

Abstract

Introduction: As COVID-19 disease has rapidly spread across the world, its impact has grown with increasing number of cases and mortality rate in Turkey.

Aim: The aim of this study is to examine epidemiologic and clinical features of the patients that admitted to the hospital with the pre-diagnosis of coronavirus disease-2019 (COVID-19) in Turkey.

Method: In this retrospective study, epidemiologic and clinical features, laboratory findings, radiologic features, therapeutic approaches and survival conditions of the patients with the pre-diagnosis of COVID-19 from March 11th to June 30th, 2020. The all data of the cases were compared in 4 groups: 1st group for the confirmed cases reverse transcriptase polymerase chain reaction (RT-PCR) +, chest computed tomography (CT) +, 2nd group for the clinically diagnosed cases (RT-PCR- CT +), 3rd group for the mild and asymptomatic cases (RT-PCR + CT-), 4th group for the suspected cases (RT-PCR - CT -). Post-hoc analysis was performed to evaluate the differences among the groups.

Results: In total, 3334 patients with the pre-diagnosis of COVID-19 admitted to the emergency department. Based on the post-hoc analyses, significant differences were found among the four groups in terms of their test results of leucocytes, hemoglobin, platelets, neutrophils, urea and C-reactive protein (CRP) ($p < 0.001$). Furthermore, the factors of age groups, hospitalization, intensive care follow-up and mortality rate of the four groups showed a significant difference among the groups ($p = 0.001$).

Conclusion: Mean of leucocytes, neutrophile and platelet values of the patients with tested positive for the RT-PCR was found lower compared to the ones with tested negative for the RT-PCR. Mean of CRP values was found higher in patients with lung involvement compared to other patient groups.

Key words: SARS-CoV-2, COVID-19, pneumonia, epidemiology, Turkey

What is already known about this topic?

In cases with confirmed COVID-19 disease individuals over 65 years and hospitalization rates were higher than the other groups.

What is added by this report?

No deaths were found in cases with confirmed COVID-19 disease. The chest CT imaging results of only 23% of the patients that tested positive in RT-PCR test showed COVID-19 pneumonia findings. Most patients with COVID-19 had normal leucocyte and lymphocyte counts in blood test examinations. CRP value of the cases with lung involvement was higher.

Introduction

World Health Organization (WHO) reported pneumonia cases of unknown etiology in Hubei State, Wuhan city of China on December 31st, 2019. Fever, shortness of breath and radiologic findings of bilateral lung pneumonic infiltration (1). On January 7th 2020, Chinese scientists isolated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus from the patients and the disease was called as a coronavirus disease - 2019 (COVID-19) infection by WHO in February 2020 (2, 3). On January 10th 2020, COVID-19 Science Committee of the Ministry of Health of the Republic of Turkey was established in Turkey. The committee prepared up-to-date diagnosis and treatment guidelines based on the available scientific evidences and ensured that the patient diagnosis and treatment management is performed through following these guidelines in all hospitals in Turkey. The first COVID-19 case was recorded on March 11th 2020 considerably later than the COVID-19 outbreaks in the neighboring countries such as European countries and Iran (4). WHO declared COVID-19 as a pandemic on March 11th 2020 (5).

Confirmed number of cases has been continuously rising daily all around the world. The pandemic that originated from Asia spread to Europe first, and then America and Africa continents; the highest number of cases has been so far reported in USA, Brazil, Russia, India, and United Kingdom (6). As the outbreak has been rapidly spreading all around the world, as of October 30th, 2020, the number of confirmed COVID-19 cases worldwide stands at 44.888.869 and the total number of deaths is 1.178.475 while the number of cases and deaths in Turkey were reported as 373.154 and 10.177, respectively (7). Identifying the epidemiological characteristics of this disease will help to make appropriate decisions and thus control the pandemic.

This study aims to present the details of epidemiologic and clinical features, laboratory findings, radiologic features, therapeutic approaches and survival conditions of the patients with the pre-diagnosis of COVID-19 retrospectively in Samsun Gazi State Hospital that is one of the pandemic hospitals authorized to apply diagnosis and treatment protocols of COVID-19 in Turkey.

Methods

Study design and participants

The study presents a retrospective evaluation of the patients that admitted to the Emergency Department of Samsun Gazi State Hospital with the pre-diagnosis of COVID-19 between March 11th 2020 that is the date of first reported case in Turkey and June 30th 2020

The patient data on age, symptoms, vital findings, comorbid diseases, smoking, and pre-application 14-day clinical history of the patients were obtained in the triage area of the emergency department and the patients that are considered to be a potential or confirmed COVID-19 case were directed to the isolation area in the service. A potential case is defined as a case that shows at least one of the symptoms and findings of fever or acute respiratory tract disease (coughing and shortness of breath), by the fact that his/her clinical presentation cannot be classified as any other disease, by the history of going abroad or contacting the relatives that went abroad in the 14 days prior to the beginning of symptoms or as a case that were in close contact with a confirmed COVID-19 patient. On the other hand, the confirmed cases are defined who were found to have SARS-CoV-2 in nasopharyngeal swab samples obtained from potential cases. Laboratory studies and lung imaging studies of the patients that were taken to the isolation area were carried out, and the nasopharyngeal swab samples were obtained from the people that were in close contact with a confirmed COVID-19 patient in order to perform SARS CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) test. Furthermore, full blood count, electrolytes, glucose, urea, creatinine, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), C-reactive protein (CRP), D-dimer, troponin tests were performed on each case. Unenhanced chest computed tomography (CT) imaging was applied for lung imaging and the acquired CT findings were categorized under two main groups. The findings considered as COVID-19 pneumonia in the foreground are occurrences of peripheral, bilateral, ground glass opacity, multifocal round ground glass opacity (they can be accompanied by other findings of organized pneumonia such as paving stone appearance, consolidation, reverse-halo). The findings not considered as COVID-19 pneumonia in the foreground are the chest CT findings regarded as atelectasis, lobar consolidation, and parenchymal band formation.(4)

In the study, the patients are categorized in 4 main groups (8). The first group as the confirmed cases are those that admitted to the hospital with fever and acute respiratory tract symptoms, tested positive in RT-PCR, and with the chest CT imaging results considered as COVID-19 lung involvement. The second group as the clinically diagnosed cases are those

that admitted to the hospital with fever and acute respiratory tract symptoms, tested negative in RT-PCR, but with chest CT imaging results considered positive in terms of COVID-19 lung involvement. The third group as the mildly symptomatic or completely asymptomatic cases, are those tested positive in RT-PCR but the chest CT imaging yielded negative results. The fourth group as the suspected cases, are patients that applied to the hospital with fever and acute respiratory tract symptoms, tested negative in RT-PCR and showed no COVID-19 lung involvement in the chest CT imaging.

Data collection

Epidemiologic, demographic, clinical, laboratory, treatment and result data of the patients admitted to the isolation area were obtained from the electronic database of the hospital retrospectively.

Ethical approval

Ethics committee approval was obtained with the Ethics Committee Decision dated 30st June 2020 and No. 10 of the Health Sciences University Samsun Education and Training Hospital Ethics Committee.

Data analysis

Descriptive statistics are presented with mean and standard deviation values for continuous data; they are presented with numbers and percentages for categorical data. Compatibility of continuous data with normal distribution was evaluated by Kolmogorov-Smirnov test. Mann-Whitney U, Kruskal Wallis H and chi square test were used in the statistical analysis. Post-hoc analysis was made for the differences arising from Kruskal Wallis H test and Bonferroni correction was made in the evaluation. For the statistical significance, p values in the confidence interval of 95% and below 0.05 were considered significant. The program IBM SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA), version 21.0 was used for the statistical analysis.

Results

3334 patients admitted to the emergency department in total with the pre-diagnosis of COVID-19. 55.5% of the patients are male. Age mean of the patients is 45.46 ± 19.7 ; the median age is 42(6-106). While 34.7% of the patients belong to the age group 31-50 years, 19.8% is above 65 years of age. Of the total cases, 12.7% had hypertension, 7.5% had diabetes, 7.1% had chronic obstructive pulmonary disease (COPD). 28.1% of the patients

were smoker. The demographic features and the co-morbid diseases of the cases are given in Table 1.

The most frequent symptoms reported by the patients were coughing (22.8%), shortness of breath (22.6%), muscle and joint pains (11.1%), fever (6.2%), and fatigue (6.2%). The less frequent symptoms were, in order of frequency, the complaints of sore throat, chest pain, nausea-vomiting-diarrhea, headache-dizziness. While 22.1% of the patients were hospitalized, 2.2% was monitored in the intensive care. Of the total cases, 0.4% (n=12) resulted in exitus. Mortality rate was found 0.8% (n=7) in cases considered to have COVID-19. 2.4% of the patients were referred to other health centers for various reasons (Table 2). 9.8% of all the cases were tested positive in RT-PCR test. 16.4% of the cases showed COVID-19 pneumonia findings in CT imaging results. 13.7% of the cases whose CT imaging results showed COVID-19 pneumonia was tested positive in RT-PCR. No pathology was found in CT results of 53.5% of the cases (Table 3).

Age groups, laboratory studies, hospitalization, intensive care unit monitoring and exitus condition of the cases were compared in 4 groups: 1st group represents the confirmed cases (RT-PCR + CT +); 2nd groups consist of the clinically diagnosed cases (RT-PCR- CT +); 3rd group represents the mild or asymptomatic cases (RT-PCR+ CT -); 4th group consists of the suspected cases (RT-PCR- CT -). While a significant difference was found among leucocytes ($p<0.001$), hemoglobin ($p<0.001$), platelets ($p<0.001$), neutrophils ($p<0.001$), urea ($p<0.001$), ALT ($p=0.007$), and CRP ($p<0.001$) values in the laboratory results between the groups based on the post-hoc analyses; no significant difference was found among lymphocytes, Na, K, Cl, serum creatinine, AST, D-dimer, and troponin values. We found in the post-hoc analyses that the difference between leucocytes and neutrophils values is due to the difference between groups 1-4 ($p<0.001$), 1-2 ($p<0.001$), 3-4 ($p<0.001$), 3-2 ($p<0.001$); whereas the difference between CRP values is due to the groups 3-2 ($p=0.001$), 4-2 ($p<0.001$). Although no statistical difference was found in lymphocyte values among the groups ($p=0.017$), average value of lymphocyte was found to be lower in group 1 than other groups. Comparison of the laboratory test results among the groups is given in Table 4. A significant difference was found for each parameter among the groups in comparison of age groups, hospitalization, intensive care unit monitoring and exitus condition for 4 groups ($p=0.001$). 35.6% of RT-PCR + (groups 1-3) patients are in the age group of 19-30 years. Rate of admission to service of RT-PCR + patients is 52.2%. This rate is significantly higher than that of RT-PCR – (groups 2-4) patients (Table 5).

We found that the doctors started treatment for 19.4% of (n=646) the patients in total. In our analysis of the medications administered to the patients, we found that Hydroxychloroquine sulfate (89.8%, n=580) is the most preferred medication (Table 2).

In our monthly basis analysis of RT-PCR and CT imaging results showing COVID-19 pneumonia findings, we found that 54.3% (n=177) of all RT-PCR positive cases admitted to the hospital in June. The rate is 1.2% (n=4) in March (Fig 1).

Discussion

Three types of coronavirus infections broke out all over the world in the last twenty years. They are Severe Acute Respiratory Syndrome (SARS) in 2002, Middle East Respiratory Syndrome (MERS) in 2012, and COVID-19 pandemic in 2019 (9). This study involves retrospective examination of the patients that admitted to the hospital with the pre-diagnosis of COVID-19 in the period of approximately four months starting on March 11th 2020. WHO classified COVID-19 pandemic as international public health emergency on January 30 and defined it as a pandemic on March 11th as 113 countries reported COVID-19 outbreaks after China where it appeared first, and due to the rapid spread and severity of the virus (5). The first studies on COVID-19 started on January 10 in Turkey, and the first COVID-19 case was reported on March 11th significantly later than the neighboring European countries and Iran (4). We found in examination of the test results in this study that only 1.2% of RT-PCR + cases applied to hospital on March. The rate is 54.3% in June, and lifting inter-province travel and the beginning of normalization process on June 1, 2020 are thought to have an effect on the rate increase.

3334 patients were examined in the study in total in which 55.5% of the cases is male. In the meta-analysis by Wang *et al.* on 1994 patients, the rate of males is 60% (10). Other studies in literature reports that MERs-CoV and SARS-CoV infected males more than females (11, 12). The less susceptibility to infection among women could be attributed to the X chromosome and sex hormones, which have been reported to play a role in innate and adaptive immunity (13).

We found in our study that the most common symptoms reported by the patients are coughing (22.8%), shortness of breath (22.6%), muscle-joint pains (11.1%), fever (6.2%), and fatigue (6.2%). The fewer common symptoms are found to be the complaints of nausea, vomiting, diarrhea, headache, dizziness, and chest pain. In the meta-analysis that comprises 38 studies carried out in China, the most frequent symptoms are fever (80.4%), coughing (63.1%),

fatigue (46%), and muscle pain (33%) (14). The study by Wang *et al.* indicates that the most frequent clinical symptoms are fever, coughing, fatigue, myalgia, and shortness of breath. In addition to the common respiratory syndromes, some patients were also reported to have headache or dizziness (12.1%), diarrhea (4.8%), and nausea and vomiting (3.9%) symptoms (10). In a retrospective study on 393 patients in New York state of USA, the most common symptoms were reported to be coughing, fever, shortness of breath, muscle pain, nausea, vomiting, and diarrhea by prevalence (15). While the common respiratory symptoms are found to be similar in cases in different geographic locations, the non-respiratory syndromes also stand out in COVID-19 infections.

9.8% of the total cases in the study tested positive in the RT-PCR tests. The chest CT imaging is applied on 84.8% of the patients that admitted to hospital. 13.7% of the cases in which the CT imaging results showed COVID-19 pneumonia findings also tested positive in the RT-PCR tests. The chest CT imaging results of 23% of the patients that tested positive in RT-PCR test showed COVID-19 pneumonia findings. As of July 1, the number of total tests was reported to be 3.433.963, and total number of cases was reported to be 201.098 in Turkey. Positive rate of the tests that were performed until that date is 5.8% (16). The positive rate of the tests in the hospital (9.8%) where we run our study is above the average of Turkey. The difference between the rates is thought to arise from the fact that the screening tests performed by the contact tracing teams on asymptomatic cases or contacts are also included in the country-wide results. RT-PCR and chest CT are the main diagnosis methods for COVID-19. Chest CT is recommended as an alternative and reliable method in diagnosis of COVID-19 patients in China (17). In the study by Fang *et al.*, the sensitivity of chest CT (98%) is reported to be higher than that of the RT-PCR (71%) ($p < 0.001$). The study favors the use of chest CT imaging for patients with clinical and epidemiologic features corresponding to the COVID-19 infection particularly when they are tested negative in RT-PCR. The current practical issues with RT-PCR testing such as vendor related instrument variability, immature nucleic acid assays, low sensitivity to low viral load, and incorrect / unreliable clinic sampling are among the reasons for low precision of viral nucleic acid determination (18). Chung *et al.* reported that the chest CT imaging results can be negative for COVID-19 viral pneumonia in the first admission to hospital (three out of twenty-one patients, 86% sensitivity) (19). Xie *et al.* reported that five out of 167 patients (3%) can be tested negative in RT-PCR testing for COVID-19 in the first admission to hospital in spite of the chest CT imaging shows findings specific to a COVID-19 pneumonia (20). A meta-analysis comprising 9 studies that were carried out until April 2020 in the databases of Medline, Embase, Scopus, and Web of

Science inferred that neither of the two diagnostic modalities is reliable alone, and final diagnosis must be made based on both CT scanning and RT-PCR (21). Another study carried out in China does not favor the routine use of CT imaging due to its poor specificity in spite of high sensitivity. Other disadvantages are reported to be unnecessary exposure of patients to radiation and the rise in the risk of nosocomial infection due to the potential contamination during imaging (22). Actual sensitivity ratio between CT and PCR is investigated in other objective studies in a meta-analysis comprising 37 studies on 9610 patients; no significant difference was found between the two methodologies (75% and 78% respectively) (23).

Laboratory findings were examined by separating the patients into 4 groups: 1st group (RT-PCR + CT +), 2nd group (RT-PCR- CT +), 3rd group (RT-PCR+ CT-), and 4th group (RT-PCR- CT-). Most patients had normal leucocyte and lymphocyte counts in blood test examinations. The mean values of leucocyte and lymphocytes counts are 7.160 (2.500-22.800) and 1.800 (300-3.700) in 1st group, respectively. A significant difference was found in leucocytes, neutrophile, and platelet values between the 1st and 3rd Group and the 2nd and 4th Group ($p < 0.001$). The average of leucocytes, neutrophile, and platelet values in RT-PCR + patients is found to be lower compared to those with RT-PCR -. There wasn't any statistically significant difference in the average of lymphocyte values among the groups. In this study, average value of CRP was found significantly higher in 2nd group compared to 3rd and 4th Groups ($p < 0.001$). CRP value of the cases with lung involvement was higher. However, the average value was found to be lower in 1st Group compared to other groups. In the meta-analysis by Zhu et al., 3062 patients were examined, and normal leucocyte values (69.7%), lymphopenia (56.5%), increased CRP levels (73.6%), and ESR (65.6%) were found in most patients (14). 90% of 393 patients reported in USA had lymphopenia, 27% of them had thrombocytopenia and most of them had high liver function values and inflammatory markers (15). The study by Zhang *et al.* found that CRP values of the patients with negative imaging findings were significantly higher than those with normal imaging findings ($p < 0.05$) (24). This finding indicates that the symptom of pneumonia can be associated with a serious illness; therefore, such patients are in tendency to have more serious clinical features. Although there was an increase in AST, ALT, and creatinine levels in some confirmed COVID-19 cases, no significant difference was found in average values of the groups. Critical organ functions such as liver and kidney functions in COVID-19 patients must be closely monitored and evaluated.

23.4% of all the cases had a comorbid disease. The most frequent comorbid diseases are hypertension (12.7%), diabetes (7.5%), COPD (7.1%), cardiovascular disease (3.3%), chronic

renal failure (0.8%), and malignancy (0.7%). Comorbidity rate is 10.89% in a study that examines 2968 patients that were admitted to hospital with the diagnosis of COVID-19 in Iran. Diabetes (3.81%), chronic pulmonary disease (2.02%), hypertension (1.99%), cardiovascular disease (1.25%), chronic renal failure (0.60%), and malignancy (0.57%) were reported to be the most frequent comorbid diseases (25). While the rate of underlying diseases is 31.9% in a meta-analysis that studies 135 infected patients in China, the most frequent medical histories were hypertension, diabetes, cardiovascular disease, and malignancy (26). A meta-analysis by Yang *et al.* on 1576 infected patients reported that the most common comorbidities are hypertension, diabetes, cardiovascular disease, and respiratory disease. This study evaluated the comorbid diseases of the patients that have acute or mild COVID-19 infection and found that underlying diseases pose a risk to acute infection (27).

22.1% of the patients that applied to the hospital are treated by admission to the service. The rate is 52.2% in RT-PCR + patients. 2.2% of all the cases were monitored in the intensive care unit. 12 patients (0.4%) in total died. The case fatality rate is found 0.8% diagnosed with COVID-19. In Turkey, the case fatality rate was reported until July 1 2020 is 2.5%. The case fatality rate around the world is 4.9% as reported until July 1 2020 (16). The case fatality was reported to be 2.6% worldwide on October 30, 2020 (7). The meta-analysis by Wang *et al.* dealt with 10 studies in the literature and reported the mortality rate to be 5% (10). Another meta-analysis studying 3062 patients found the case fatality rate 5.5% (14). In a study on 2968 patients in a single center in Iran, the case fatality rate is reported to be 1.85% (25). The reason for low case fatality rate in this study can be attributed to inclusion of asymptomatic/mild cases that are treated and monitored at home as well as the hospitalized patients.

Conclusions

The case fatality rate caused by COVID-19 is found to be lower in Samsun province than the rates in Turkey and around the world. Mean of leucocytes, neutrophile, and platelet count values in RT-PCR + patients are found to be lower than those of RT-PCR – patients. Mean of CRP values in patients with lung involvement is found to be higher than those of other patient groups included in the study.

COVID-19 infection continues to spread across the whole world as the number of cases and mortality rates increase daily. Changes in the seasonal conditions, social and economic life has a significant influence on the process, and we think that further studies should be carried out on a broader context including larger number of cases in the future.

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Authors' contribution:

Simsek Yurt, N: protocol/project development, data collection, data analysis, writing/editing, management

Ocak, M: data collection, data analysis, manuscript reviewing

Yurt, YC: protocol/project development, data collection, manuscript reviewing

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