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Abstract

Background: Clinical features of confirmed COVID-19 cases cover a wide spectrum.

Aims: To study the clinical, radiological and virological features of the first 150 patients with COVID-19 in Lebanon.

Methods: Our university hospital was designated as the primary COVID-19 care centre in Lebanon. Between 21 February 2020, the date of the first confirmed case of COVID-19 in Lebanon, and 3 April 2020, our team treated 150 patients diagnosed with COVID-19. In this prospective descriptive study, we present our experience in treating these patients, specifically the diagnostic criteria, outcome, and demographic, clinical, radiological and biological characteristics.

Results: Ninety-five (63.33%) of the patients were male and 55 (36.67%) were female. Most patients (58%) were aged > 50 years, and 8 (5.33%) were healthcare workers. Diagnosis was based on reverse transcription polymerase chain reaction, and patients were classified as mild, moderate or critical. Fifteen (10%) patients had a critical presentation and fever was the most prominent symptom at presentation. One hundred and thirty-eight (92%) patients underwent radiological evaluation. The most common laboratory findings were lymphocytopenia (34.38%), followed by neutropenia (28.13%), but leukocytosis was not prevalent (1.56%). Old age and comorbidity were significant indicators in patient risk stratification. Chest computed tomography was an invaluable method of diagnosis and management. Our radiological findings were consistent with the published literature.

Conclusion: Our study underlines the variable presentation of COVID-19, the difference in severity, and the diverse methods of diagnosis. This suggests the need for a tailored approach, taking into consideration the wide spectrum of presentation.

Keywords: COVID-19, epidemiology, Lebanon, diagnosis, treatment

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Introduction

In December 2019, in Hunan, China, 4 cases that fulfilled the definition of pneumonia of unknown etiology were detected (1). On 31 December 2019, the Chinese Government formally announced the outbreak, and the virus was rapidly isolated and sequenced, and identified as a

new type of coronavirus. It was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19) (2,3). Thereafter, person-to-person transmission was officially confirmed (4,5). On 30 January 2020, after spreading to other countries, the World Health Organization (WHO) declared it a Public Health Event of International Concern. The exceptional situation created by COVID-19, which was declared a pandemic by WHO on 11 March 2020 (6), led to the designation of our university hospital as the primary COVID-19 care centre in Lebanon. COVID-19 is an emerging disease that has presented a global challenge which has overwhelmed healthcare institutions worldwide (7,8).

Clinical features of confirmed cases of COVID-19 vary over a wide spectrum, including asymptomatic infection, mild upper respiratory tract illness, lower respiratory tract illness with fever, dry cough, and dyspnoea, neurological symptoms, gastrointestinal symptoms (mainly diarrhoea), and severe viral pneumonia with respiratory failure, multisystem inflammatory syndrome, thromboembolism, and even death (1,5,9).

In this study, we investigated the different characteristics of the first 150 COVID-19 patients in Lebanon, including the diagnostic criteria, outcome, demographics, and clinical, radiological and biological characteristics. Given the novelty and impact of SARS-CoV-2, this study provides an important insight locally, regionally and globally, on the treatment trends of a large university hospital serving as the primary coronavirus response centre in Lebanon.

Methods

Study design

This prospective descriptive study was conducted at Rafik Hariri University Hospital (RHUH), Beirut, Lebanon. We included the first 150 patients diagnosed with COVID-19 in Lebanon between 21 February and 3 April 2020, as well as a few sporadic cases in other hospitals. Institutional Review Board approval was obtained, and all medical, social and ethical considerations were respected.

During the study period, as the country was not in the community spread phase of the disease, patients with a travel history to endemic regions, contacts of confirmed COVID-19 cases, or symptomatic patients were all screened using reverse transcription polymerase chain reaction (RT-PCR) of nasopharyngeal swab, oropharyngeal swab or sputum specimen. A positive RT-PCR test implied a confirmed diagnosis of COVID-19. A total of 5088 patients were tested for COVID-19 during the period. Criteria for inclusion in the study were based on a positive diagnosis of COVID-19, as per WHO guidelines (10). We excluded patients who had negative RT-PCR test.

All included patients were admitted to RHUH and classified as mild, moderate, severe or critical, according to the severity criteria outlined below. No healthcare, administrative, medical, paramedical, maintenance or environmental service staff at the hospital tested positive for COVID-19 during the of the study.

Severity criteria

Clinical severity was stratified as follows: (1) asymptomatic: no symptoms; (2) mild: upper respiratory symptoms with no imaging abnormalities; (3) moderate: symptoms defined by 2 of dyspnoea, cough and temperature > 38 °C, with imaging abnormalities; and (4) severe/critical: O2 saturation ≤ 93%, respiratory rate ≥ 30 breaths per minute and ratio of arterial oxygen partial pressure to fractional inspired oxygen ≤ 300 mmHg. Patients in the asymptomatic/mild/moderate categories were admitted to the regular isolation wards. Patients with the severe and critical forms were admitted to the COVID-19 intensive care unit (ICU).

Discharge criteria

Based on WHO recommendations, cured status was conditional on 2 consecutive negative RT-PCR tests 24 hours apart, or in patients with total resolution of symptoms and findings. All patients were discharged on the condition of home quarantine until RT-PCR conversion took place.

Data collection

Data was collected prospectively. Several demographic, biological, clinical and radiological characteristics were assessed, as well as the clinical course and outcome. Our data collection took into consideration the WHO/International Severe Acute Respiratory and Emerging Infection (ISARIC) Consortium case record form for severe acute respiratory infections (11). All patients' names were removed and coded to protect their privacy. All data were checked by 2 physicians and analysed by a statistician and a physician.

Laboratory testing

Upper (nasopharyngeal swabs) and lower (when possible) respiratory tract samples for SARS-CoV-2 diagnostic testing were obtained according to WHO guidelines from all patients at admission and maintained in a viral-transport medium (12). Samples were immediately transported to the laboratory where procedures for RNA extraction and real-time RT-PCR using the Charité protocol were conducted (13). For each patient, samples were obtained upon admission, and subsequently once every 2 or 3 days until they were discharged or died. Viral RNA was extracted manually from 140 µl of nasopharyngeal swab fluid, sputum or both, using

the QIAamp Viral RNA Mini kit (Qiagen, Hilden, Germany). Automatic extraction was performed using the MagNA Pure Compact (Roche, Basel, Switzerland) with 200 µl as the primary sample volume. An RT-PCR corresponding to the Charité protocol (published on 17 January 2020) was used for detection of SARS-CoV 2 (13). The assay uses a first-line screening with the E gene and a confirmatory assay with the RdRp gene and a synthetic RNA positive control. A 25-µl reaction was set up containing 5 µl RNA, 12.5 µl 2 reaction buffer provided with the Superscript III One Step RT-PCR system, with Platinum Taq Polymerase (Invitrogen, Carlsbad, CA, USA), 1 µl reverse transcriptase/Taq mixture from the kit, and 0.4 µl 50 mM magnesium sulphate solution.

Thermal cycling was performed at 55°C for 10 minutes for reverse transcription, followed by 95°C for 3 minutes, and then 45 cycles of 95°C for 15 seconds, 58°C for 30 seconds, using an ABI 7500 instrument (Thermo Fisher Scientific, Waltham, MA, USA).

Although the laboratory parameters were assigned, for the first 22 patients who were all categorized as mild or asymptomatic, no blood workup was taken. As the cases became more heterogeneous in presentation, it was decided that all subsequent patients would undergo routine blood examinations. The recorded parameters included a complete blood count with differential, electrolytes, blood urea nitrogen, creatinine and C-reactive protein (CRP). Other types of laboratory workup were taken in specific cases, but not included in the overall design of this study.

Radiology

For the first 24 patients, who were all categorized as asymptomatic or mild, and included paediatric patients, chest X-ray was the radiological procedure of choice, with plain chest computed tomography (CT) reserved for the more severe cases. As the cases became more heterogeneous in presentation, and after including the added benefits of chest CT imaging, it was decided that all subsequent patients would undergo plain chest CT. Chest X-ray and CT findings were interpreted by our team and confirmed by the radiology team. The parameters taken into consideration were ground glass appearance, lobe predominance, and diffuse consolidation.

Statistical analysis

In total, 122 parameters were collected, analysed and classified according to epidemiological factors, demographics, medical history, clinical findings and factors, course of hospitalization, laboratory findings, simple radiography and CT findings, complications, supportive treatment, medications, outcome, and time to conversion. For categorical data, number and valid percentage were calculated. For continuous data, the mean and standard deviation were

measured. The statistical calculations were performed using SPSS version 20.

Results

RT-PCR

All patients were diagnosed based on RT-PCR testing of nasopharyngeal and oropharyngeal swabs. RT-PCR using the E Gene assay was used on 146 specimens, while RT-PCR using RdRP assay was used on 104 specimens.

Demographics and epidemiological factors

Most patients were male (95; 63%), of Middle-Eastern origin (143; 95%) and with a mean age of 45 (5–86) years. Around 42% of the patients were aged

Concerning the known mode of exposure, 44 (29.33%) patients had a history of travel to an area with documented cases of SARS-CoV-2 infection; 102 (68.0%) were in close contact with a confirmed or probable symptomatic case of SARS-CoV-2 infection; and 2 (1.33%) patients were present in a healthcare facility where SARS-CoV-2 infections were managed. Two (1.33%) cases had unknown mode of exposure. Of the 44 patients with history of travel, 41 had travelled in the 14 days prior to symptom onset. Fifteen travellers came from the Islamic Republic of Iran, 7 from France or the United Kingdom of Great Britain and Northern Ireland, 4 from the United Arab Emirates, and 1 each from Austria, Egypt, Germany, Italy, Netherlands, Spain and Turkey. One patient was from an unknown country of origin.

Medical history

Table 1 summarizes the prevalence of medical conditions in this population. One hundred and fifteen (76.67%) patients never smoked, 27 (18%) were active smokers, and 8 (5.33%) were former smokers.

Initial presentation

Sixty-eight (45.33%) patients presented with mild symptoms, 67 (44.67%) with moderate symptoms and 15 (10%) with severe symptoms. Fever (89; 59.33%) was the most prominent symptom at presentation, followed by cough (87; 58%), and sore throat (27; 18%) (Table 2) . The average temperature at presentation was 37°C (35.6–39.3°C).

Management and clinical course

The overall ICU or high dependency unit admission rate was 10% (15 patients). Nine of these patients required invasive ventilation. The 6 remaining patients required noninvasive

positive-pressure ventilation. Eight (5.33%) ICU patients required inotropes or vasopressor support. One patient required prone ventilation and one required renal replacement therapy. Of the 135 patients admitted to the regular non-ICU floor, 3 required oxygen therapy. Most patients (132; 88%) did not receive any form of oxygen treatment. Thirty (20%) patients received antibiotic therapy; 8 (5.33%) received antiviral treatment, specifically Lopinavir/Ritonavir combination; and 12 (8%) received chloroquine. These medications were based on drug availability in the country and were tried randomly, given the lack of clear treatment guidelines and awaiting the relevant WHO trial. None of the patients received convalescent plasma, corticosteroids or antifungal treatment.

Table 3 summarizes the complications during admission in hospital. Patients who developed acute respiratory distress syndrome (ARDS) had a more complicated course in hospital than other patients. They required longer stay and more invasive treatment. Of the 11 patients (7.33%) who developed ARDS, 8 died.

One hundred and thirty-five (90%) patients were discharged from hospital with a favourable outcome; 5 (3.33%) were still hospitalized at the end of the study; and 2 (1.33%) were transferred to another hospital. The overall death rate was 5.33% (8 patients). The average length of stay was 13.9 (1–42) days. Patients were discharged if they tested negative for 2 consecutive RT-PCRs, within 24 hours, as per WHO guidelines. Patients were also discharged if they became fully asymptomatic, with normal laboratory results, on the condition that they remained quarantined at home until RT-PCR conversion took place. One hundred and thirteen (75.33%) patients had a conversion of their RT-PCR test over 2 consecutive days. The average time to conversion was 21.5 (7-–64) days.

Admission date

Figure 1 shows the number of confirmed positive cases according to admission date.

Laboratory findings

One hundred and twenty-eight patients underwent laboratory testing, and on admission, 12 (9.38%) had leukopenia and 2 (1.56%) had leukocytosis, with a mean of 6.38×109/l. Forty-four (34.38%) patients had lymphocytopenia and 7 (5.47%) had high lymphocyte count, with a mean of 1.87×109/l. Thirty-six (28.13%) patients had neutropenia and 5 (3.91%) had high neutrophil count, with a mean of 3.7×109/l. Ninety-five (74.22%) of the 128 tested patients had haemoglobin level within the normal range, 16 (12.5%) were anaemic, and 17 (13.28%) had high haemoglobin level, with a mean of 13.72 g/dl. Platelets were below the normal range in 16 (12.5%) patients and increased in 5 (3.9%). Of the 123 patients who underwent creatinine level testing, 36 (29.27%) had an elevated level. The most common electrolyte disturbance was

hyponatraemia, which was detected in 16 (13.33%) of 120 tested patients. CRP levels were higher than normal values in 71 (58.2%) of 122 tested patients.

Radiological findings

Twelve patients underwent chest X-ray, 126 underwent plain CT scan of the chest (Table 4), and 12 asymptomatic cases underwent no imaging.

Discussion

This study describes the clinical, epidemiological and radiological features of the first 150 COVID-19 patients in Lebanon. The results show that middle-aged men were more affected than women, with the majority showing mild-to-moderate symptoms. The most prominent comorbidities were hypertension and diabetes. Fever, cough and sore throat were the most prevalent symptoms. Moreover, lymphocytopenia and neutropenia were predictors of disease severity and chest CT was the gold standard for diagnosis.

In our study, the mean age of the patients was 45 years, which is lower than that reported previously (5,14–17). The latest demographic statistics for Lebanon estimates the median age as 33.7 years, with almost 50% aged 25–54 years (18). The fact that Lebanon has a young population explains the variations in the median ages reported. The present study shows that men were more affected than women, which is consistent with previous studies showing that men are more predisposed to contracting COVID-19 (5,14,16,17). Approximately 5% of the patients were healthcare workers but none were members of the RHUH staff. This proportion is lower than that reported in other similar studies (15) and can be attributed to the meticulous planning and extensive reorganization of departments and divisions before receiving patients, along with the strict precautions observed by the staff.

Around 25% of the patients had previous comorbidities, with hypertension and diabetes mellitus being the most common, which is similar to previous studies (5, 14). Although the underlying pathogenesis of hypertension and diabetes among COVID-19 patients have not been fully elucidated, it is hypothesized that activation of the renin–angiotensin system induces a cytokine storm that causes lung injury (19). Also, decreased innate immunity and vascular dysfunction, along with the prothrombotic state in diabetic patients, worsen the prognosis of COVID-19 patients (20).

The prevalence of smokers in our cohort was 25%, compared with 42% in a larger study of COVID-19 patients conducted in Lebanon (21). This discrepancy in proportions could be

attributed to the difference in sample size and the questions about smoking.

Consistent with the findings of several studies, including systematic reviews, the most prominent symptoms at presentation were fever, cough and sore throat (5,19,22). The symptoms, however, were variable and at many times nonspecific, ranging from digestive symptoms to generalized weakness. The most prevalent haematological disorder was lymphocytopenia, followed by neutropenia and elevated creatinine level. Our findings agree with the laboratory abnormalities reported by other studies, which shows that these inflammatory markers are predictors of the clinical severity of COVID-19 (5,14,16).

Regarding the complications, the majority of the patients developed pneumonia (bacterial and viral). ARDS was a major complication associated with poor prognosis and high mortality rate, and 8 of 11 patients who developed ARDS died. The findings of a global literature review substantiate our data, confirming that ARDS is a common complication of COVID-19 and that moderate-to-severe ARDS is associated with a higher risk of mechanical ventilation and death (23).

In accordance with previous studies, the predominant CT finding of COVID-19 was multifocal bilateral air space opacities, characterized by ground glass opacity of the subpleural and peripheral area (5,24). Given that different radiological patterns are observed at different stages of COVID-19, CT remains a crucial diagnostic tool to predict clinical worsening. According to some studies, 50% worsening of CT findings is classified as severe COVID-19, while diffuse consolidation leads to ARDS. Moreover, imaging scores correlate well with mortality risk factors (15,25,26). Although CT remains the gold standard for diagnosis of COVID-19, the radiological findings overlap with those of other pulmonary diseases, thus requiring further attention and precision at the time of diagnosis (27).

The average length of stay in our study was 13.9 days, which is consistent with a systematic review that reported a median length of stay of 14 days in China (28). However, it should be noted that the length of stay in our study could have been overestimated, because at the beginning of the pandemic, all patients with positive RT-PCR results were admitted to the hospital regardless of disease severity, and were only discharged after testing negative for 2 consecutive RT-PCRs as per the initial WHO recommendations (12). Thus, further studies should be carried out to determine an accurate length of stay, taking into consideration the difference between ICU and non-ICU patients.

The novelty of this disease and the rapid and consistent change in the proposed management were a major limitation in this study. We could not provide accurate estimates of the average length of stay among critical and noncritical patients due to the change in recommendations regarding RT-PCR testing. Besides, the descriptive nature of this study and the small sample size impeded us from investigating the correlation between the risk factors and severity of the disease. We could not determine which risk factors were associated with higher mortality. Thus, larger studies should be conducted to identify the underlying factors associated with disease severity and to design interventions to improve outcomes.

Conclusion

The management of COVID-19 requires a global approach that takes into consideration the variable presentation of the disease, differences in severity, the diverse methods of diagnosis, and different proposed treatment plans. We described our experience in treating the first 150 cases of COVID-19 in Lebanon, a country in major turmoil with a debilitating economic crisis that puts a strain on all resources. Our findings were similar to those in the literature. We propose a combination of clinical, biological and radiological methods to optimize diagnosis, risk stratification, and eventual management of patients.

Funding: None

Competing interests: None declared.

Caractéristiques cliniques et épidémiologiques des 150 premiers patients atteints de COVID-19 au Liban : étude descriptive prospective

Résumé

Contexte : Les caractéristiques cliniques des cas confirmés de COVID-19 couvrent un large éventail.

Objectifs : Étudier les caractéristiques cliniques, radiologiques et virologiques des 150 premiers patients atteints de COVID-19 au Liban.

Méthodes : Notre hôpital universitaire a été désigné comme le principal centre de prise en charge de la COVID-19 au Liban. Entre le 21 février 2020, date du premier cas confirmé de

COVID-19 au Liban, et le 3 avril 2020, notre équipe a traité 150 patients diagnostiqués avec COVID-19. Dans la présente étude descriptive prospective, nous présentons les enseignements tirés du traitement de ces patients, en particulier les critères diagnostiques, les résultats et les caractéristiques démographiques, cliniques, radiologiques et biologiques.

Résultats : Quatre-vingt-quinze des patients (63,33 %) étaient des hommes et 55 (36,67 %) étaient des femmes. La plupart des patients (58 %) étaient âgés de plus de 50 ans et 8 (5,33 %) étaient des agents de santé. Le diagnostic était basé sur une réaction en chaîne par polymérase après transcription inverse et les patients étaient classés comme légers, modérés ou critiques. Quinze patients (10 %) étaient atteints d'une forme critique de COVID-19 et la fièvre était le symptôme le plus important lors de la consultation. Cent trente-huit patients (92 %) ont été soumis à une évaluation radiologique. Les résultats de laboratoire les plus fréquents étaient une lymphocytopénie (34,38 %), suivie d'une neutropénie (28,13 %) ; par contre, la leucocytose n'était pas prévalente (1,56 %). La vieillesse et les comorbidités étaient des indicateurs significatifs de la stratification du risque chez les patients. La tomodensitométrie du thorax était une méthode de diagnostic et de prise en charge indispensable. Nos résultats radiologiques étaient conformes à la littérature publiée.

Conclusion : Notre étude souligne la variabilité des formes que prend la COVID-19, la différence de gravité de ses symptômes et les diverses méthodes de diagnostic. Ceci suggère la nécessité d'une approche personnalisée, en tenant compte du large éventail des symptômes.

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WHO EMRO | Clinical and epidemiological characteristics of the first 150 patients with COVID-19 in Leba

: صُنِّف مستشفانا الجامعي على أنه مركز الرعاية الرئيسي لمرضى كوفيد -19 فيطُرق البحث
لبنان . وعالج فريقنا 150 مريضًا شُخِّصت إصابتهم بمرض كوفيد -19 في الفترة ما بين 21
فبراير / شباط 2020 ، وهو تاريخ اكتشاف أول حالة إصابة مؤكَّدة بمرض كوفيد -19 في لبنان،
و3 أبريل / نيسان 2020. ونعرض في هذه الدراسة الوصفية الاستباقية تجربتنا في علاج هؤلاء
المرضى، وتحديدًا المعايير التشخيصية، والنتائج، والسمات السكانية والسريرية
والإشعاعية والبيولوجية .

: ضمَّت مجموعة المرضى 95 (63.33%) من الذكور و 55 (36.67%) من الإناث . وكان عمرالنتائ ج
معظم المرضى (58%) أكثر من 50 عامًا، وكان من بين المجموعة 8 مرضى (5.33%) من العاملين
في مجال الرعاية الصحية . واستند التشخيص إلى التنسخ العكسي لتفاعل البوليميراز
المتسلسل، وصُنِّفت حالات المرضى إلى خفيفة أو متوسطة أو حرجة . وكان 15 مريضًا (10%) قد
ظهرت عليهم أعراض حرجة وكانت الحُمَّى أبرز الأعراض التي ظهرت . وخضع 138 مريضًا (92%)
للتقييم الإشعاعي . وكانت أكثر النتائج المختبرية شيوعًا قلة اللمفاويات (34.38%) ،
يليها قلة العدلات (28.13%) ، ولكن كثرة الكريات البيضاء لم تكن سائدة (1.56%). وشكَّل
كلٌ من الشيخوخة وحالات المراضة المصاحبة مؤشرات مهمة في التقسيم الطبقي للمخاطر التي
تواجه المرضى . وكان التصوير المقطعي المحوسب للصدر طريقة بالغة الأهمية للتشخيص
والعلاج . وجاءت نتائجنا الإشعاعية متوافقة مع المصنفات المنشورة .

: تؤكِّد دراستنا التفاوت في أعراض كوفيد -19 ، وتبايُن وخامة المرض،الاستنتاجات
وتنوُّع أساليب تشخيصه . ويشير ذلك إلى الحاجة إلى اتباع نهج مخصص يأخذ في الاعتبار
الطيف الواسع لأعراض المرض وسماته .

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