncel, Nazife Sultanoglu, Marco Farronato, Gianluca Martino Tartaglia, Munis Dundar, Giampietro Farronato, Irfan Suat Gunsel, Matteo Bertelli, and Tamer Sanlidag. 2020. “A Pilot Study on the Preventative Potential of Alpha-Cyclodextrin and Hydroxytyrosol against SARS-CoV-2 Transmission.” Acta Biomedica 91:1–7. doi: 10.23750/abm.v91i13-S.10817.

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