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RESEARCH ARTICLE

Evaluation of SARS-CoV-2 patients with annual RT-PCR analysis results

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ABSTRACT

Background: Nowadays, people have faced with a pandemic called COVID-19. The reliable detection of the virus is important to prevent transmission of the virus. RT-PCR is a gold standard method for the diagnosis of the disease used at all over the world. The highest number of sample size (1,461,258 patient sample) and differing results are reported with our study regarding the PCR positivity rates.

Method/Study Design: The study was aimed to evaluate the positivity and negativity of the patients with RT-PCR from all the samples studied between March 25, 2020 and March 25, 2021, when the pandemic was declared and started to be seen in Turkey, and to investigate its contribution to the total test capacity of our country.

Results/Conclusions: 1,461,258 patient is observed, and this frequency male is 58% and female is 42% of the population. The maximum number of admissions is noticed during the Autumn-2020 involved age ranged from 25 to 35. 14.6% positive result is got while the 85.4% negative result is observed. When the age distribution of COVID-19 (+) patients is evaluated, COVID-19 (+) rate is highest in the 6-15 age range, followed by the 66-75 age range and the highest COVID-19 (+) rate are November and October, respectively. Additionally, the highest COVID-19 (+) rate is in Autumn. According to the test results, it was determined that 7.5% of the male participants were COVID-19 (+) and 7.1% of the female participants were COVID-19 (+).

Keywords: COVID-19, q-RT-PCR, SARS-CoV-2

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a beta type of coronavirus that leads to coronavirus-19 disease (COVID-19) infection. It is the 7th coronavirus described in humans after 229E, NL63, OC43, HKU1, MERS-CoV, and the previous SARS-CoV. The severe acute respiratory syndrome (SARS-Co-V-1) is emerged as outbreak at China in 2002, and the coronavirus that caused MERS (Middle East respiratory syndrome) infection started at Jordan in 2012 [1]. The complete genome of SARS-CoV-2 is composed of around 30kb and two-third of 5' contains orf1ab encoding orf1ab polyproteins. On the other side of the genome as 3′ consists of genes encoding structural proteins, currently known as surface glycoprotein (S), an envelope protein (E), membrane protein (M), and nucleocapsid (N) proteins. The infection of the virus is occurred by binding affinity with host and receptor communication with binding affinities of the spike protein (S proteins) of the SARS-CoV-2 to the human angiotensin-converting enzyme 2 (ACE2) [2]. S protein is also composed of two main parts: first an amino-terminal subunit (S1) and a carboxyl-terminal subunit (S2) by host furin-like proteases [3]. When the interaction occurs between S protein and host receptor, S protein is divided into these two subunits. The recognizing of virus-host binding actually is created in the C-terminal of the S1 subunit (S1 CTD) because of having a receptor-binding domain (RBD) [4]. Moreover, zoonotic transmission of coronaviruses and determining cell tropism

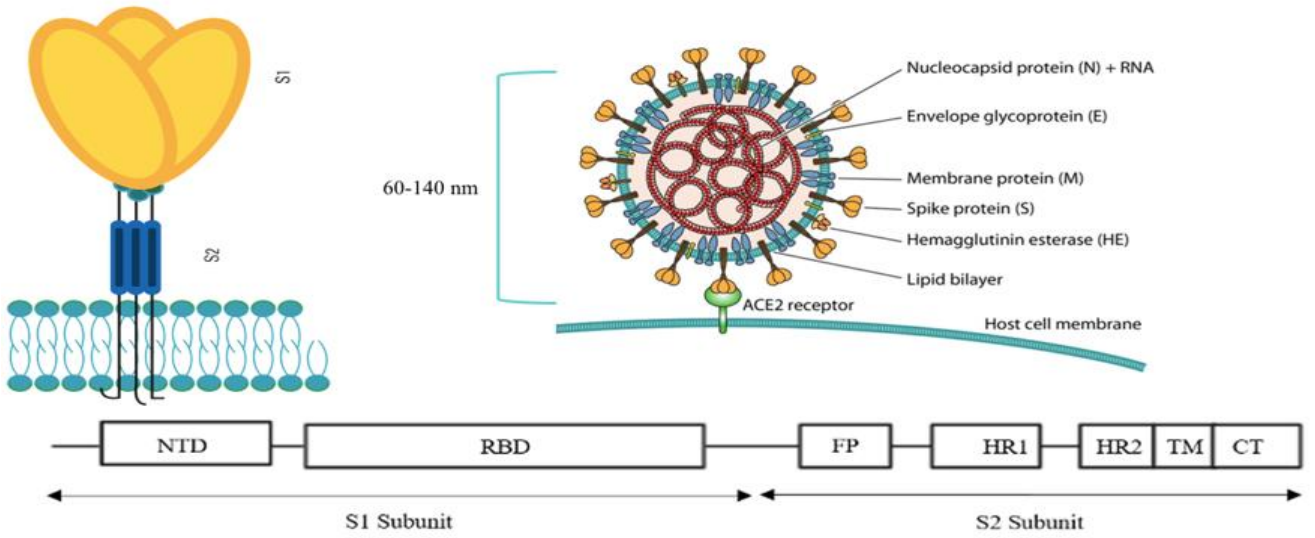

Figure 1. Structural form of SARS-CoV-2

is the role of in this domain. On the other side, S2 subunit of S protein includes a hydrophobic fusion loop and two heptad repeat regions (HR1 and HR2) which are significant for membrane charge fusion as shown in **Figure 1** [5].

The transmission of the disease is through air droplets that especially spread around coughing, sneezing, and speech. The first case of COVID-19 was announced in China, December 2019 and in March 2020, the World Health Organization (WHO) declared SARS-CoV-2 infection as a pandemic [6, 7]. Afterwhile, 16 August 2022, there have been 588.757.628 confirmed cases of COVID-19, including 6.433.794 deaths, reported to WHO. As of 8 August 2022, a total of 12.355.390.461 vaccine doses have been administered [8-10]. Because of the lack of efficient and effective antiviral therapy to the disease and the undeniable fact that vaccination studies have just begun after the disease outbreaks, early diagnosis of symptomatic and asymptomatic patients take a significant role in controlling the epidemic. Generally, symptomatic patients show some common clinical manifestations of the disease usually including fever (body temperature 37◦C to 38◦C), cough, nasal congestion, and fatigue after less than a week. Moreover, pneumonia mostly occurs in the second or third week of symptomatic infection [11]. On the other hand, laboratory studies declare that SARS patients also have demonstrated high level of C-reactive protein (CRP), leukopenia, lymphopenia, lactate dehydrogenase (LDH), aminotransferase, and creatine kinase [12]. In some critical cases of patients could be obtained acute respiratory distress syndrome (ARDS), acute respiratory failure, other serious complications, and even death [13]. Nowadays, the majority of people with COVID-19 disease do not show symptoms called asymptomatic carriers that are detected by positive polymerase chain reaction (PCR) results depending on their viral loads [14]. Approximately, asymptomatic cases range from 8% to 80% [15]. This group is the actual problem to control the pandemic. In a community, they could infect many people without any consciousness. While symptomatic patients can be detected as much several techniques such as computed tomography (CT), The enzyme-linked immunosorbent assay (ELISA) or serological test, chosen most effective technique is the critical point for the true diagnosis to control the transmission of virus. ELISA is an immunoassay that is less costly but also less sensitive than RT-PCR the gold standard method. The diagnosis is ensured by the presence of immunoglobulin (Ig) G in immunofluorescence assay (IFA). On the other side, serological tests are blood-based tests that are used for whether the person had an infection used by antibodies levels. Especially, IgM and IgG antibodies and antigens are used as key lock compatibility [16].

Principally, antigens are recognized by the immune system of an infected person as foreign elements and specific antibodies are produced to prevent the infection. Generally, antibodies are produced after the second week of the virus infection within the body used as a marker for diagnosis. The actual disadvantage of these tests is that while IgM antibodies can be detected after 10-20 days, IgG is determined after 20 days of SARS-CoV-2 infection [17]. Nowadays, point of care (POC) is utilized for the diagnosis of SARS-CoV-2. However, tests are available only in research settings recommended by WHO and can just determine actively replicating viruses in samples. At the same time, recently the loop-mediated isothermal amplification (LAMP) method is chosen rather than RT-PCR because of the easy usage and sensitivity as the gold standard technique [18]. However, when the LAMP is compared with the RT-PCR technique, some unverified results can be obtained, and less sensitivity can be observed. Thus, real-time reverse transcription-polymerase chain reaction (RT-PCR) has been chosen as a gold standard method referenced standard by the T.R. Ministry of Health [19].

RT-PCR is a version of PCR method explicitly developed for (genomic) RNA detection quantitatively gold standard method that used three main target genes for SARS-CoV-2 virus detection including the Orf1b gene (human RNA polymerase protein), N-gene (N protein), and the E-gene (E protein). The test confirmation is dependent on the probe-target sequence. In this technique, two consecutive reactions are actualized, first conversion of RNA into complementary DNA (cDNA) through reverse transcription enzyme and second amplification of the cDNA sample by polymerase chain reaction using gene-specific primers. DNA produced in the first step is used in the second step throughout thermal cycles [20]. Within the second step of the reaction, gene-specific primers guide the reaction as a complementary element and amplification of only the selected region on the genome. The probes with primers produce a signal fluorescently allowing a quantifiable reaction system. Generally, TagMan probes are utilized. For the RT-PCR, the patient's samples are taken from nasopharyngeal or oropharyngeal [21]. In the presented study, we evaluated the 1-year RT-PCR results according to the patient's age, gender, amount of positivity throughout the year, and seasonal variation. We think that these results will help in estimating the number of future cases.

MATERIAL AND METHOD

Sample Collection, Transportation and Storage

For the test process, nasopharyngeal swap samples are utilized by SARS-CoV-2 patients and were collected by trained personnel and transferred to Kanuni Sultan Suleyman Training and Research Hospital in a VTM solution tube. 1,461,258 randomly selected patients' samples were tested with Bio-Speedy (SARS CoV-2 Double Gene RT-qPCR kit [version 1]).

RT-PCR Tests

Throughout process, extra RNA extraction step is not required because of the use of VTM solution which is included enzyme with nucleic acid extraction property. Only swap samples of patients within the VTM solution are enough with vigorous vertexing for RNA extraction which is the key step of process. For the RT-PCR, 1,461,258 randomly selected patients' samples are tested with Bio-Speedy (SARS CoV-2 Double Gene RT-qPCR Kit [version 1]). The primers are designed with conserved regions of ORF1ab and RNaseP genes of SARS-CoV-2. Channels of Fam and phosphonamidite (Hex) are preferred for ORFlab and RNaseP gene, respectively. Experiments are performed in Biorad CFX96 platforms. According to the kit protocol, 5 µl patient samples with VTM were added to a 15 µl ready kit mixture to achieve 20 µl PCR mixture in totally. Thermal cycle parameters of RT-PCR amplification were, as follows: 52 °C for 5 minutes for reverse transcription, 95 °C for 10 seconds for holding, then 40 cycles of 95 °C for 1 second and 55 °C for 30 seconds for denaturation, annealing, and extension, respectively.

Table 1. Gender Distribution

Variable	Variable levels	Frequency	Percentage (%)
Gender	Male	848,111	58.0
	Female	613,147	42.0
	Total	**1,461,258**	**100.0**

Test interpretation

The test interpretation is arranged based on kit protocol as 200 for the Biorad CFX96 platform. The Ct values below 32 for Fam channel irrespective of Hex values is accepted as positive with sigmoidal curve. Non-sigmoidal signals and sigmoidal signals with Ct values above 32 in the Fam channel and sigmoidal signals with Ct values below 32 in the Hex channel were interpreted as negative based on kit protocol. Non sigmoidal signals and sigmoid below 32 Ct on both Fam and Hex channels were interpreted as an invalid result.

Statistical Analyzes

Statistical package program was used in the analysis of the data obtained as a result of the research. While analyzing the obtained data, descriptive statistical methods (frequency, percentage and mean) were used and they were turned into tables and graphics. Also, ratio charts are scaled to ×1,000.

Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. This study protocol was reviewed and approved by Ethics Committee of Kanuni Sultan Suleyman Training and Research Hospital No: 2021.05.164, Subject No: KAEK/2021.05.164 Date: 06.05.2021 – 09:57 – E-80929729-000-8438 and Republic of Turkey, Ministry of Health, COVID-19 Scientific Research Studies Approval No: YakupArtik-2021-03-16T19_12_58.

RESULTS

Subjects who applied to Kanuni Sultan Suleyman Training and Research Hospital COVID-19 diagnostic laboratory between 25 March 2020-25 March 2021 were collected. A total of 1,461,258 subjects were included.

Table 1 and **Figure 2** show the gender distribution of 1,461,258 patients who had PCR analysis done in the lab between March 25, 2020, and March 25, 2021. It was discovered that 58%, or 848,111, of the participants were male and 42%, or 613,147, were female shown in **Table 1**.

The age distributions of 1,461,258 participants who underwent PCR analysis in the laboratory between March 25, 2020, and March 25, 2021, are shown in **Table 2** and **Figure 3**. The annual data revealed that the majority of the patients who applied for the test were between the ages of six and 45. Within this distribution, it was discovered that the 16-25 age group, or the young population, had the highest test rate and concentration.

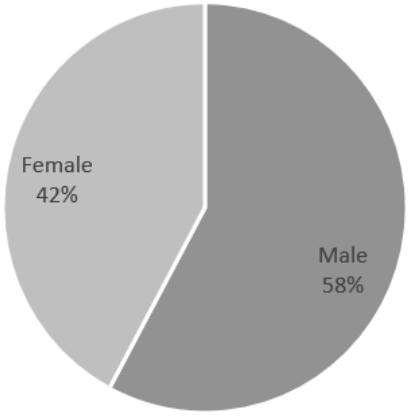

Figure 2. Gender distribution

Table 2. Frequency Percent Plots of Number of Tests by Age

Variable	Variable levels	Frequency	Percentage (%)
Age	<5	17,495	1.2
	6-15	42,039	2.9
	16-25	285,122	19.5
	26-35	390,765	26.7
	36-45	312,093	21.4
	46-55	217,732	14.9
	56-65	114,909	7.9
	66-75	50,654	3.5
	76<	30,449	2.1
	Total	**1,461,258**	**100.0%**

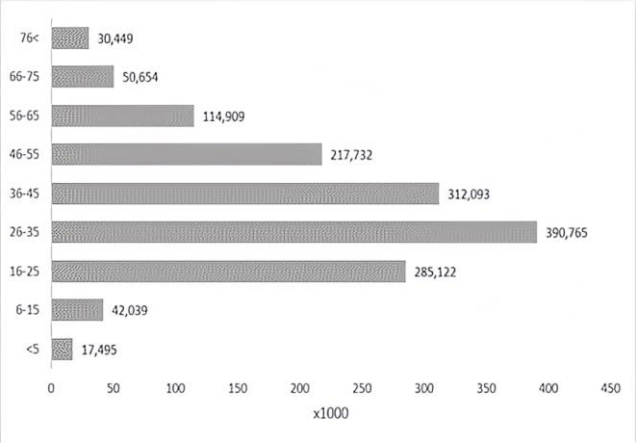

Figure 3. Frequency percent plots of number of tests by age

The monthly average age of the participants who underwent PCR analysis in the laboratory between March 25, 2020, and March 25, 2021, is shown in the **Figure 4**.

According to **Figure 4**, the average age in March-2020 was 44, which is the highest average age in a year. In the months that followed, it was discovered that the average age decreased over time, with the lowest average age occurring in September-2020.

The seasonal distribution of 1,461,258 participants who underwent PCR analysis in the laboratory between March 25, 2020, and March 25, 2021, is shown in the **Table 3** and **Figure 5**.

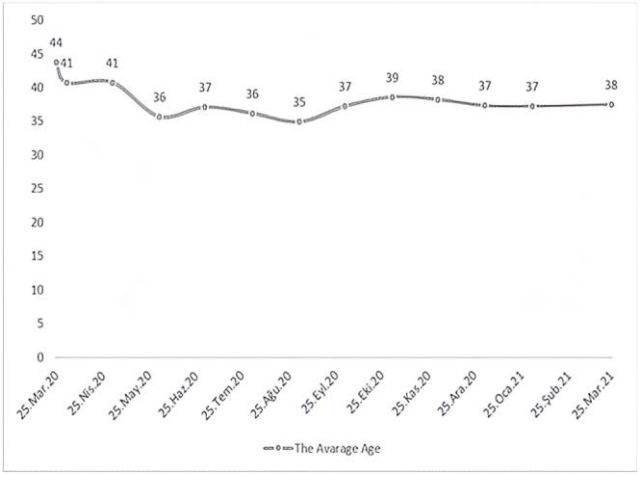

Figure 4. RT-PCR result of monthly average of patients

Table 3. Seasonal Distribution of Participants

Variable	Variable levels	Frequency	Percentage (%)
Season	Spring-2020(25 March>)	154,517	10.6
	Summer-2020	478,155	32.7
	Autumn-2020	600,155	41.1
	Winter-2021	171,630	11.7
	Spring-2021(25 March <)	56,801	3.9
	Total	**1,461,258**	**100.0**

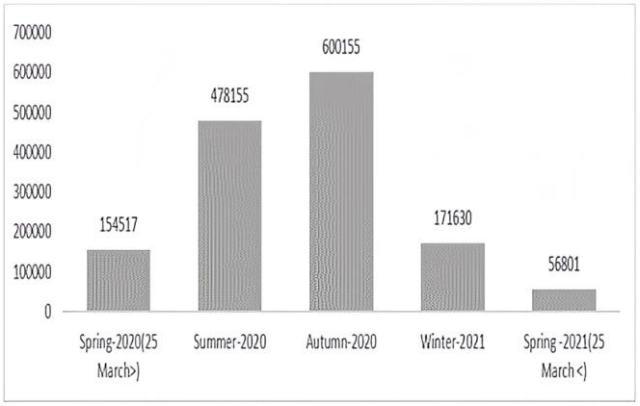

Figure 5. Seasonal distribution of participants

In this context, the maximum number of admissions is noticed during the Autmn-2020 season, after which it begins to decline.

The monthly distribution of 1,461,258 subjects who underwent PCR analysis in the laboratory between March 25, 2020, and March 25, 2021, is shown in the **Table 4** and **Figure 6**.

In this context, the number of people admission for the test has been increasing since Seprember-2020, and it has been determined that the highest number of admissions was seen in August-2020, followed by a decrease.

In the **Table 5** and **Figure 7**, the qualitative analysis results [COVID-19 (+), COVID-19 (-)] of 1461258 subjects who underwent PCR analysis in the laboratory between 25 March 2020, and 25 March 2021, are shown.

Table 4. Monthly Distribution of Patients' Results

Variable	Variable levels	Frequency	Percentage (%)
Months	25-Mar-20>	1,818	0.1
	Apr-20	73,522	5.0
	May-20	79,177	5.4
	Jun-20	137,370	9.4
	Jul-20	132,285	9.1
	Aug-20	208,500	14.3
	Sep-20	222,014	15.2
	Oct-20	202,239	13.8
	Nov-20	175,902	12.0
	Dec-20	90,151	6.2
	Jan-21	42,996	2.9
	Feb-21	38,483	2.6
	25-Mar-21<	56,801	3.9
	25-Mar-20>	1,818	0.1
	Total	**1,461,258**	**100.0%**

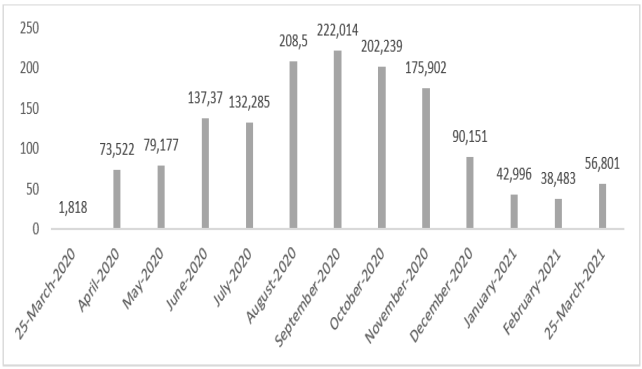

Figure 6. Monthly distribution of patients' results

Table 5. Distribution of COVID-19 (+) and COVID-19 (-)

Variable	Variable levels	Frequency	Percentage (%)
Test result	Negative	1,247,768	85.4
	Positive	213,490	14.6
	Total	**1,461,258**	**100.0%**

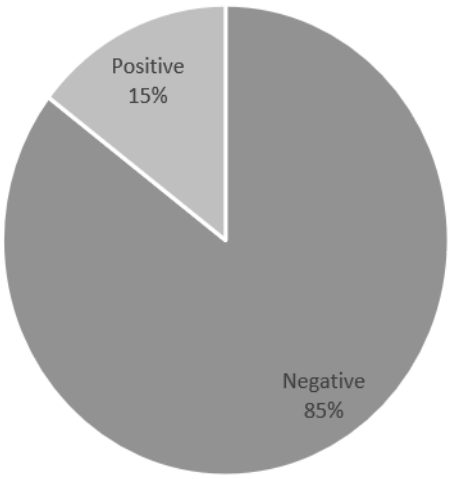

Figure 7. Distribution of COVID-19 (+) and COVID-19 (-)

In this context, it was determined that 14.6% of the participants were COVID-19 (+) in this context, 213,490, and 1,247,768 out of 85.4% were COVID-19 (-).

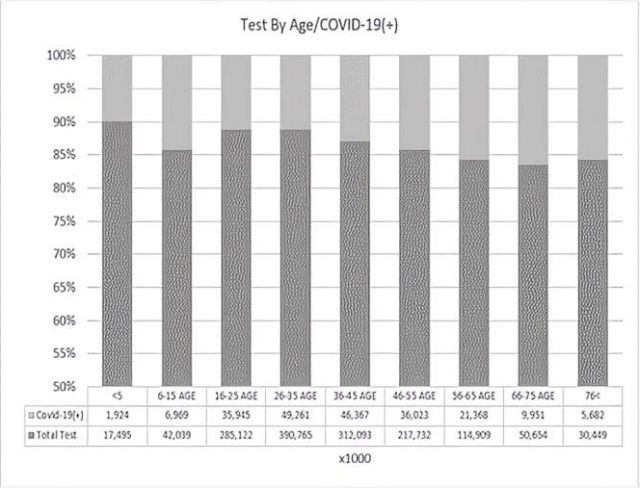

Figure 8. Age distirubition of COVID-19 (+) patients

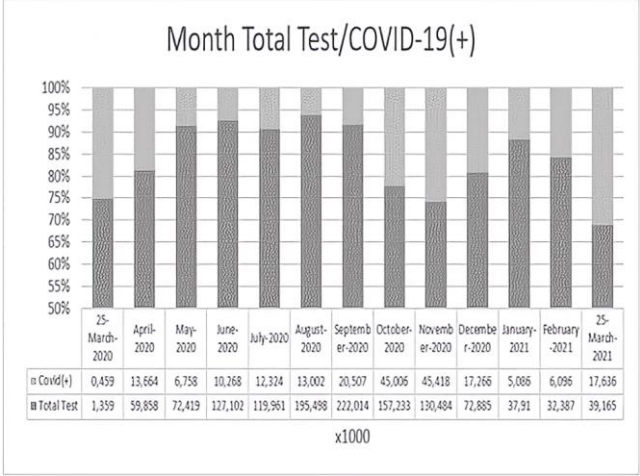

Figure 9. Total tests by month/COVID-19 (+)

In the **Figure 8**, the status of being COVID-19 (+) according to age distribution of the subjects who underwent PCR analysis in the laboratory between March 25, 2020-March 25, 2021, are given.

In this context, the intensity of the COVID-19 (+) rate is highest in the 6-15 age range, followed by the 66-75 age range. Although the age range of 26-35 is the most intense admission range, it has been determined that being COVID-19 (+) is the lowest range.

In the **Figure 9**, the status of being COVID-19 (+) according to months of the subjects who underwent qualitative PCR analysis in the laboratory between March 25, 2020-March 25, 2021, are given.

In this context, the months with the highest COVID-19 (+) rate are November and October, respectively.

In the **Figure 10**, between March 25, 2020, and March 25, 2021, the COVID-19 (+) density of the subjects who underwent qualitative PCR analysis in the laboratory was measured according to the seasons. In this context, it has been determined that the season with the highest COVID-19 (+) rate is Autumn.

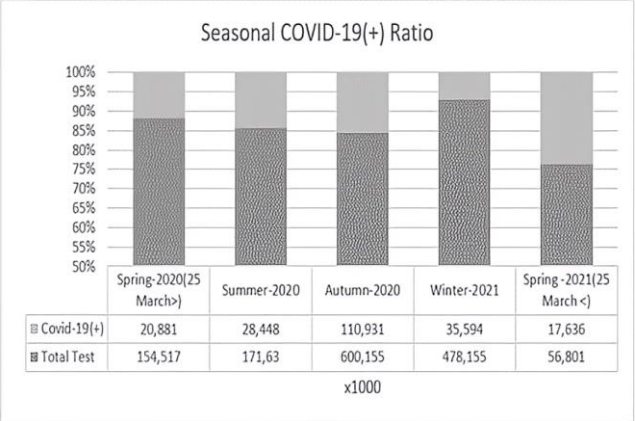

Figure 10. Seasonal COVID-19 (+) rate

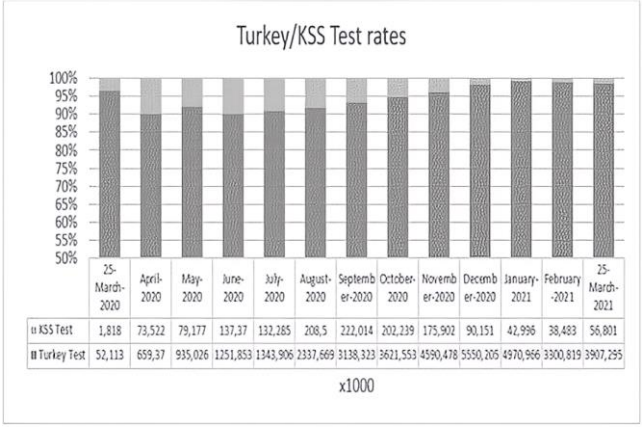

Figure 12. Turkey/our hospital test rates

Table 6. Gender Distribution of Patients

	COVID-19 (-)		COVID-19 (+)		Total
	F	%	F	%	
Male	738,242	50.5	109,869	7.5	848,111
Female	509,526	34.9	103,621	7.1	613,147
Total	1,247,768	85.4	213,490	14.6	1,461,258

Note. F: Frequency & %: Percentage

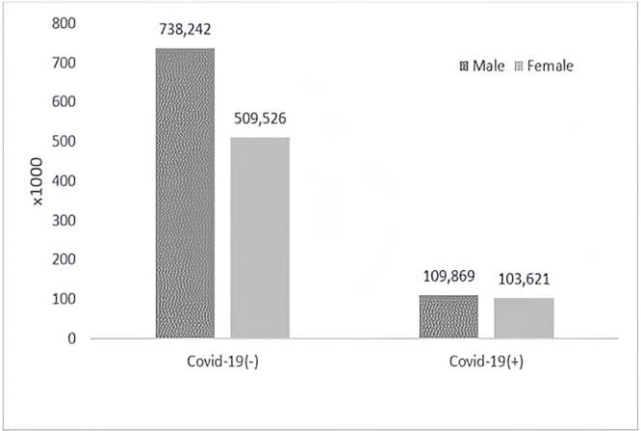

Figure 11. Gender distribution of patients

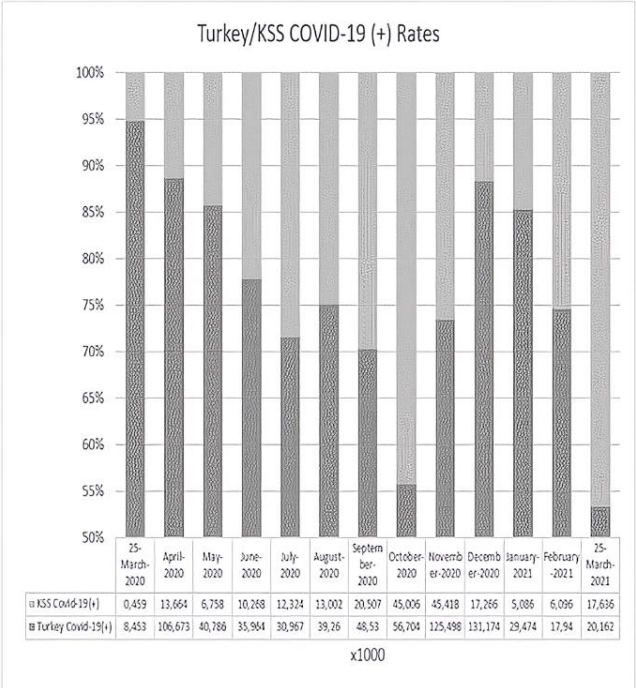

Figure 13. Turkey/ our hospital (KSS) COVID-19 (+) rates

In the **Table 6** and **Figure 11**, the gender distribution of 1,461,258 subjects who underwent PCR analysis between 25 March 2020, and 25 March 2021, according to the qualitative analysis result [COVID-19 (+), COVID-19 (-)] is shown.

In this regard, according to the test results, it was determined that 7.5% of the male participants were COVID-19 (+) and 7.1% of female participants were COVID-19 (+).

Figure 12 is presented by comparing the monthly COVID-19 test numbers of the Turkish Ministry of Health with the monthly test numbers of the Kanuni Sultan Suleyman Training and Research Hospital COVID-19 Diagnostic Laboratory.

As a result of the test based on these data, it is seen that the highest rate of taking the test in the Kanuni Sultan Suleyman Training and Research Hospital COVID-19 Diagnostic Laboratory in June, April, and July, respectively.

Figure 13 is presented by comparing the monthly COVID-19 (+) test numbers of the Turkish Ministry of Health with the COVID-19 (+) monthly test numbers of Kanuni Sultan Suleyman Training and Research Hospital COVID-19 Diagnostic Laboratory.

As a result of the test based on these data, it was determined that the highest rate of COVID-19 (+) was in October, July, and November, respectively.

DISCUSSION

Throughout history, mankind has struggled with many pandemics caused by viral infections that are SARS, swine flu, ebola, MERS, and eventually COVID-19. Especially, in 2020, COVID-19 disease was a challenging endeavor to the entire medical world.

The scientific world tried to carry out studies to reveal the virus characteristics in these periods. Although many time has been left behind, actual characteristic of virus has not still been understood. To control the pandemic, the actual focus should be diagnosis of the virus effectively and also to manage the spreading of infections. Since January 2020, the novel coronavirus was isolated from Wuhan's patients nasopharyngeal and oropharyngeal secretions and viral genetic sequencing are provided by the Global Initiative on Sharing All Influenza Data–GISAID.

According to known genetic code of the virus, diagnostic methods for COVID-19 through quantitative reverse-transcription polymerase chain reaction (RT-PCR) systems are developed up to present time. Moreover, RT-PCR technique is chosen as a gold standard for the confirmation of COVID-19 disease in upper respiratory samples (nasopharyngeal and oropharyngeal secretion). Several RT-PCR methods are offered by WHO to ensure a suitable diagnosis, help testing populations and contribute to controlling the spread of the disease [22].

In this article, we evaluate the annual RT-PCR result of patients. In this content, 1,461,258 patient is observed, and this frequency male is 58% and female is 42% of the population. Moreover, when the age scale of the patients is examined the most population is observed ranged from 25 to 35 and the maximum number of admissions is noticed during the Autmn-2020 season.

Within the 1,461,258 patient 14.6% positive result is got while the 85.4% negative result is observed. When the age distribution of COVID-19 (+) patients is evaluated, COVID-19 (+) rate is highest in the 6-15 age range, followed by the 66-75 age range and the highest COVID-19 (+) rate are November and October, respectively. On the other hand, in literature this value is presented as that mean age of patients is 33.9 years [23]. Additionally, the highest COVID-19 (+) rate is in Autumn.

According to the test results, it was determined that 7.5% of the male participants were COVID-19 (+) and 7.1% of the female participants were COVID-19 (+). The aim of the study was to evaluate a large number of patients, and while the distribution of test rates by age, season, gender, and months was examined, the values in the same parameters were shown in the positivity rates. We think that this study will provide a perspective to the studies in 2022 in terms of risk management activities. In this way, we have shown how the population trend is in case of possible virus mutation or any new variant. At the same time, we made sense of how the positivity rates progressed by month, season, age, and gender, retrospectively. Although in literature there are many studies about the RT-PCR result of COVID-19 patients, the highest number of sample size and differing results are reported with our study regarding the PCR positivity rates [24, 25].

Author contributions: SZMK: provided support on academic consultancy and administrative process management throughout the entire research process and in the analysis of PCR results; **YA:** developed the protocol, summarized, and analyzed the data, wrote the article, and vouched for it; **NPC:** developed the protocol and methodology and reviewed the article; **CK:** provided administrative process management throughout the entire research process; & **YTS:** analyzed the PCR results. All authors have agreed with the results and conclusions.

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Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Gulec EY, Cesur NP, FazlioGlu GY,Kazezoğlu C. Effect of different storage conditions on COVID-19 RT-PCR results. J Med Virol. 2021;93(12):6575-81. doi:10.1002/jmv.27204 PMid:34260086 PMCid: PMC8426709
2. Khailany RA, Safdar M, Ozaslan M. Genomic characterization of a novel SARS-CoV-2. Gene Rep. 2020;19:100682. doi:10.1016/j.genrep.2020.100682 PMid:32300673 PMCid:PMC7161481
3. Artik Y, Cesur NP, Turkoglu Lacin N. SARS-CoV-2 mutations, diagnosis and their concern. Arch Mol Biol Genet. 2022;1(2):57-65.
4. Artik Y, Cesur NP. General evaluation of COVID-19 diagnosis methods. Cohesive J Microbiol Infect Dis. 2022;5(5):000621
5. Walls AC, Park Y-J, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell. 2020;181(2):281-92. doi:10.1016/j.cell.2020.02.058 PMid:32155444 PMCid:PMC7102599
6. Artik Y, Varol N, Cesur NP. Hospital disaster and emergency plan in biological disasters (HDEP): Coronavirus (SARS-CoV-2) COVID-19 pandemic system model example. J Contemp Stud Epidemiol Public Heal. 2022;3(1):ep22003. Doi:10.29333/jconseph/11975

7. Artik Y, Kurtulmus MS, Cesur NP, Komurcu SZM, Kazezoglu C, Kocatas A. Clinic evaluation of the destrovir spray effectiveness in SARS-CoV-2 disease. Electron J Gen Med. 2022;19(2):em357. doi:10.29333/ejgm/11578
8. Komurcu SZM, Artik Y, Cesur NP, et al. The evaluation of potential global impact of the N501Y mutation in SARS-COV-2 positive patients. J Med Virol. 2021;94(3):1009-19. doi:10.1002/JMV.27413 PMid:34676574 PMCid:PMC8661766
9. Artik Y, Cesur NP, Kenar L, Ortatali M. Biological disasters: An overview of the COVID-19 pandemic in the first quarter of 2021. J Disaster Risk. 2021;4(2):163-82. doi:10.35341/AFET.977488
10. WHO Coronavirus (COVID-19) Dashboard. Available at: https://covid19.who.int/
11. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: A report of 1014 cases. Radiology. 2020;296(2):E32-40. doi:10.1148/radiol.2020200642 PMid:32101510 PMCid:PMC7233399
12. Wang J-T, Sheng WH, Fang C-T, et al. Clinical manifestations, laboratory findings, and treatment outcomes of SARS patients. Emerg Infect Dis. 2004;10(5):818-24. doi:10.3201/eid1005.030640 PMid:15200814 PMCid:PMC3323212
13. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive. Lancet. 2020;395(10223):507-13. doi:10.1016/S0140-6736(20)30211-7
14. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. JAMA. 2020;323(14):1406-7. doi:10.1001/jama.2020.2565 PMid:32083643 PMCid:PMC7042844
15. Byambasuren O, Cardona M, Bell K, Clark J, McLaws ML, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: Systematic review and meta-analysis. J Assoc Med Microbiol Infect Dis Canada. 2020. doi:10.3138/jammi-2020-0030
16. Ehrhart J-C, Bennetau B, Renaud L, et al. A new immunosensor for breast cancer cell detection using antibody-coated long alkylsilane self-assembled monolayers in a parallel plate flow chamber. Biosens Bioelectron. 2008;24(3):467-74. doi:10.1016/j.bios.2008.04.027 PMid:18547800
17. Erdem O, Derin E, Sagdic K, Yilmaz EG, Inci F. Smart materials-integrated sensor technologies for COVID-19 diagnosis. Emergent Mater. 2021;4(1):169-85. doi:10.1007/s42247-020-00150-w PMid:33495747 PMCid:PMC7817967
18. Artik Y, Cosgun AB, Cesur NP, et al. Comparison of COVID-19 laboratory diagnosis by commercial kits: Effectivity of RT-PCR to the RT-LAMP, J Med Virol. 2022;94(5):1998-2007. doi:10.1002/JMV.27559 PMid:34997587 PMCid:PMC9015626
19. Demirbilek Y, Pehlivanturk G, Ozguler ZO, Mese EA. COVID-19 outbreak control, example of ministry of health of Turkey. Turkish J Med Sci. 2020;50(SI-1):489-94. doi:10.3906/sag-2004-187 PMid:32304192 PMCid:PMC7195985
20. Holland PM, Abramson RD, Watson R, Gelfand DH. Detection of specific polymerase chain reaction product by utilizing the 5'----3'exonuclease activity of Thermus aquaticus DNA polymerase. Proc Natl Acad Sci. 1991;88(16):7276-80. doi:10.1073/pnas.88.16.7276 PMid:1871133 PMCid:PMC52277
21. Hatcher EL, Zhdanov SA, Bao Y, et al. Virus variation resource–improved response to emergent viral outbreaks. Nucleic Acids Res. 2017;45(D1):D482-90. doi:10.1093/nar/gkw1065 PMid:27899678 PMCid:PMC5210549
22. Wang M, Wu Q, Xu W, et al. Clinical diagnosis of 8274 samples with 2019-novel coronavirus in Wuhan. MedRxiv. 2020. doi:10.1101/2020.02.12.20022327
23. Hasanoglu I, Korukluoglu G, Asilturk D, et al. Higher viral loads in asymptomatic COVID-19 patients might be the invisible part of the iceberg. Infection. 2021;49(1):117-26. doi:10.1007/s15010-020-01548-8 PMid:33231841 PMCid:PMC7685188
24. Peng L, Liu J, Xu W, et al. SARS-CoV-2 can be detected in urine, blood, anal swabs, and oropharyngeal swabs specimens. J Med Virol. 2020;92(9):1676-80. doi:10.1002/jmv.25936 PMid:32330305 PMCid:PMC7264521
25. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA. 2020;323(18):1843-4. doi:10.1001/jama.2020.3786

