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Severity of radiographic changes in patients with COVID-19 pneumonia - experience from secondary-level hospital

Степен радиографских промена код пацијената са ковид 19 пнеумонијом – искуство из болнице секундарног нивоа

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SUMMARY

Introduction/Aim Chest X-ray (CXR) is a common diagnostic procedure for monitoring the course and outcome of pneumonia.

The aim of the study was to examine the frequency, type and degree of CXR changes in COVID-19 pneumonia and compare it with demographic data and the presence of comorbidities.

Methods In this retrospective study, CXRs taken on the day of admission were analyzed for 620 patients with COVID-19. CXR were defined as ground-glass opacification (GGO), consolidation, reticular changes, pulmonary nodules, and pleural effusions. CXR severity score (CXR-SS) was determined based on the adjusted Radiographic Assessment of Lung Edema score. SPSS version 17.0 was used for statistical analyses.

Results The average age was 62.75 ± 14.8 years 66.5% of analyzed patients had comorbidities. CXR changes were bilateral in 53.2%, dominant in the lower lung in 68.1% and diffuse in 24.5%. GGO were present in 55%, reticular changes in 37.3%, and consolidations in 24% of patients. Based on CXR-SS, 47.2% of patients had mild pneumonia, 40.2% moderate, 7.9% severe, and 4.6% very severe. Severe/very severe pneumonia was in 71.8% of older than 65 years. Bilateral changes were found in 97.4% of people with severe/very severe pneumonia, diffuse in 56.4%, and consolidation in 66.7% of the patients. GGO were in 58.1% of subjects with mild/moderate pneumonia.

Conclusion CXR in patients with COVID-19 pneumonia are more frequently bilateral, dominantly peripheral, in the lower lung zone. The degree of diffuse changes is proportional to older age and more frequent comorbidities. In a severe form of the disease, consolidation and reticular opacification dominate.

Keywords: chest X-ray; pulmonary severity score; COVID-19 pneumonia

САЖЕТАК

Увод/Циљ Радиографија грудног коша је уобичајен дијагностички поступак за праћење клиничког тока и исхода болести код пацијената са ковид19 пнеумонијом. Циљ истраживања је био да се испита учесталост, тип и степен радиографских плућних промена код ковид 19 пнеумоније и упореди са демографским подацима и присуством коморбидитета лечених болесника.

Методе Подаци су прикупљени ретроградно, на дан пријема у болницу, код 620 пацијената са ковид 19 пнеумонијом. Радиографске промене су дефинисане као *ground glass* опацификације (ГГО), консолидације, ретикуларне промене, плућни нодули и плеуралне ефузије. Степен промена је одређиван према адаптираној радиографској процени едема плућа. За статистичку обраду је коришћен статистички пакет *SPSS,* вер. 17.0.

Резултати Просечни узраст пацијената је био 62.75 ± 14.8 година. Коморбидитете је имало 66.5% пацијената. Радиографске промене су биле обостране код 53.2%, доминантно у доњим плућним пољима код 68.1%, а дифузне код 24.5% испитаника. ГГО су виђене код 55%, ретикуларне промене код 37.3%, а консолидације код 24% пацијената. На основу радиографског скоринг система, 47.2% пацијената је имало лаку пнеумонију, 40.2% умерену, 7.9% тешку, а 4.6% врло тешку. Код 71.8% старијих од 65 година виђена је тежа упала плућа. Билатералне промене су виђене код 97.4% особа са тежом пнеумонијом, дифузне код 56.4%, а консолидације код 66.7% истих пацијената. ГГО промене су виђене код 58.1% испитаника са лакшом упалом.

Закључак Радиографске промене код пацијената са ковидом 19 су најчешће обостране, доминантно периферне и у доњој плућној зони. Степен дифузних промена пропорционалан је старијем узрасту и учесталијим коморбидитетима. Код тешког облика болести доминирају консолидације и ретикуларне опацификације.

Кључне речи: радиографски налаз; степен плућних промена; ковид 19 пнеумонија

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has different clinical manifestations. In 80–90% of cases, the disease has no symptoms or the symptoms are mild [1]. A severe clinical course can occur in patients with comorbidities [2]. Severe courses of COVID-19 are often complicated by acute respiratory distress syndrome [3].

Chest X-ray (CXR) is an important part of non-invasive diagnostics of lung diseases. It represents an easy-to-implement and affordable method. In addition to the clinical examination, there was a common diagnostic procedure for monitoring the course and outcome of COVID-19 pneumonia. The ability of CXR to visualize changes typical of pneumonia caused by the SARS CoV 2 virus was highlighted [4].

Ground-glass opacifications are the most common radiographic finding in COVID-19 pneumonia [5].

The aim of the research was to examine the frequency and type of radiographic changes in our patients with COVID-19 pneumonia, determine the CXR score and compare it with demographic characteristics and comorbidities.

METHODS

The study included total of 620 patients with COVID-19 who had been treated in the General Hospital in Užice, from June 01 to December 31, 2020. All collected data were analyzed retrospectively. The diagnosis of COVID-19 is established by the detection of SARS-CoV-2 virus in the nasopharyngeal swab. Testing was performed in reference laboratories in the Republic of Serbia. A rapid immunochromatographic antigen test and a polymerase chain reaction (PCR) test were used according to international guidelines [6].

Demographic data (gender and age), comorbidities and CXR were collected from the day of admission. Radiography was performed anteroposteriorly in immobile patients and

anteroposteriorly in others, at full inspiration. The recording was made with a portable device (Vision M, Visaris).

The Fleischner Society's nomenclature was used to determine the CXR changes described as ground-glass opacity (GGO), consolidation, reticular alteration, pulmonary nodules and pleural effusion [7]. The distribution of pulmonary changes was defined as perihilar or peripheral. The dominance of changes was described based on the involvement of the upper and middle lung fields, or a diffuse distribution of the changes.

CXR severity score (CXR-SS) was determined based on the Radiographic Assessment of Lung Edema (RALE) score. This type of radiographic assessment was first performed by Warren et al. [8].

Each lung field is scored from 0 to 4 depending on the presence of changes. A score of 0 means no lung changes, score of 1 means that they are present in less than a quarter of the lung field. Scores 2 and 3 indicate involvement of 25-50% and 50-75%, respectively. A maximum score of 4 means that more than 75% of the lung field is affected. The maximum total score for changes in both lungs was 8 [9].

Statistical analysis

The Statistical Package for Social Sciences (SPSS Inc., Chicago, IL.US) version 17.0 was used for statistical analyses.

The results were expressed as means ± SD and as percentages. Non-parametric variables were calculated by chi-square test. A probability value of $P < 0.05$ was considered significant.

The manuscript was approved by the Ethics Committee of the Uzice Health Center, on February 2, 2024, number 0303/850.

RESULTS

A total of 620 patients with confirmed SARS-CoV-2 infection were examined. The median age was 62.75 +/-14.8 (range 20–92 years). Age groups of the respondents is shown in Figure 1. The largest number of our patients were aged 61-70 (25.9%). Two patients were over 90 years old. Age, gender, and the presence of comorbidities are shown in Table 1.

The presence of comorbidities was significant (66.5%). The most common comorbidities found were hypertension (HTN)/cardiovascular diseases (CVD) (77.4%) and diabetes mellitus (DM) (29%). Followed by chronic obstructive pulmonary disease (COPD)/asthma in 15%, chronic (CH) neurological diseases in 11.7%, kidney diseases in 9%, obesity in 8.7%. Psychiatric diseases, autoimmune diseases, malignancies, gastrointestinal (GI) and liver diseases were the least common (4.9%, 3.4%, 1.5%, 1%, respectively) (Figure 2).

CXR alteration are shown in Table 2. In relation to the CXR, alterations were bilateral in 330/620 patients (53.2%), unilateral in the left lung in 158/220 (25.5%) and right lung in 132/220 (21.3%). Alterations were predominantly in the lower lung field in 411/620 (68.1%), diffuse in 152/620 (24.5%) and in the upper zone in 46/620 (7.4%). Changes in the peripheral lung fields were in 434/620 (70%), central zones in 186/220 (30%). GGO alone was present in 258/620 (41.6%), reticular alteration alone in 152/620 (24.5%), consolidation alone in 63/620 (10.2%), pulmonary nodules in 10/620 (1.6%), pleural effusion in 3/620 (0.5%). In total (with/without other changes), GGO was present in 341/620 (55%), reticular alteration in 231/620 (37.3%), consolidation in 149/620 (24%). The total number of pleural nodules was 22/620 (3.5%), pleural effusion 17/620 (2.7%).

Bilateral alterations were significantly more frequent than unilateral left ($p = 0.002$), or right ($p < 0.001$). Lung changes were significantly more frequent in the lower fields compared to the upper zone ($p = 0.00$) or diffuse changes ($p < 0.001$).

The described changes of the peripheral zones were significantly more frequent than perihilar ($p < 0.001$). The total frequency of GGO was significantly higher than the total frequency of consolidation ($p < 0.001$). GGO alone was significantly more frequent than reticular alteration alone ($p = 0.035$).

No significant difference was observed in the total number of GGO and reticular alterations ($p = 0.065$). Pulmonary nodules and pleural effusion, alone or in combination with other findings, were significantly less frequent then other alterations ($p < 0.001$ in every relationship).

CXR-SS is shown in table 3. Score from 1 to 8 was in 21.1%, 26.1%, 22.6%, 17.6%, 5.2%, 2.7%, 2.7%, 1.9% of patients, respectively. CXR showed mild involvement (score 1-2) in 293/620 (47.2) patients. Moderate involvement (score 3-4) was found in 249/620 (40.2%) patients, severe involvement (score 5-6) was found in 49/620 (7.9%) patients and very severe involvement (score 7-8) was found in 29/620 (4.6%) patients.

In relation to the severity of the disease according to the CXR-SS, respondents were grouped into two groups. The first group included patients with CXR-SS from 1 to 4, the second group included patients with CXR-SS from 5 to 8.

Characteristics by patient groups are shown in the table 4.

Persons over 65 years of age had a statistically significantly more severe disease (71.8%, $p = 0.019$).

Patients with a more severe form of the disease had more frequent comorbidities (93.6%, $p = 0.013$). The most common comorbidities were HTN/CVD and DM, found in 77.4% and 29.4%, respectively. Patients with severe disease significantly more often had HTN/CVD, DM, obesity and chronic kidney failure ($p < 0.001$, $p = 0.031$, $p = 0.004$, $p = 0.010$, respectively). Radiographic alterations by patient groups are shown in Table 5.

Bilateral (97.4%) and diffuse (56.4%) alterations were significantly more common in patients with severe diseases ($p < 0.001$ for both parameters). The zonal distribution of lung changes was not significantly different between the groups. Consolidations in combination with other findings (66.7%) were significantly more frequent in the group of severe diseases ($p = 0.009$). Patients with mild/moderate disease had significant unilateral frequency of alterations by type of GGO. This was in both cases, alone GGO (46.9%) and with other findings (58.1%) ($p = 0.00$, $p = 0.009$, respectively). In relation to the presence of unilateral changes, there was no difference between the left and right sides. Reticular alterations in combination with other findings were most common in severe disease (59%) ($p = 0.009$).

DISCUSSION

Regular CXR was the most important method of rapid diagnosis of pneumonia during the COVID-19 pandemic. The evaluation of changes was often crucial for the decision on further treatment. Baseline CXR sensitivity in literature is estimated between 69 and 90 percent [9]. Modified and improved radiological techniques are presented in the literature [10]. They are based on a number of characteristics of the radiological image. New methods will contribute to the precise diagnosis of lung changes by selecting the lung region of interest according to pixel intensity. The improvement of the X-ray image is achieved by the filtering process with equalization of the histogram [10]. These techniques are not yet available in our institution.

In our study, CXR findings and CXR-SS of patients with COVID-19 upon admission in the hospital were analyzed. All our subjects had CXR changes. Some authors describe a third or a quarter of negative CXR [9, 11]. The first CXR of their subjects was done at the onset of symptoms, which does not apply to our patients. The general hospital is a secondary-type medical institution, so patients were usually treated in primary care facilities beforehand.

Most of our respondents had a lower CXR-SS (1–4). Progression of the CXR-SS during the course of the disease is expected [11, 12]. The low CXR-SS of our patients indicate a shorter time from the onset of the disease.

The largest number of our patients were aged 61–70 (25.9%). We did not observe a significant difference between younger and older than 65, while patients older than 65 showed a higher CXR-SS. The result is expected and in accordance with other authors [13]. Older age is accompanied by comorbidities and a decrease in the defense functions of the immune system. Regression of defense mechanisms implies reduced function of immune cells, such as dendritic cells and macrophages. Consequently, the activation of T lymphocytes was reduced. The mentioned processes create conditions for the occurrence of pneumonia [13].

Most of our respondents were men (57.3%). A similar result is presented in the literature [14]. At the beginning of the pandemic, patients were often male. With the increase in the number of patients, there were no differences according to gender [14]. The authors agree that immunoregulatory functions of sex hormones, physiological factors and different lifestyles play an important role in the development of infection [13].

The frequency of presence of comorbidities in our patients was significant. Our subjects most often had hypertension, cardiovascular diseases and diabetes mellitus. More than half of Fang, et al. [15] respondents had associated diseases. Hypertension and diabetes mellitus were most often present, as in our subjects.

These comorbidities were significantly more common in our patients with severe CXR score. The results of Zhang and the authors also showed the frequent presence of associated diseases in patients with severe form of COVID-19 pneumonia [2]. We also agree in the conclusion with other authors that COPD and asthma are not risk factors for COVID-19 infection, nor for higher CXR-SS. The explanation of this finding assumes use of long-acting

beta agonists and muscarinic antagonists in asthma and COPD therapy. These drugs reduce viral load in nasopharyngeal and tracheal tissue cultures [16].

Severe COVID-19 pneumonia was common in our patients with previously diagnosed hypertension and diabetes. Hypertension and cardiac strain are caused by the angiotensin II. This is affected by SARS-CoV-2 binding to the enzyme converter [17]. This mechanism is also used by SARS-CoV-2 to affect lung tissue, as well as other organs such as the pancreas. An elevated level of pro-inflammatory cytokines was measured in the serum of patients with diabetes. SARS-CoV-2 also leads to an increase in the level of these cytokines. The consequence of an increased level of pro-inflammatory cytokines can be the appearance of a cytokine storm in diabetics with COVID-19 pneumonia [18]. Some authors also report diabetes mellitus as a predictive factor for poor prognosis of COVID-19 pneumonia [19].

Due to the diffuse alveolar damage caused by SARS-CoV-2, GGO occur, which was a common CXR finding in COVID 19 pneumonia. This finding was confirmed by computed tomography [20].

GGO, alone or with other alterations, was most often in our subjects. The GGO present on both sides was also the most frequent finding of subjects with COVID 19 pneumonia analyzed by Kuhajda et al. [5]. This finding corresponds to result of other authors and confirms the assumption that not much time has passed from the onset of symptoms to admission [11]. The conclusion of Yasin et al. is the most frequent presence of consolidations [12]. This is also the finding of Wong et al. [9].

Total described consolidations and reticular alteration were significantly more frequent in our subjects with severe pneumonia, which correlates with the findings of other authors [9]. Pleural effusion and pulmonary nodules were uncommon, both here and in literature [9, 12]. A pronounced pleural effusion was seen in a patient with COVID-19 pneumonia and associated with rheumatoid arthritis [21].

Lung field involvement on CXR in our subjects was most often bilateral with peripheral distribution and more present in the lower lung. Our result is similar to the findings of other authors [9, 12, 22, 23]. In the mentioned studies, the relationship between the distribution of pulmonary changes and the severity of pneumonia was not analyzed. The result of our research showed that mostly bilateral, at the peripheral and dominance diffuse lung alterations corresponded to a higher CXR-SS.

Yacobi et al. [4] suggest that CXR is an easy and accessible procedure for diagnosing lung changes in COVID-19 pneumonia. According to them, SARS-CoV-2 most often causes reticular opacities and GGO. Basal positioned consolidations are typical changes in pneumonia caused by this virus. CXR changes are usually in the peripheral lung zones, as in our patients [4].

CXR changes in COVID-19 pneumonia differ according to disease stages. The first stage is characterized by rapid progression of only GGO, GGO with reticular pattern or consolidation. This stage lasts up to seven days. Advanced stage also lasts up to seven days and is characterized by GGO associated with consolidations and reticular changes. The absorption stage occurs after the 14th day of the disease. In this stage, absorption occurs. CXR absorption indicators are subpleural and fibrotic changes [25]. As in the case of other pathogens, the most severe consequence of COVID-19 pneumonia is the development of pulmonary fibrosis [25]. A significant occurrence of pulmonary fibrosis after 6 months from the onset of the disease in patients with COVID-19 pneumonia was described [15]. Spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema were also complications of COVID-19 pneumonia described in the literature [5]. Thromboembolic complications were also described, and not only in the lungs [26]. The pathogenetic mechanism of SARS-CoV-2 leads to coagulopathy and consequent damage to the endothelium of blood vessels [27].

There are different phases of the body's response to inflammation caused by the SARS-CoV-2. The beginning of the infection is characterized by a high level of virus and the activation of interferon and macrophages. The second phase is characterized by a lower level of virus and less presence of defense cells. In this way, the evolution of diffuse alveolar damage and CXR alterations occurs [28].

We analyzed only the radiographic changes on the day of admission to the hospital, without further follow-up, which would certainly be interesting and important. We analyzed patient data when vaccines were still not in use in our population. Vaccination protection for COVID-19 was important factor for the occurrence and clinical course of the diseases. Vaccination had a significant effect on the reduction of CXR-SS [29]. The clinical course and prognosis of vaccinated patients was more favorable [30].

CONCLUSION

The radiographic changes in patients with COVID-19 pneumonia were often present in both lungs. Their distribution was most often peripheral. The changes were dominantly present in the lower lung zones. The most present alterations were ground-glass opacity.

Pulmonary changes were more severe in elderly patients with comorbidities, the most often cardiovascular and diabetes mellitus. The severity of the lung field involvement is accompanied by diffuse distribution of lung changes by type of consolidations and reticular opacification.

Conflict of interest: None declared.

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Figure 1. Age groups of the respondents

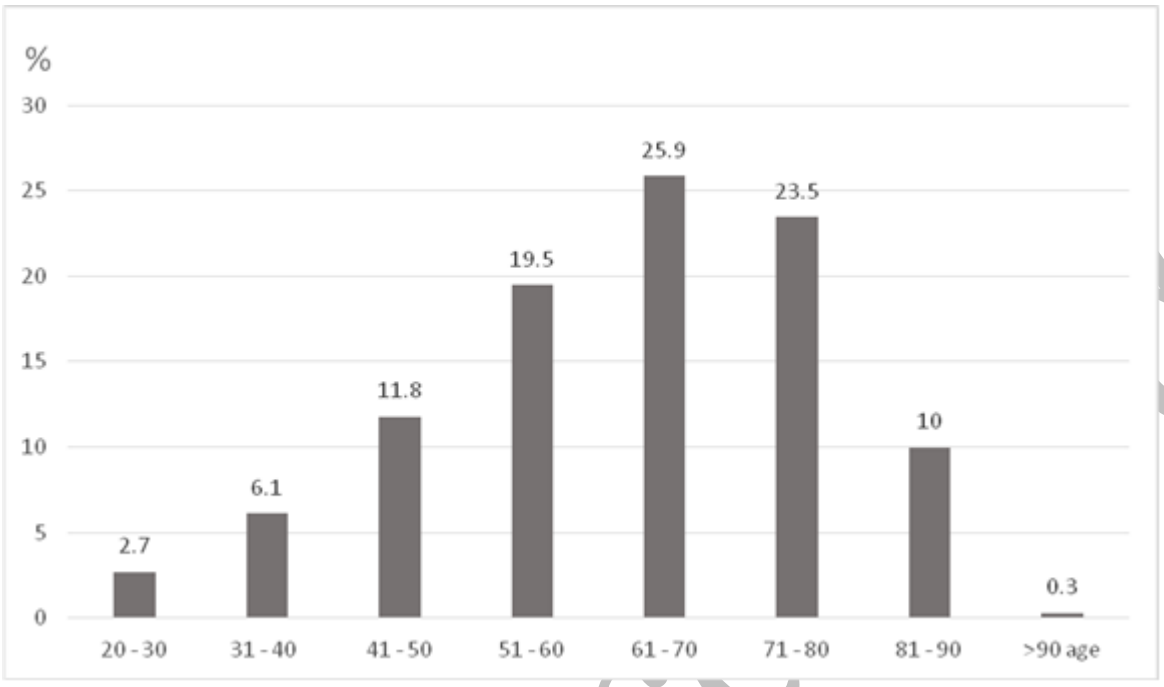
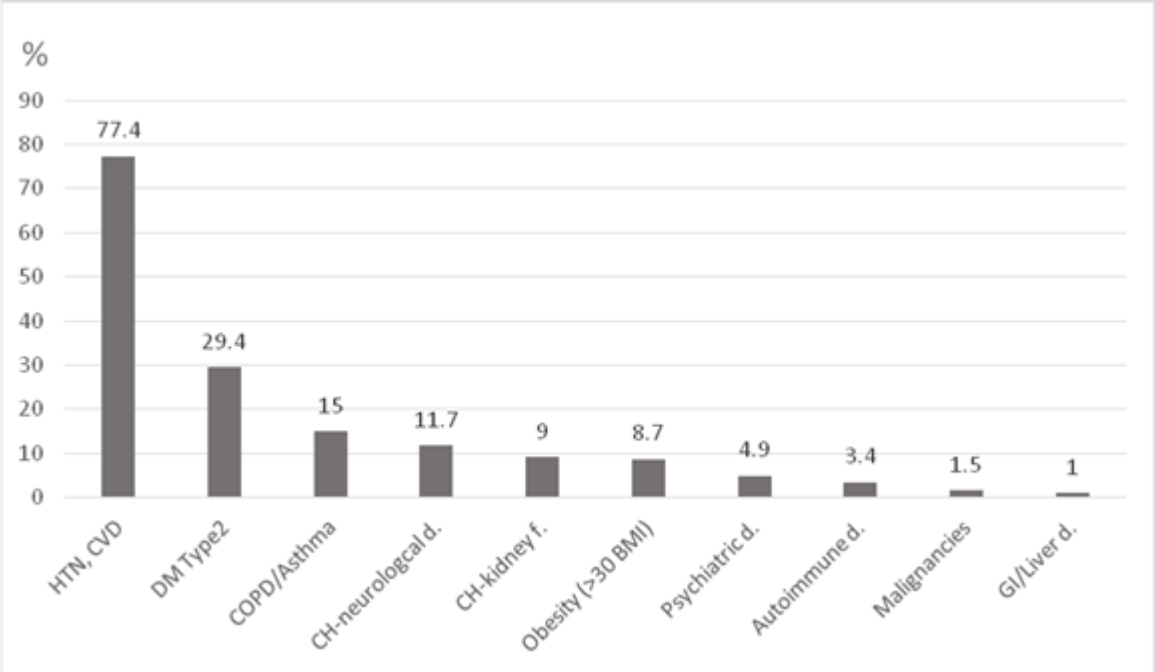


Figure 2. Comorbidities in patients with COVID-19



HTN – hypertension; CVD – cardiovascular diseases; DM – diabetes mellitus; COPD – chronic obstructive pulmonary disease; CH – chronic; BMI – body mass index; GI – gastrointestinal

Table 1. Characteristics of patients with COVID-19

Variable		*N* 620	% patients Total 100	*P* value
Age group	≥ 65 < 65	313 307	50.5 49.5	0.920
Gender	Men Women	355 265	57.3 42.7	0.144
Comorbidity	Yes No	412 208	66.5 33.5	< 0.001

Table 2. Radiographic alterations in COVID-19

Variable		*N*	% patients
Positive CXR		620	100
Lung field involvement	Bilateral	330	53.2
	Left unilateral	158	25.5
	Right unilateral	132	21.3
	Lower zone	422	68.1
	Diffuse	152	24.5
	Upper zone	46	7.4
	Peripheral	434	70
	Perihilar	186	30
Type of alteration	GGO (alone)	258	41.6
	Reticular alteration (alone)	152	24.5
	Consolidation (alone)	63	10.2
	Pulmonary nodules	10	1.6
	Pleural effusion	3	0.5
	GGO (total)	341	55
	Reticular alteration (total)	231	37.3
	Consolidation (total)	149	24
	Pulmonary nodules (total)	22	3.5
	Pleural effusion (total)	17	2.7

CXR – chest X ray; GGO – ground-glass opacity

Table 3. Chest X-ray severity score (CXS-SS) in patients with COVID-19

Variable		*N*	% patients
Positive chest radiographs		620	100
CXR-SS	1	131	21.1
	2	162	26.1
	3	140	22.6
	4	109	17.6
	5	32	5.2
	6	17	2.7
	7	17	2.7
	8	12	1.9
CXR-SS (total)	Mild (1, 2)	293	47.2
	Moderate (3, 4)	249	40.2
	Severe (5, 6)	49	7.9
	Very severe (7, 8)	29	4.6

Table 4. The relationship between patients characteristics and chest X-ray severity in COVID-19

Variable		Mild/moderate Total 542		Severe/very severe Total 78		p value
		N	% patients	*N*	% patients	
Age group	≥ 65	251	46.3	56	71.8	0.019
Gender	Men	305	56.3	50	64.1	0.477
Comorbidity	Yes	339	62.5	73	93.6	0.013
	HTN, CVD	253	46.7	66	90.4	< 0.001
	DM type 2	84	15.5	22	30.1	0.031
	Obesity (> 30 BMI)	39	7.2	17	23.3	0.004
	COPD/Asthma	37	6.8	12	16.4	0.046
	CH-Neuro disorders	37	6.8	7	9.6	0.489
	CH-kidney failure	25	4.6	12	16.4	0.010
	Psychiatric disorders	16	2.9	4	5.5	0.369
	Autoimmune diseases	14	2.6	1	1.4	0.549
	Malignancies	6	1.1	2	2.7	0.412
	GI/liver disease	3	0.6	0	0	0.439

HTN – hypertension; CVD – cardiovascular diseases; DM – diabetes mellitus; COPD – chronic obstructive pulmonary disease; CH – chronic; BMI – body mass index; GI – gastrointestinal

Table 5. The relationship between radiographic alterations and chest X-ray severity in COVID-19

Variable		Mild/moderate Total 542		Severe/very severe Total 78		*P* value
		N	% patients	*N*	% patients	
Lung field involvement	Bilateral	254	46.9	76	97.4	< 0.001
	Left unilateral	156	28.8	2	2.6	< 0.001
	Right unilateral	132	24.4	0	0	0.00
	Lower zone	390	72	32	41	0.004
	Diffuse	108	19.9	44	56.4	< 0.001
	Upper zone	44	8.1	2	2.6	0.093
	Peripheral	377	69.6	5	73.1	0.769
	Perihilar	165	30.4	2	26.9	0.644
Type of alteration	GGO (alone)	254	46.9	4	5.1	0.00
	Reticular alteration (alone)	138	25.5	14	17.9	0.249
	Consolidation (alone)	51	9.4	12	15.4	0.228
	Pulmonary nodules	10	1.8	0	0	0.179
	Pleural effusion	3	0.6	0	0	0.439
	GGO (total)	315	58.1	26	33.3	0.009
	Reticular alteration (total)	185	34.1	46	59	0.009
	Consolidation (total)	97	17.9	52	66.7	0.00
	Pulmonary nodules	19	3.5	3	3.8	0.913
	Pleural effusion	13	2.4	4	5.1	0.324

GGO – ground-glass opacity

