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Pattern and prevalence of different findings in high resolution computed tomography images in patients with coronavirus disease and kidney injury; a pilot study

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ABSTRACT

Introduction: Since December 2019, an outbreak of pneumonia caused by a new coronavirus has emerged. The standard diagnostic method for COVID-19 infection is the real-time reverse transcriptase-polymerase chain reaction (RT-PCR). High-resolution computed tomography (HRCT) has been proven as a sensitive, feasible and accessible test in Iran. In addition to respiratory system, other organs could also be involved in this disease. The exact mechanism of renal involvement is unknown; however, acute kidney injury (AKI) occurs in almost 5-15% of cases. Different HRCT patterns might be associated with AKI presence and severity of the disease.

Objectives: To investigate patterns and prevalence of different HRCT findings in COVID-19 patients with concurrent AKI.

Patients and Methods: In this retrospective study, we reviewed all hospitalized patients with COVID-19 infection, from February to April 2020 in Razi hospital, Rasht. Twenty-two cases who had AKI were enrolled. The HRCT findings of the patients were reviewed independently by two radiologists. Percentage and prevalence of HRCT findings were analyzed in SPSS 21 software.

Results: All 22 cases had multifocal distribution on HRCT. Around 95.5% had peripheral involvement, 86.4% had central zones opacity while 72.2% of cases had peribronchovascular pattern. Bilateral lung involvement was found in 90.9%, but only 9.1% had unilateral involvement. There was 59.1% of lower lobe predominance for COVID-19 involvement since sub-pleural regions were spared in 18.2% of individuals. All the patients' HRCTs showed ground glass opacity. Reticular pattern (81.8%), consolidation (77.3%), vascular enlargement in involved zones (68.2%) and airway changes (68.2%) were the next more prevalent findings. Half of the subjects showed crazy paving, 45.5% had pleural effusion and 13.6% had also lymphadenopathy. We found 40.9% of the patients had arcade-like sign. Less frequent findings were nodular opacities (13.6%), halo sign (9.1%) and reverse-halo sign (9.1%), respectively.

Conclusion: This study demonstrated that atypical patterns are likely to be more common in COVID-19 patients with kidney injury.

Implication for health policy/practice/research/medical education:
In this retrospective study, we reviewed patients with COVID-19 infection, who had also acute kidney injury. All 22 cases had multifocal distribution on high-resolution computed tomography (HRCT). About 95.5% of cases had peripheral involvement, 86.4% had central zones opacity while 72.2% had peribronchovascular involvement. Bilateral lung involvement was found in 90.9%; however, only 9.1% had unilateral involvement. There was 59.1% lower lobe predominance. We found the reticular pattern in 81.8% of cases, consolidation in 77.3%, vascular enlargement in involved zones in 68.2% of patients and airway changes in 68.2% of participants. Half of the subjects showed crazy paving, 45.5% pleural effusion and 13.6% lymphadenopathy. We also detected, 40.9% of the patients had arcade-like sign. Less frequent findings were nodular opacities (13.6%), halo sign (9.1%) and reverse-halo sign (9.1%) respectively. Our study showed that atypical patterns are likely to be more common in COVID-19 patients with acute kidney injury.

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Original

Introduction

In late December 2019, in the capital of Hubei province in China, a cluster of pneumonia of unknown origin was reported (1). In January 2020, Chinese scientists isolated a new coronavirus (SARS-COV-2) from these patients (2). When 118 598 cases of patients were reported to be infected with COVID-19 in more than 100 countries on March 11, 2020, The World Health Organization (WHO) called this as a pandemic (3). This disease was also rapidly spread in most provinces of Iran at that time (4).

It has been reported a wide spectrum of signs and symptoms among 291 pediatric (age <18 years old) and 10 944 adults (age 18-24 years old) (5). The gold standard method for diagnosis of COVID-19 is real-time reverse transcription-polymerase chain reaction (RT-PCR) of viral nucleic acid (6).

Recent studies have revealed that RT-PCR has low sensitivity of 61%-71% for diagnosis. This may be due to low-viral load in the samples or laboratory errors (7). During the beginning of the outbreak in Iran, the gold standard RT-PCR diagnostic test was not available. Therefore, imaging findings played a major role in diagnosis and evaluation of the disease severity (1).

The cost of high-resolution computed tomography (HRCT) is subsidized in Iran and it is covered by all insurances. Hence, in comparison to RT-PCR, it was more available and accessible for the health community (8). While bilateral ground-glass opacities and consolidations are known to be predominant findings of COVID-19 in HRCT, other radiological findings on chest computerized tomography (CT) scan have been detected as well (9, 10).

Here is some explanation on a few radiology signs that might be seen in patients with COVID-19 infection. The atoll sign (reversed halo sign) is characterized by a central ground-glass opacity bordered by denser consolidation of crescentic shape. This pattern was seen in several COVID-19 cases and it could be related to disease progression (11).

Airway changes such as irreversible bronchial dilation which is called bronchiectasis are another manifestation. Based on previous findings, bronchiectasis and bronchial wall thickening were significantly higher in critical patients with COVID-19 (2).

Ground-glass opacification/opacity

On HRCT, ground glass opacity is characterized as a hazy region of lung increased attenuation in which the vessels are visible (12). Recent studies have shown that ground-glass opacification/opacity (GGO) is the earliest respiratory manifestation of COVID-19 patients in CT scan (13). The reticular pattern is associated with interlobular septal or interstitial thickening, which is characterized by a fine network of lines within lobules. Recent studies have revealed that this pattern has a higher incidence when the disease course gets longer (6). Likewise, in recent surveys consolidative lesions were more frequent in older patients and longer course of disease. Consolidation is defined as a homogeneous enhanced lung opacity that results in the obscuration of vessels (6). Another important finding in chest CT scan is crazy-paving, as the combination of GGO and interlobular septal thickening in the same region (6), this pattern resembles the peak stage of COVID-19 (11,14).

As a national guideline, Iranian Society of Radiology (ISRCC) of COVID-19 consultant group has published a report template to help radiologists and clinicians in order to use CT scan for evaluation of suspicious patients with COVID 19 infection. This protocol is available for all practitioners and radiologists (8). The lung is reported to be the most commonly affected organ. Other organs can be involved as well (15). Organ damage could be due to direct damage or body response inflammation. Previous studies on severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome–related coronavirus (MERS-CoV) have revealed that acute kidney injury (AKI) occurs in 5-15% of cases, and has mortality rate of 60-90%. Preliminary reports have indicated a low-incidence of AKI in patients with COVID-19 (3-9%); however, recent studies have pointed out a greater prevalence of kidney involvement presenting as massive albuminuria, proteinuria, hematuria and blood urea nitrogen (BUN) and serum creatinine rise in such patients (16). The exact mechanisms of renal involvement are not fully known yet. It has been found that angiotensin converting enzyme (ACE) and dipeptidyl peptidase-4 (DPP-4) are SARS-COV and MERS-COV receptors and both are expressed in renal tubular cells (16). ACE2 receptors facilitates the entry of some types of coronavirus into human body cells. Association between ACE2 and SARS-COV infection has been shown in previous studies (15). Symptoms and outcomes of SARS-COV-2 infection could be related to different expression levels and patterns of ACE2 gene in different tissues (15). Brush border of proximal tubular cells and to a lesser extent, podocytes have been shown to express ACE2, but not in glomerular endothelial and mesangial cells (15). Coronavirus has been isolated in kidney tissue and urine (13).

Objectives

Due to the great importance of accurate and early diagnosis and management of COVID-19 patients who experience lung and other organs involvement such as the kidney, we aimed to investigate different patterns of pulmonary involvement in patients with COVID-19 and AKI.

Patients and Methods

Study design

We conducted a cross-sectional study involving all hospitalized patients with COVID-19 infection who had AKI and lung involvement at the same time, from February 21, 2020 to April 30, 2020 in Razi hospital, Rasht, Guilan province.

After obtaining informed consent, patients with confirmed SARS-COV-2 infection, based on a positive RT-PCR test, clinical signs and symptoms in addition to kidney involvement based upon AKI 2012 diagnostic criteria, were studied.

Patients with normal renal function and patients under 18 years of age were excluded.

Demographic information as age, gender and past medical history were collected by reviewing the history. Laboratory data were obtained from electronic files of patients with the primary diagnosis of COVID-19 infection.

Materials

Criteria for admission of patients such as AKI were defined as follows:

- Elevation in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
- Elevation in serum creatinine to ≥1.5 times baseline, known or presumed to have occurred within the prior seven days; or
- Urine volume <0.5 mL/kg/h for 6 hours.

First chest CT-scan of each patient during hospitalization course were evaluated using a multi-detector computed tomography scanner (general high speed dual)with this protocol; 120 kV, 140 mM and 1.2 mm slice thickness. The scan range, ranged from long apex to the diaphragm in the axial plane. Prevalence of different HRCT patterns in these patients was evaluated independently by two expert radiologists and disagreements were resolved by concurrent review and discussions until arriving at a consensus. All studied patients had previously undergone routine CT scan of the lungs at the discretion of their physician and no additional radiation was given to the patients.

Data analysis

Qualitative variables were expressed as number and percentage. All analyses were conducted by Statistical Package for the Social Sciences (SPSS) 16.0 (SPSS Inc., Chicago, IL). Statistical significance was defined as $P<0.05$ and 95% confidence interval was also considered to be a reliable estimate.

Results

Our review showed a different prevalence of HRCT pattern in the subjects. The results are summarized in Table 1. A total of 22 patients were studied (15 males and 7 females) with an age range of 24-84 years. All of cases had multifocal distribution while in 95.5% of cases peripheral involvement were predominant. Around 86.4% of cases had opacities in central zones and 68.2% had peribronchovascular pattern of involvement (Figure 1; peribronchovascular distribution). The majority of cases had bilateral lung involvement (90.9%); however, unilateral involvement was seen only in 9.1% of subjects. Moreover, we detected lower lobe predominant involvement in 13 patients (59.1%). Sub-pleural regions were spared in 18.2% of cases. There was no unifocal involvement in the subjects. Also, ground glass opacity was the most prevalent pattern. All patients' HRCT (100%) showed areas of ground glass opacity. Reticular pattern (81.8%), consolidations (77.3%), vascular enlargement (68.2%) and airway changes (68.2%) were the next more prevalent findings, respectively. Fifty percent of patients showed crazy paving, 45.5% of cases had pleural effusion (10 patients), 40% of patients had arcade sign and three patients (13.6%) had lymphadenopathy. Less frequent findings included nodular opacities (13.6%), halo sign (9.1%) and reverse halo sign (9%) (Figure 2; crazy paving and Figure 3; halo sign).

Table 1. Prevalence of HRCT characterizations

	No.	Percent
Peripheral dominancy	17	77.3
Lower lobe dominancy	13	59.1
Peribronchovascular pattern	16	72.7
Vascular enlargement	15	68.2
Arcade-like sign	9	40.9
Ground glass pattern	22	100.0
Consolidation	17	77.3
Reticular pattern	18	81.8
Crazy-paving pattern	11	50.0
Air-bronchogram	11	50.0
Airway changes	15	68.2
Nodular opacity	3	13.6
Halo sign	2	9.1
Reverse halo sign	2	9.1
Unifocal	0	0.0
Multifocal	22	100.0
Bilateral	20	90.9
Unilateral	2	9.1
Peripheral involvement	21	95.5
Central involvement	19	86.4
Pleural effusion	10	45.5
Lymphadenopathy	3	13.6
Sub-pleural sparing	4	18.2

Discussion

As we know from earlier studies, AKI is associated with worse outcomes in COVID-19 patients (17). In previous studies of SARS and MERS-COV, AKI was seen in 5-15% of cases and mortality rate was reported between 60%-90%. Preliminary reports indicated a low-incidence (3%-9%) of AKI in patients with COVID-19 (18).

Prior studies demonstrated that bronchial wall thickening, reticular pattern, consolidation and crazy paving are HRCT patterns that should increase our concerns about COVID-19 patients, since it has been reported that in severe critical cases and longer course of

Figure 1. In a 39-year-old female COVID-19 patient, lung HRCT shows focal consolidation surrounded by ground glass opacity named halo sign in right lung base.

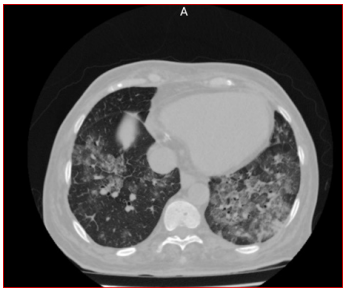

Figure 2. A 58-year-old female with COVID-19 disease, CT scan shows interlobular septal thickening superimposed on ground glass opacity named crazy-paving sign in bilateral lower lobes predominantly on left side.

Figure 3. A 39-year-old male with COVID-19 pneumonia and concurrent kidney injury, CT scan shows peribronchovascular pattern of distribution on both longs.

the disease, these patterns are significantly higher than other patients (6).

In this survey, 50% of the study population who were COVID-19 patients with AKI had crazy-paving, 81% had reticular pattern, 77% had consolidation and 68% had air way changes, which showed that atypical patterns can be seen more commonly in kidney involved patients. In addition, the prevalence of pleural effusion and lymphadenopathy showed that although in other patients these findings are inconsistent for COVID-19, they can be observed in COVID-19 patients with concurrent AKI and their presence does not rule out COVID-19 pneumonia.

In the study by Zheng et al, chest CT scan and its features were utilized to diagnose COVID-19 disease, then its typical and atypical manifestations were evaluated. In their results, GGO pattern was the earliest radiological pattern in CT scan. According to the result of their study, ground glass opacities, consolidation, reticular pattern and crazy paving were typical CT presentations. Moreover, atypical CT manifestations such as pleural changes, airway changes, nodules and fibrosis were observed in COVID-19 patients (6). In another study, Pan et al evaluated the course of the disease and the findings of CT scans, the results showed that crazy-paving pattern was a sign of disease progression in its peak stage (14).

Conclusion

Overall, the results of the current study demonstrated that atypical patterns should be expected more common in AKI patients with COVID-19 infection, which can be related to a progressive course of the disease.

Limitations of the study

The current study has some limitations including the unavailability of polymerase chain reaction (PCR) test in the early days of the outbreak in this province. In addition, in false negative results, the diagnosis of COVID-19 was based on clinical findings and imaging. Another limitation of this study was the limited number of patients who underwent HRCT, because a number of patients were admitted to our center without imaging and some were admitted only with a routine X-ray.

Authors' contribution

Conceptualization: ARD, ER, FSF.
Methodology: AV, EM, MN.
Validation: ER, ARD.
Formal analysis: AV, EM, MN.
Investigation: ARD, ER, FSF.
Resources: MN, SS, EM, AV.
Data curation: AV, EM, MN.
Visualization: ARD, ER.
Supervision: ER, ARD.
Project administration: ER.
Writing–original draft: ER, ARD, SS, EM, ES, FSF.
Writing–review and editing: All authors.

Conflicts of interest

Authors declare no conflict of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The ethics committee of Guilan University of Medical Sciences approved this study (Ethical code#IR.GUMS.REC.1399.197). Informed consent was obtained from patients. This study was extracted from M.D thesis of Fahime Soleimani Farsani at this university (Thesis

#1194). Additionally, ethical issues including plagiarism, data fabrication and double publication were also completely observed by the authors.

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