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Analysis from Statistical Perspective of 2019 Novel Coronavirus Cases in Turkey: How are the Things Going on?

Türkiye'deki 2019 Yeni Koronavirüs Vakalarının İstatistiksel Bakış Açısı ile Analizi: Süreç Nasıl Gidiyor?

[©] Özlem TOLUK^{a,b}, [©] Burcu DİNÇGEZ ÇAKMAK^{a,c}, [©] İlker ERCAN^d, [©] Yeşim UNCU^e

^aBursa Uludağ University Institute of Health Sciences, Department of Biostatistics, Bursa, TURKEY ^bBezmialem Vakif University Faculty of Medicine, Department of Biostatistics and Medical Informatics, İstanbul, TURKEY ^cBursa Yüksek İhtisas Research and Training Hospital, University of Health Sciences, Department of Obstetrics and Gynecology, Bursa, TURKEY ^dBursa Uludağ University Faculty of Medicine, Department of Biostatistics, Bursa, TURKEY ^eBursa Uludağ University Faculty of Medicine, Department of Family Practice, Bursa, TURKEY

ABSTRACT Objective: There is only limited data about 2019-novel coronavirus (2019-nCov) outbreak from Turkey. Here, we aimed to analyse 2019-nCov cases in Turkey from statistical perspective. Material and Methods: Data were obtained from Republic of Turkey Ministery of Health website. The statistical modeling was performed for tests between 27 March and 18 April. The ratios were computed for according to test numbers, number of cases, number of patients in intensive care care, deaths for statistical analysis. An association between related ratios and time was analyzed by using curve estimation approach. Curves were drawn with 95% confidence interval. Results: The ratio of number of cases/number of tests were increased until 7 April and then decreased while the ratio of daily recovered cases/number of daily cases were decreased until that date and then increased. The ratio of deaths/number of cases were increased rapidly initially whereas it later increased more slowly. Although the ratio of number of intubated cases/number of cases and the ratio of number of cases in intensive care unit/number of cases have tendency to decrease in same rate, the ratio of number of deaths/number of cases in intensive care unit has tendency to increase from the beginning of pandemia until this date. Conclusion: The increasing trend of recovered cases, decreasing of deaths, requirement of intensive care unit and intubation are the main satisfactions for Turkey. The statistical modeling used here could shed some light on the control of process. While more cases than modeling estimate can show uncontrolled process, less cases could indicate well-controlled process.

ÖZET Amaç: Dünyada salgın oluşturan 2019-yeni koronavirüse (2019-nCov) ilişkin Türkiye'den kısıtlı veri mevcuttur. Bu çalısmadaki amacımız ülkemizdeki olguların istatistiksel yönden analizidir. Gereç ve Yöntemler: Veriler Türkiye Cumhuriyeti Sağlık Bakanlığı'nın internet sitesinden alınarak, 27 Mart ve 18 Nisan arasındaki testler için istatistiksel modelleme yapıldı. Test sayılarına, vaka sayılarına, yoğun bakımdaki hasta sayısına ve ölüm sayısına göre istatistiksel analizler yapılarak oranlar hesaplandı. İlişkili oranlar ve zaman arasındaki ilişki eğri tahmin yaklaşımı ile değerlendirildi. Eğriler %95 güven aralığı ile çizildi. Bulgular: Vaka/test oranının 7 Nisan'a kadar artış gösterip sonra azaldığı, günlük iyileşen hasta sayısı/günlük vaka sayısı oranının önce azalıp, o tarihten sonra arttığı bulundu. Ölüm/vaka oranının başlangıçta hızlı bir artış hızı gösterirken daha sonra yavaş bir artış hızına ulaştığı saptandı. Pandemi başlangıcından son analiz tarihine kadar entübe vaka/vaka sayısı ile yoğun bakımdaki vaka/vaka sayısı oranlarında aynı hızda bir azalma mevcut olmasına rağmen, ölüm/yoğun bakımdaki vaka oranında aynı hızda artış mevcuttu. Sonuç: İyileşen vakaların artış, ölümlerin, yoğun bakım ünitesindeki vakaların ve entübe hastaların azalma eğiliminde olması Türkiye için olumlu bir gelişme olarak görülebilir. Burada kullanılan istatistiksel modelleme sürecin kontrolüne ışık tutabilir. İlerleyen günlerde, modelin tahmin ettiğinden çok vaka saptanması sürecin kontrol altında olmadığını gösterirken, tahminden daha az vaka olması sürecin kontrol altında olduğunu göstermektedir.

Keywords: Coronavirus; outbreak; statistical perspective; Turkey

Anahtar Kelimeler: Koronavirüs; salgın; istatistiksel yaklaşım; Türkiye

Coronaviruses, a member of Coronaviridiae family, are an enveloped positive-sense RNA

viruses.¹ In previous years, severe acute respiratory coronavirus (SARS-CoV) and Middle East respira-

Correspondence: Burcu DİNÇGEZ CAKMAK Bursa Uludağ University Institute of Health Sciences, Department of Biostatistics, Bursa, TURKEY/TÜRKİYE E-mail: burcumavis@gmail.com



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2146-9040 / Copyright © 2020 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). tory syndrome coronavirus (MERS-CoV) caused epidemias, the mortality of which varies between nearly 10-37%.^{2,3} Nowadays, there is an outbreak of a new type coronavirus named as 2019 novel coronavirus (2019-nCov) among worldwide. This new virus was first established in December 2019 in Wuhan, China among adult patients with severe pneumonia with unknown etiology on bronchoalveolar lavage samples.^{4,5} Evidences indicate that it firstly transmitted to humans via wild animals sold in Seafood Wholesale Market.⁶ Although the transmission mechanism of 2019-nCov still remains unclear, human to human transmission with respiratory droplets is the most acceptable theory.

According to the data from China, the incubation period of 2019-nCov is changing between 3 to 14 days. After then, prodromal phase of the disease starts with generally mild symptoms such as fever, sore throat, fatigue, dry cough and myalgia.^{7,8} It is asymptomatic in 80% of cases and it has generally good prognosis whereas it can cause acute respiratory distress syndrome, pulmonary oedema and multiple organ failure in severe cases.

Detection of 2019-nCov rapidly and accurately has crucial role to limit the outbreak. Since 2019nCov is a newly introduced pathogen, the available diagnostic procedures are not enough. Nasopharyngeal and oropharyngeal swab tests are standard assessment tools for the infection and the current tests include reverse-transcription or real time polymerase chain reaction. Unfortunately they are time consuming and populations have limited commercial kits to detect 2019-nCov. Thus clinical or imaging parameters could be used with their additional diagnostic roles. Computed tomography of the chest is a very useful and available diagnostic tool which can give a chance to a clinician to detect pneumonia in early stages of the disease.^{6,7} It is known that ground glass shadow, pulmonary consolidation and nodules are the most common signs of infection on computed tomography of the chest.

Isolation, social distancing and quarantine have crucial role to control the outbreak.⁹ There is no fully recommended anti 2019-nCov treatment. Lopinavir, ritanavir, remdesivir and ribavirin are the most commonly used antiviral agents.⁶ Chloroquine and hyTurkiye Klinikleri J Med Sci. 2020;40(2):228-35

droxychloroquine are widely used antimalarial agents which are both used in prophylaxis and treatment.¹⁰ Corticostreroids, anticoagulant agents and antibodies are the other treatment options for this infection. Although vaccination studies are going on rapidly, there is no vaccines available during the outbreak.^{6,11} It is important to guide clinicians and government during pandemia by analysing data from own country and all around the world. Because all populations in the world require well-coordinated effort to eliminate 2019-nCov infection.

There is only limited data about 2019-nCov from Turkey in the literature and the outbreak going on in our country is still a major challenging issue for all clinicians. In this study we aimed to analyse 2019nCov cases from statistical perspective. In case we accept the number of tests can represent a sample for population; number of cases per tests, number of deaths, number of intubated cases, number of cases requiring intensive care unit per number of cases, number of deaths of patients who admitted intensive care unit and daily recovered cases per daily cases were assessed day by day and statistical modeling was based on these variables.

MATERIAL AND METHODS

The routine procedure to diagnose definite 2019nCov cases in our country is defined according to these criterias.

The criteria to define suspected 2019-nCov cases are as the following: A: Fewer or any respiratory symptom (cough or dyspnea) and having no other reason to explain these clinical state and a travel history of a person or a relative to abroad country within 14 days before symptom onset or B: Fewer or any respiratory symptom (cough or dyspnea) and contact with definite 2019-nCov case within 14 days before symptom onset or C: Fewer or any respiratory symptom (cough or dyspnea) and requirement of hospitalization (occurence of fewer, cough, dyspnea, tachypnea, hypoxemia, hypotension, extensive radiographic evidences in chest imaging and change of consciousness) and having no other reason to explain these clinical condition or D: Sudden onset fewer and cough or dyspnea without rhinorrhea.

After the case is accepted as suspected, the samples are obtained from oropharynx followed by nasopharynx for definitive diagnosis. The samples are obtained from oropharynx followed by nasopharynx from suspected 2019-nCov cases. These samples are routinely assessed by laboratories in some centers determined by Public Health General Directorate (HSGM) by using nucleic acide amplification tests (polymerase chain reaction). Then, the results of the tests are reported to Republic of Turkey Ministery of Health via websites. Suspected patients whose swabs are positive in terms of SARS-CoV-2 by using molecular examination were defined as definite 2019nCov cases (confirmed cases). Negative suspected cases are followed in a period of time and are tested if they have clinical sypmtoms for 2019-nCov.

Since the number of tests may be a representative of the community, they were taken into consideration in our study. Data were obtained from Republic of Turkey Ministry of Health internet website.¹²

The date of the first case reported and death was recorded in our study. The regular testing, explaining the data of cases, deaths, patients who require intensive care unit, patients who require intubation and number of patients who recover were started at 27 March 2020 in our country. Thus the statistical modelling was performed for tests between the dates of 27 March 2020 and 18 April 2020.

In our study, we took into account the number of tests, the number of confirmed cases, patients who were intubated, patients who require intensive care unit, patients who died and recover from illness and number of deaths in intensive care unit. The ratio of the number of confirmed cases to test numbers, the ratio of deaths to the number of cases, the ratio of cases in intensive care unit to the number of cases, the ratio of intubated cases to the the number of cases, the ratio of deaths to the number of cases in in intensive care unit and the ratio of daily recovered cases to the number of daily cases were used in our analysis and was modelled based on time.

An association between related ratios and time was analyzed by using curve estimation approach. The most appropriate ones among adopted models in curve estimation were determined in terms of coefficient significance, model significance and determination coefficient. Curves were drawn with 95% confidence intervals. Statistical significance was taken as α = 0.05 and data analysis was done by using NCSS 07.1.8 Program.

In this study, data were obtained from official website and no additional data were collected from hospital records and patients. Thus, ethical committee approval and informed consent were not necessary for this study. This study were in accordance with the 1964 Helsinki Declaration and its later amendments.

RESULTS

The first case was reported in 10 March 2020, the first death was reported in 17 March 2020 and regular testing and data sharing were started in 27 March 2020. Model was based on the data between 27 March and 18 April 2020.

The most appropriate models in curve estimation were quadratic model in terms of coefficient significance, model significance and determination coefficient for the ratio of cases to number of tests, the ratio of daily recovered patients to daily case number and the ratio of number of deaths to number of cases in intensive care unit; logarithmic model for the ratio of number of deaths to number of case and exponential model for the ratio of number of intubated cases to number of cases and the ratio of number of cases in intensive care unit to number of cases (Table 1).

Statistical model for the ratio of number of cases to number of tests based on time was shown in Table 1. The alterations in the ratio of number of cases to number of tests based on time were presented in Figure 1. According to this figure, the ratio of number of cases to number of tests were increased until 7 April 2020 and after then it was decreased.

Statistical model for the ratio of number of deaths to number of cases based on time was demonstrated in Table. The alterations in the ratio of number of deaths to number of cases were presented in Figure 2. It was found that the ratio of deaths to number of cases were increased rapidly in first week whereas it increased more slowly after first week.

TABLE 1: Statistical modeling of 2019-nCov cases based on time.			
Ratio (y: ratio)	Model* (t: day)	\mathbb{R}^2	Figure no
$\left(\frac{\text{cases}}{(\text{number of tests})}\right)$	y=0.1234+0.0045t-0.0002t ²	0.876	Figure 1
()	y=0.0068(ln(t +7.9092))	0.827	Figure 2
(y=exp(-0.0479(t+54.1320))	0.899	Figure 3
()	y=exp(-0.0560(t+51.9598))	0.880	Figure 4
(daily recovered daily cases	y=0.0815-0.0192t+0.0015t ²	0.875	Figure 5
()	y=0.2011+0.0112t+0.0010t ²	0.993	Figure 6

*: All models and coefficients in models: p<0.001.

Statistical model for the ratio of number of cases in intensive care unit to number of cases based on time was presented in Table 1. The alterations in the ratio of number of cases in intensive care unit to number of cases were shown in Figure 3. This model showed that this ratio has a tendency to decrease in the same rate from the beginning of the pandemia.

Statistical model for the ratio of number of intubated cases to number of cases based on time was demonstrated in Table 1. The alterations in the ratio of number of intubated cases to number of cases based on time were shown in Figure 4. The ratio of number of intubated cases to number of cases has a tendency to decrease in the same rate from the beginning of the pandemia.

Statistical model for the ratio of number of daily recovered cases to number of daily cases based on time was presented in Table 1. The alterations in the ratio of number of daily recovered cases to number of daily cases based on time were demonstrated in Figure 5. According to this figure, the ratio of number of daily recovered cases to number of daily cases were decreased until 7 April 2020 and after that date it was increased.

Statistical model for the ratio of number deaths to number of cases in intensive care unit based on time was shown in Table 1. The alterations in the ratio of number of deaths to number of cases in in-

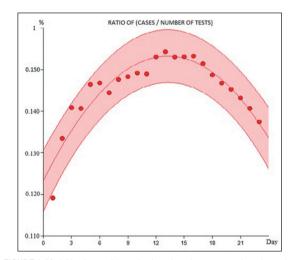


FIGURE 1: Model for time and the ratio of number of cases to number of tests (27 March-18 April 2020).

tensive care unit based on time were demonstrated in Figure 6. The ratio of number of deaths to number of cases in intensive care unit has a tendency to increase from the beginning of the pandemia until this date.

DISCUSSION

A series of pneumonia cases with unknown etiology and mimicking viral pneumonia were the initial cases of outbreak in China in 2019. Scientists from China had isolated a new type coronavirus named as 2019nCov from bronchoalveolar lavage samples by deep sequence analysis.^{13,14} The source of the outbreak was

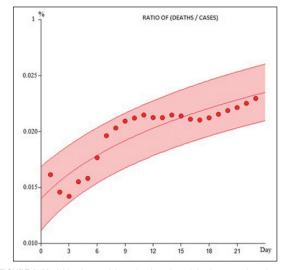


FIGURE 2: Model for time and the ratio of number of deaths to number of cases (27 March-18 April 2020).

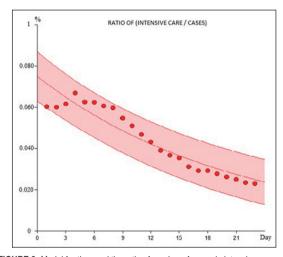


FIGURE 3: Model for time and the ratio of number of cases in intensive care unit to number of cases (27 March-18 April 2020).

claimed to be a market selling live animals named as Huanan Seafood Wholesale Market in China. The outbreak of 2019-nCov started at December 2019 in China and then spread worldwide rapidly. From 18 to 29 December 2019, five cases were admitted to hospitals and one of them died.^{15,16} By 2 January, 41 laboratory confirmed individuals were determined in Wuhan. More than half of these cases were directly in contact with seafood market. In the following of these patients, 68% of the them were discharged and 15% were died in 22 January 2020.¹⁴ At the same time 571 cases were reported in 25 provinces in China.¹⁷ At the end of January, 7736 confirmed cases, 170 deaths and 124 recovered and discharged patients were reported in China.7 Similarly, in that date, 90 cases with 2019nCov infection have been reported in many countries such as Hong Kong, Taiwan, Australia, Japan, Malaysia, The Republic of Korea, Singapore, Germany, France, Canada, Vietnam and the United States of America.^{15,18} The virus had an exponential rise rate and spread rapidly day by day. A total of 20 438 definite cases, 2788 patients in intensive care units, 425 deaths, 632 recovered patients and 23214 suspected individuals were announced at 4 February in China.¹⁹ By the first half of March, 2019-nCov infection was detected in 192 countries and at the end of March, 800 000 cases of all age groups and nearly 7900 deaths were reported all over the world.²⁰ If we look into the patients numbers by 18 April 2020 all over the world, 2 309 176 patients were diagnosed as 2019-nCov, 158 063 were died and 575 619 cases were recovered. There are 725 368 cases, 37 697 deaths with a death rate of 5.2%, 7861 patients in intensive care unit and 43 828 recovered patients in United States, 191 202 cases, 20 019 deaths with a death rate of 10.47%, 7871 patients in intensive care units and 72 963 recovered patients in Spain; 175 925 cases, 23 227 deaths with a death rate of 13.2%, 2733 patients in intensive care units and 44 927 recovered patients in Italy; 141 752 cases, 4372 deaths with a death rate of 3.08%, 2119 patients in intensive care units and 87 500 recovered

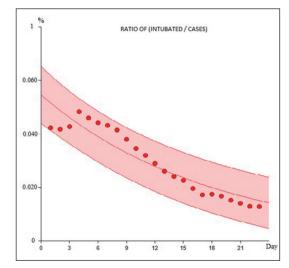


FIGURE 4: Model for time and the ratio of number of intubated cases to number of cases (27 March-18 April 2020).

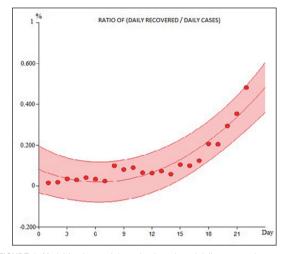


FIGURE 5: Model for time and the ratio of number of daily recovered cases to number of daily cases (28 March-18 April 2020).

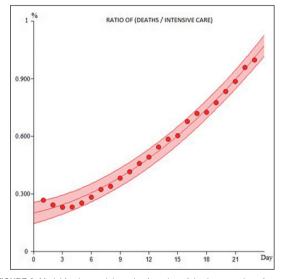


FIGURE 6: Model for time and the ratio of number of deaths to number of cases in intensive care unit (27 March-18 April 2020).

patients in Germany.²¹ In Turkey, the first case was detected in 10 March, the first death was reported in 17 March. By 27 March 2020, a total of confirmed cases was 5698, a number of deaths was 92, the number of patients in intensive care units was 344, the number of intubated patients was 241 and the number of patients recovered was 42. In 18 April 2020, a total of confirmed cases was 1890, the number of patients in intensive care units was 1894, the number of intubated patients in intensive care units was 1894, the number of patients was 1054 and the number of patients recovered was 10

453.¹² The average death rate is nearly 2% in our country. In addition to this findings, we found in this statistical model that the ratio of number of cases to number of tests were increased until 7 April 2020 and after then it was decreased while the ratio of number of daily recovered cases to number of daily cases were decreased until that date and then it was increased. The ratio of deaths to number of cases were increased rapidly in first week whereas it increased more slowly after the first week. Although the ratio of number of intubated cases to number of cases and the ratio of number of cases in intensive care unit to number of cases have a tendency to decrease in the same rate, the ratio of number of deaths to number of cases in intensive care unit has a tendency to increase from the beginning of the pandemia until this date.

One of the most important issue for transmission for the outbreak was traveling abroad. In a study searching the estimated size of outbreak was focused on the data about the number of confirmed cases outside China and travel, Wu et al. showed that 75 815 people is estimated to be infected with 2019-nCov by 25 January 2020 and to be doubled in 6.4 days time period.²² In the world, many efforts were made to control the outbreak. Firstly, Chinese government isolated the provinces, which the cases were most detected, holidays and festivals were restricted, two new hospitals with 2600 beds were opened for the patients with pneumonia. School openings were postponed, many medical teams went Hubei from other provinces to help local medical teams. Research teams were created to search for the prevention and management of the disease. Moreover, protective equipment and drugs were transferred to the epidemic area.¹⁹ In our country, the first case who were detected in 10 March 2020, had an history of traveling. Furthermore, the first case death from 2019-nCov infection had an history of trip abroad. Other factor that results increment in our case number was Umrah. Our government and the scientific committee analysed the risk factors and they decided to quarantine people, who came from Umrah at the beginning of the outbreak, announced continuously for social distancing via media and advise people to wear protective equipment in marketing and crowded areas. In some provinences, some hospitals were selected as pandemic hospitals and reconstructed for the outbreak. In addition to this, distance learning programs were started for education, international flights were stopped, a rule of 3 meters distance was ordered in market places, travel ban was scheduled at 28 March and order a curfew for the weekends at 10 April for all ages and continuous curfew above 65 years and below 20 years old. We suggest that taking precautions in the early period of the outbreak in Turkey by analysing and understanding the policy of China to control outbreak is one of the reasons of this decreasing curve. Supporting this idea, United Kingdom claimed that social distancing and quarantine are not necessary for controling the outbreak and this idea was resulted with 108 692 cases with a high death rate of 13% in their country.²³

The diagnosis of infection is based on molecular methods. Since they are time-consuming, quicker methods to define cases is essential. Although blood tests are not specific for the disease, chest tomography can give a chance to us for early diagnosis. Patients with symptoms and chest imaging findings are hospitalized and started to treat in our country until molecular tests result. So, early treatment avoid clinical worsening and viral replication that leads to decreased intensive care unit and intubation rates. The other advantage of this condition is the opportunity of isolation of patients in early periods. Contrary to other countries, we have more tomography machines in our country and this is one of the factors that help us to fasten the process and control the spread rate.

Another reason of the decrement in serious cases and deaths can be the country-specific and new algorythims in our country. Government ordered medical companies to product hydroxychloroquine in the early period of the outbreak and we could start hydroxychloroquine at early stages. Moreover we administered favipravir during early viral replication period before critical illness. The other approach applied was noninvasive ventilation techniques versus intubation, which prevents lung injury due to intubation. Coagulopathy is claimed to be one of the etiologic factors for the disease so we started to use low molecular weight heparin in treatment. Furthermore antibody treatment was started to be administered in selected cases.

CONCLUSION

Recently, we concluded that the increasing trend of daily recovered cases and decreasing trend of number of deaths, requirement of intensive care unit and intubation are the main satisfactions for our country. In this study, number of tests was taken into account because number of tests are samples represents population. Evaluation of case numbers independently from test number may not be an appropriate approach. Case numbers per tests could give more correct knowledge about the spread of the infection. The two critical points for modeling for pandemia are the correct selection of the statistical modeling and updating the model according to the new cases. The statistical modeling used in this study about 2019nCov infection would provide a benefit to scientists and the population. Moreover it could shed some light on the control of the process. While more cases than modeling estimates can show the uncontrolled process, less cases could indicate the well-controlled process.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: İlker Ercan; Design: İlker Ercan, Özlem Toluk; Control/Supervision: İlker Ercan; Data Collection and/or Processing: İlker Ercan, Özlem Toluk; Analysis and/or Interpretation: İlker Ercan, Burcu Dinçgez Çakmak; Literature Review: Burcu Dinçgez Çakmak, Yeşim Uncu; Writing the Article: Burcu Dinçgez Çakmak, Yeşim Uncu; Critical Review: İlker Ercan, Yeşim Uncu; References and Fundings: İlker Ercan, Burcu Dinçgez Çakmak; Materials: Burcu Dinçgez Çakmak, Özlem Toluk.

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