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Research Article

Case Series of COVID-19 Patients Hospitalized in Tishreen- Lattakia University Hospital Between 2020 and 2021

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological agent of the coronavirus disease (COVID-19) pandemic. The expression of the diseases varies among patients, ranging from asymptomatic, or non-pulmonary lesions in mild cases, to cytokine storm leading to severe disease indicating hospitalization and ultimately to ARDS: $PaO_2/FIO_2 < 300$ requiring mechanical ventilation and consequently predisposing to high mortality rates. In Syria, we wanted to participate to the international effort by tracking the characteristics of our COVID-19 hospitalized patients, who tested positive for Rt-PCR and to give our recommendations.

Methods: We conducted a prospective case series study for the year 2020 - 2021, of our hospitalized COVID-19 patients confirmed by positive Rt-PCR.

A clinical record was filled for each patient: clinical characteristics, SPO_2, acute phase reactants when available, CT scan findings and treatment was monitored. The need for mechanical ventilation (NIV or intubation) and mortality were the main outcomes of interest.

Results: 139 patients were included. Their characteristics were: mean age 62 years (SD: 53 - 71), males in 68.7%, any comorbidity in 62.7% (50.7% with hypertension, 10 with asthma and COPD, 26.9 with diabetes, 24% with cardiac failure).

Prevalence of main symptoms during hospitalization was as follows: Fever in 77.6%, cough and shortness of breath in 68.7%, gastrointestinal symptoms in 36.6%, anosmia and agnosia in 9.7%. We noticed that silent hypoxia without shortness of breath was present in 15 patients, and antibiotics were prescribed in all but 8 patients.

A CT scan was performed in all patients showed Ground Glass Opacities (GGOs) in 82.2% (11.1% unilateral, 88.9% bilateral). 19 patients needed mechanical ventilation and 31 died. Death was associated with older age, severity of hypoxia, need of mechanical ventilation and presence of comorbidities.

Conclusion and Recommendations: We should obtain diagnostic tests for COVID-19 in suspected cases. We advise to daily monitor SPO_2 even in non-severe patients, in order to detect silent hypoxia which could damage the lungs. Lastly, we stress on the threatening attitude of prescribing unindicated antibiotics which will lead to antibiotic resistance.

Keywords: *COVID19; Severe Hypoxia in COVID; Silent Hypoxia; Ventilators for COVID16; Antibiotics in COVID 19*

Introduction

In March 2019 WHO declared COVID-19 as a pandemic caused by the virus SARS-CoV-2. The transmission is mainly by droplets while the infected patient can either be symptomatic or asymptomatic [1]. The global burden of COVID-19 patients as reported by WHO end January 2022 is 356,955,754 cases including 5,610,291 deaths [2].

Immunity dysfunction leads to inflammation of the lungs, epithelial and endothelial damage, apoptosis of alveolar monocytes type 1 and 2, microthrombi in capillaries, lymphopenia and thrombocytopenia. This leads to oedema, and possibly atelectasis. Microthrombi in capillary vessels and eventually pulmonary embolism, organizing pneumonia and this could end by fibrosis [3].

The expression of diseases varies among patients, going from asymptomatic or non-pulmonary lesions in mild cases, to cytokine storm leading to severe disease indicating hospitalization, and ultimately to ARDS: $PaO_2/FIO_2 < 300$ requiring mechanical ventilation and consequently to high mortality rates [1,4-8].

Huge amount of case series and cohort studies were published, trying to highlight epidemiological, clinical, biological and radiological characteristics as well as features predicting mortality [1,4-9]. In practice, severity is defined by $SPO_2 \leq 90\%$ by WHO [1] even ≤ 94% by Europe and USA [6-9]. Taking SpO_2 as criteria is very applicable in Low and Middle Income Countries (LMIC) where blood gas measurement is not available in many hospitals. In this context, silent hypoxia is of extreme interest [3,4].

Lastly, scientific authorities around the world, raise concern on the over prescription of Broad Spectrum antibiotics in this viral pneumonia, without evidence of superinfection by bacteria or fungi, and gave guidelines [10,11].

Objective of the Study

We conducted a survey in Syria which first objective was to describe the characteristics of COVID-19 hospitalized patients, who tested positive for Rt-PCR in terms of symptoms, as well as severity-taking SPO_2 as criteria and mortality. The second objective was to investigate factors predicting severity, mechanical ventilation, and mortality. The third objective was to discuss the use of antibiotics in COVID-19.

Methods

In our hospital, outpatients' clinics for respiratory diseases were closed during the period of the study aiming to avoid widespread infection of COVID-19 to hospital workers and our policy was when a patient comes to our emergency department and we suspect COVID-19 infection, RT-PCR was done to confirm the diagnosis and when positive and severe we hospitalized them. A Computerized tomography (CT) scan was performed emergently for all hospitalized patients.

We conducted a prospective case series study for the year 2020-2021, of our hospitalized COVID-19 patients confirmed by positive Rt-PCR. The clinical record was filled for each patient about clinical characteristics, SPO_2, acute phase reactants when available, CRP, procalcitonin, lymphopenia and CT scan findings. Treatment was also monitored. Hypoxia ≤ 94% was considered as a severity criterion. The need for mechanical ventilation (NIV or intubation) and mortality were other outcomes of interest.

Median and interquartile range (IQR) were used to present the continuous variables. Categorical variables were described as the counts and percentages. The Mann-Whitney U (non-normal distribution) was used to compare continuous variables between groups. Chi square or Fisher's exact test was used to compare the categorical variables. We determine OR (odds ratio) and 95% confidence intervals to identify risk factor for hypoxia lower than 94, hypoxia lower than 90, death and the need for ventilator. In our study. $P < 0.05$ was considered to be statistically significant. SPSS version 17.0 software was used for the data analysis

Results

139 patients were included. They were aged 62 years in mean, 68.7% were men, 62.7% had comorbidities (50.7% had hypertension, 10 patients had doctor-diagnosed asthma and COPD, 26.9% diabetes and in 24% cardiac failure. Prevalence of main symptoms was as following: fever in 77.6%, cough and shortness of breath in 68.7%, anosmia and agnosia in 9.7%, gastrointestinal symptoms in 36.6%. Procalcitonin was monitored in 57 patients and was > 0.25 only in 15 patients.

While The Europeans and Americans consider severe hypoxia if SPO_2 ≤ 94%, which is reported in 69.5% of our patients, WHO consider severe hypoxia if ≤ 90%, which was present in 65% of our patients.

Table 1 shows that hypoxia ≤ 94% was significantly associated with age (P = 0.07) and shortness of breath (P = 0.001); however not all patients with hypoxia ≤ 94% suffered from shortness of breath (15 were not). As comorbidities: one comorbid condition was found in 62.7%: 66.3% of patients had hypoxia, while only 53.8% in the case of no comorbidity, 9.5% suffered from asthma and COPD as comorbidity, Procalcitonin was monitored in 57 patients, and was > 0.25 only in 15 patients.

Characteristics	Total (134)	Hypoxia (SpO_2<94%) (95)	No hypoxia (SpO_2>94%) (39)	P	OR with 95% confidence interval
Age (year) (missing 3)	62 (53-71) Median IQR	63 (56-73) Median IQR	62 (47-65) Median (IQR)	0.07	
Male Sex	92 (68.7%)	66 (69.5%)	26 (66.7%)	0.75	
Comorbidities					
Any comorbidity	84 (62.7%)	63 (66.3%)	21 (53.8%)	0.18	
Hypertension	68 (50.7%)	52 (54.7%)	16 (41%)	0.15	
Type 2 diabetes	36 (26.9%)	24 (25.3%)	12 (30.8%)	0.51	
Cardiac Ischemia	23 (17.2%)	16 (16.8%)	7 (17.9%)	0.88	

Heart Failure	10 (7.5%)	9 (9.5%)	1 (2.6%)	0.17	
Asthma - COPD	10 (7.5%)	9 (9.5%)	1 (2.6%)	0.17	
Symptoms					
Fever	104 (77.6%)	76 (80%)	28 (71.8%)	0.30	
Cough	92 (68.7%)	68 (71.6%)	24 (61.5%)	0.26	
Fatigue	101 (75.4%)	74 (77.9%)	27 (69.2%)	0.29	
Sore throat	12 (9%)	10 (10.5%)	2 (5.1%)	0.51	
Shortness of breath	92 (68.7%)	77 (81.1%)	15 (38.5%)	0.001	6.8 (3 - 15.6)
Wheezing	7 (5.2%)	6 (6.3%)	1 (2.6%)	0.67	
Rhinorrhea	11 (8.2%)	10 (10.5%)	1 (2.6%)	0.18	
Chest pain	18 (13.4%)	12 (12.6%)	6 (15.4%)	0.67	
Gastrointestinal symptoms	49 (36.6%)	35 (36.8%)	14 (35.9%)	0.92	
Anosmia	13 (9.7%)	12 (12.6%)	1 (2.6%)	0.11	
Agnosia	13 (9.7%)	11 (11.6%)	2 (5.1%)	0.35	
Laboratory findings					
PCT>0.25 (missing 81)	15 (28.3)	13 (34.2%)	2 (13.3%)	0.18	
CRP (missing 14)	97 (45 - 151) Median IQR	100 (50 - 147) Median IQR	66 (19 - 154) Median IQR	0.18	

Table 1: *Characteristics of the patients.*

Hypoxia (SpO_2 ≤ 94%+) prevalence and its relation to other variables.

+Severity is defined by SPO_2 ≤ 94% for Europe and US.

Taking SPO_2 ≤ 90% for severe hypoxia as indicated by WHO, 65% had hypoxia among our patients. Besides as expected shortness of breath (P = 0.001), wheezing (P = 0.051), rhinorrhea (P = 0.002), and cough (P = 0.032), the following characteristics were significantly associated with hypoxia: age (P = 0.01), any co-morbidity (P = 0.049), and procalcitonin > 0.25 (P = 0.0049) (Table 2).

Characteristics	Total (134)	Severe hypoxia (SpO_2<90%) (63)	No Severe hypoxia (SpO_2>90) (71)	P	OR with 95% confidence interval
Age (year) (missing 3)	62 (53-71) Median IQR	65 (59-73) Median IQR	59 (50-67) Median IQR	0.01	
Male Sex	92 (68.7%)	45 (71.4%)	47 (66.2%)	0.52	
Comorbidities					
Any comorbidity	84 (62.7%)	45 (71.4%)	39 (54.9%)	0.049	2.1 (1 - 4.2)
Hypertension	68 (50.7%)	36 (57.1%)	32 (45.1%)	0.16	

Type 2 diabetes	36 (26.9%)	17 (27%)	19 (26.8%)	0.98	
Cardiac Ischemia	23 (17.2%)	14 (22.2%)	9 (12.7%)	0.14	
Heart Failure	10 (7.5%)	7 (11.1%)	3 (4.2%)	0.19	
Asthma - COPD	10 (7.5%)	7 (11.1%)	3 (4.2%)	0.13	
Symptoms					
Fever	104 (77.6%)	50 (79.4%)	54 (76.1%)	0.65	
Cough	92 (68.7%)	49 (77.8%)	43 (60.6%)	0.032	2.3 (1.1 - 4.9)
Fatigue	101 (75.4%)	49 (77.8%)	52 (73.2%)	0.54	
Sore throat (missing 1)	12 (9%)	9 (14.5%)	3 (4.2%)	0.04	3.8 (1 - 14.9)
Shortness of breath	92 (68.7%)	57 (90.5%)	35 (49.3%)	0.001	9.8 (3.7 - 25.6)
Wheezing	7 (5.2%)	6 (9.5%)	1 (1.4%)	0.051	
Rhinorrhea	11 (8.2%)	10 (15.9%)	1 (1.4%)	0.002	13.2 (1.6 - 106)
Chest pain	18 (13.4%)	6 (9.5%)	12 (16.9%)	0.21	
Gastrointestinal symptoms	49 (36.6%)	21 (33.3%)	28 (39.4%)	0.46	
Ageusia	13 (9.7%)	3 (4.8%)	10 (14.1%)	0.07	
anosmia	13 (9.7%)	4 (6.3%)	9 (12.7%)	0.22	
Laboratory findings					
CRP (missing 14)	97 (45 - 151) Median IQR	97 (48 - 134) Median IQR	96 (38 - 155) Median IQR	0.84	
PCT > 0.25 (missing 81)	15 (28.3)	10 (41.7%)	5 (17.2%)	0.049	3.4 (1 - 12)

***Table 2**: Characteristics of the patients. Hypoxia (SpO_2 ≤90%)⁺ prevalence and its relation to other variables. Severity is defined by Hypoxia (SpO_2 ≤ 90%) for WHO.*

19 patients needed mechanical ventilation. Ventilation was associated with comorbidities, especially asthma or COPD, and as expected to shortness of breath (Table 3). 30 patients died, shortness of breath as complaint was a predisposing factor (P = 0.049), severity of hypoxia (P = 0.031), and need of ventilator (P = 0.0001).

Characteristics	Total (134)	Mechanical ventilation (19)	No Mechanical ventilation (115)	P	OR with 95% confidence interval
Age (year) (missing 3)	62 (53-71) Median IQR	66 (59-77) Median IQR	62 (53-70) Median IQR	0.07	
Male Sex	92 (68.7%)	15 (78.9%)	77 (67%)	0.30	
Comorbidities					
Any comorbidity	84 (62.7%)	16 (84.2%)	68 (59.1%)	0.04	3.7 (1 - 13.4)
Hypertension	68 (50.7%)	13 (68.4%)	55 (47.8%)	0.10	
Type 2 diabetes	36 (26.9%)	6 (31.6%)	30 (26.1%)	0.62	
Cardiac Ischemia	23 (17.2%)	3 (15.8%)	20 (17.4%)	0.86	
Heart Failure	10 (7.5%)	2 (10.5%)	8 (7%)	0.63	
Asthma - COPD	10 (7.5%)	4 (21.1%)	6 (5.2%)	0.035	4.8 (1.2 - 19.2)
Symptoms					
Fever	104 (77.6%)	16 (84.2%)	88 (76.5%)	0.56	

Cough	92 (68.7%)	15 (78.9%)	77 (67%)	0.30	
Fatigue	101 (75.4%)	16 (84.2%)	85 (73.9%)	0.40	
Sore throat (missing 1)	12 (9%)	4 (21.1%)	8 (7%)	0.07	
Shortness of breath	92 (68.7%)	17 (89.5%)	75 (65.2%)	0.035	4.5 (1 - 20)
Wheezing	7 (5.2%)	4 (21.1%)	3 (2.6%)	0.008	9.9 (2 - 48.9)
Rhinorrhea	11 (8.2%)	6 (31.6%)	5 (4.3%)	0.001	10.2 (2.7 - 38)
Chest pain	18 (13.4%)	2 (10.5%)	16 (13.9%)	0.69	
Gastrointestinal symptoms	49 (36.6%)	6 (31.6%)	43 (37.4%)	0.63	
Ageusia	13 (9.7%)	1 (5.3%)	12 (10.4%)	0.69	
Anosmia	13 (9.7%)	2 (10.5%)	11 (9.6%)	0.90	
Laboratory findings					
CRP (missing 14)	97 (45 - 151) Median IQR	85 (32 - 107) Median IQR	100 (46 - 156) Median IQR	0.42	
PCT > 0.25 (missing 81)	15 (28.3)	2 (50%)	13 (26.5%)	0.57	

Table 3: *Need for mechanical ventilation.*

Radiological finding with CT- Scan find GGOs in 82.2% (11.1% unilateral, 88.9% bilateral) [13].

131 of our patients received Broad Spectrum Antibiotics, without evidence of bacterial super-infection criteria. And few have unilateral consolidation accompanying the bilateral Ground glass opacities.

Characteristics	Total (134)	Death (30)	Non Death (104)	P	OR with 95% confidence interval
Age (year) (missing 3)	62 (53-71) Median IQR	67 (55-76) Median IQR	62 (53-69) Median IQR	0.14	
Male Sex	92 (68.7%)	22 (73.3%)	70 (67.3%)	0.53	
Comorbidities					
Any comorbidity	84 (62.7%)	19 (63.3%)	65 (62.5%)	0.93	
More than one comorbidity	45 (33.6%)	8 (26.7%)	37 (35.6%)	0.36	
Hypertension	68 (50.7%)	16 (53.3%)	52 (50%)	0.75	
Type 2 diabetes	36 (26.9%)	7 (23.3%)	29 (27.9%)	0.62	
Cardiac Ischemia	23 (17.2%)	3 (10%)	20 (19.2%)	0.24	
Heart Failure	10 (7.5%)	2 (6.7%)	8 (7.7%)	0.85	
Asthma - COPD	10 (7.5%)	4 (13.3%)	6 (5.8%)	0.17	
Symptoms					
Shortness of breath	92 (68.7%)	25 (83.3%)	67 (64.4%)	0.049	2.8 (1 - 7.8)
Laboratory findings					
CRP (missing 14)	97 (45 - 151) Median IQR	90 (41 - 142) Median IQR	100 (45 - 153) Median IQR	0.95	
PCT > 0.25 (missing 81)	15 (28.3)	3 (30%)	12 (27.9%)	0.90	
Need for mechanical ventilation	19 (14.2%)	17 (56.7%)	2 (1.9%)	0.0001	
Hypoxia (SpO_2 < 94%)	95 (71%)	26 (86.7%)	69 (66.3%)	0.031	3.3 (1.1 - 10.2)
Severe hypoxia (SpO_2 < 94%)	63 (47%)	19 (63.3%)	44 (42.3%)	0.042	2.4 (1.02 - 5.4)

Table 4: *Death prevalence and its relation to other variables.*

For all tables abbreviations are: CRP= C-Reactive Protein, mg/L; PCT= Procalcitonin ng/ml; IQR= Interquartile Range; OR= Odds Ratio.

Discussion

In our study all hospitalized patients had positive Rt-PCR test, and all have upon admission an emergency pulmonary high resolution CT-Scan.

In the medical literature, although 80% of COVID-19 patients are asymptomatic, in the resting 20% it goes from mild symptoms to severe hospitalized cases, where 10% needs mechanical ventilation followed by mortality in 5% [6].

Spontaneous cure is in the majority of cases. While post COVID with clinical, radiological and functional features is of concern [4-6].

In our case series, the most common symptoms were: Fever in 77.6%, fatigue in 65.4%, cough in 68.7%, and shortness of breath in 68.7%. Shortness of breath was only present in hypoxic patients.

Predictors of hypoxia are: age, one comorbidity or more especially COPD and asthma. However, hypoxia is not accompanied by breathlessness in 15 patients. Hypoxia without breathlessness was also described in hospitalized patients in China [4] and in Italy [7]. This is labeled in the medical literature as silent hypoxia. [3,4].

Talking about mortality: 30/139 died (21%). Old age, any comorbidity, severity of hypoxia, and need of mechanical ventilation are significantly associated with mortality.

In a Chinese cohort study in 2020, including 342 hospitalized patients from 10 hospitals: Patients characteristics were, 84% under 60 years, 53% males, 28% have at least one comorbidity CRF in 3.5%. Hypertension in 15%. Main symptoms: fever in 77%, breathlessness in 8.2%, cough in 61%. Severe illness in 10.7 %, mechanical ventilation in 4.6%, SPO_2 was not reported in this paper, 90% have abnormal CT with GGO. We noticed that Antibiotics were prescribed in 78% of patients which allude to irrational misuse of antibiotics. Fortunately, non one died and all are discharged from hospital.

However early cases reporting other series from China showed high mortality rate: The fatality rate in Wuhan was 11.0 - 23.8%. And in the summary of a report of 72,314 Cases from the Chinese Center for Disease Control and Prevention, the overall case-fatality rate of COVID-19 was 2.3%. The young age and less comorbidities could explain non mortality in the present case series [4].

An Italian team [7] edited a review of the COVID-19 literature aiming to help clinicians to take decision for COVID-19 hospitalizations. Accordingly, they recommended that COVID-19 asymptomatic or without pneumonia could stay home, but followed and monitored because the disease could progress in the future days. But if pulmonary involvement, especially over 60 years old, with comorbidities or severe extrapulmonary manifestations they should be hospitalized.

The first 40 patients diagnosed with COVID in Italy were investigated: In the 40 first patients in Italy RT-PCR positive, 16 were hospitalized. Mean age of hospitalized was 69 years, while 45 years in non-hospitalized.

In the 16 hospitalized patients, symptoms were the same with fever in 77%, cough in 56%, ageusia/dysgeusia in all (33%), but dyspnea was present only in hospitalized (33%).

All comorbidities were significantly associated with hospitalization. Radiological CT scan signs of pulmonary involvement were observed in 14 (88%) hospitalized patients and none for non-hospitalized. 2 died/16 in hospitalized, but none in non-hospitalized. Criteria for hospitalization seems valid.

In an Indian series [8], in a one center study, 71 hospitalized patients were enrolled, predictors of hypoxia: $SPO_2 \leq 94\%$ are any co-morbidity, dyspnea and CRP > 25 mg/L. While in our series CRP did not correlate with hypoxia.

Churpek, Gupta, Spicer., *et al*. were interested in variation in hospital mortality for COVID-19. They wanted to track mortality in hospitalized COVID-19 patients, and why it is different from one hospital to the other. A total of 4,019 patients were included, 1,537 (38%) of whom died by 28 days. Mortality varied considerably across hospitals (0 - 82%). the factors that explain these differences remain unclear. This variation was mostly explained by hospital-level, socioeconomic status, strain, and physiologic differences. They suggested that individual mortality was driven mostly by patient-level factors [9].

ARIA-EAACI-GA^{2}LEN are proposing a questionnaire in a clinical community setting to help distinguish COVID-19 from Allergic Rhinitis and the Common Cold [12].

In this questionnaire, Bousquet., *et al*. raised the problem that, besides the management of severe COVID-19, one of the major problems of the infection is how to screen citizens with COVID-19 and distinguish them from patients with similar symptoms caused by allergic rhinitis or the common cold. They aimed to establish a digitalized consensus for this purpose. Given the limited availability in many developing countries of RT-PCR testing, and even of antigen rapid diagnosis testing, the consensus will prioritize testing persons presenting with COVID-19 profile.

Their main results were as follows: In COVID-19 patients, the following symptoms were highly prevalent compared to AR or the common cold, p = 0.0001: Smell dysfunction in 77%, taste dysfunction in 83%, shortness of breath in 77% and cough in 79 % [12].

Shortness of breath was only present in 68.7% of our patients, all had hypoxia. While 15 patients have “silent hypoxia” and non-breathlessness [3].

The same was reported in Chinese, Italian and Indian series [4-9]. The mechanism of silent hypoxia is possibly first the impact of the virus on the brain and nervous system, altering the mechanism of ventilation. And secondly vasoconstriction due to hypoxia is absent [3,4,6].

We should pay attention and manage hypoxia the same as in symptomatic patients. Because if not it could silently damage the lung and lead to cytokine Storm [3].

Consequently, we would also emphasize on monitoring of all COVID patients, with pulse oximetry because even if mild or asymptomatic and home isolated, silent hypoxia could be present and could damage lungs silently.

Second when viewing the filles audits to prepare our publication, we were surprised by the prescription upon admission to hospital of Broad spectrum antibiotics in all patients but 8. Following we scheduled a meeting in partnership and issued guidelines for antibiotics in COVID-19 pneumonia according to international guidelines [9,10]. Upon admission Chest XR or CT-Scan showing unilateral consolidation should be considered as community acquired bacterial pneumonia, while bacterial superinfection was excluded if only bilateral ground glass opacities were present on CT scan, or if Procalcitonin level was less than 0,25 it is not considered to be a bacterial superinfection. While purulent sputum, is in favor of bacterial superinfection [10,11].

Following, the prescription of antibiotics was restricted, and daily reviewing of COVID-19 files by pulmonologists supervisors for antibiotics was decreed.

Finally, to this day all around the world COVID-19 pandemic is progressing with the omicron variant. Vaccination, distancing, and personal protection equipment are still priority. And we should certainly continue our health and social programs for other chronic diseases, tuberculosis, climate change, and keep the discussion open with health authorities, patients, and the society [14].

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Conflict of Interest

We do not have any conflict of interest.

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