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Epidemiological Analysis of the Second Wave of COVID-19 in a Moroccan Hospital

Zakaria Chahbi[1*], M. Badaoui[1], M. Raiteb[1], M. Mouharir[1], I. Belatik[1], S. Kaddouri[1], H. Qacif[1], M. Zyani[1]

[1]Internal Medicine Department, Avicenna Hospital, Marrakesh, Morocco

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***Corresponding author:** Zakaria Chahbi
Internal Medicine Department, Avicenna Hospital, Marrakesh, Morocco

Abstract **Original Research Article**

The 2019 coronavirus pandemic (COVID-19), due to the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a sudden and substantial worldwide increase in hospitalizations for pneumonia with multi-organ disease. The aim of this work was to study the demographic, clinical, diagnostic, therapeutic and evolutionary aspects, as well as the study of risk factors associated with an unfavorable evolution of SARS-CoV-2 infection. Our work consisted of a retrospective descriptive and analytical study of 192 cases of COVID-19, collected at the Avicenna Hospital of Marrakech, during a 3-month period from July 26 to October 31, 2021. Our patients were predominantly (65%) male, with a median age of 65 years. Diabetes was the most frequent comorbidity (37.5%) followed by hypertension (28.1%). 62% were vaccinated. Fever was the most frequent symptom in 74% of cases followed by dyspnea which was present in 65.5% of patients. 76.6% of patients had an SpO2%<95%. The biological profile of our study series was diverse, RT-PCR was positive in 68.2%, CRP was increased in 97.9%, LDH was increased in 96.1% of cases, Ferritinemia was increased in 59.4%, extension of lesions on chest CT of 50-70% was predominant in 25.5% of cases. In our study, the parameters of evolution, whose statistical variation was significantly associated with an unfavorable evolution (p<0.05) were age>60 years [p: 0.036], diabetes [p: 0.029], vaccination status [p: 0.004], CRP>100mg/l [p: 0.013]. Treatment in our series was mostly corticosteroid therapy in 94.3%, anticoagulants in 90.1% with a favorable evolution in 83.9% of patients. The second wave of COVID-19 with a rapid recrudescence of cases overwhelmed the health system with a higher proportion of severe COVID-19 cases and higher mortality, thus underlining the need for advance planning, preparation and strengthening of health systems at all levels.

Keywords: Covid-19, Epidemiological study, Morocco, SARS-Cov 2.

INTRODUCTION

COVID-19 (Coronavirus Disease 2019) is a disease caused by a virus named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS Cov-2) and was discovered in December 2019 in Wuhan, China, it is highly contagious and has rapidly spread worldwide [1]. WHO (World Health Organization) officially declared it as a public health emergency of international concern on January 30, 2020 [2, 3]. The aim of this work is to describe and analyze the epidemiological profile of patients with COVID-19 and to compare it to the literature data through a retrospective study conducted in the Avicenne Military Hospital of Marrakech.

MATERIALS AND METHODS

This is a retrospective descriptive and analytical study spread over a period of 3 months from July 26 to October 31, 2021. The study included patients hospitalized for COVID-19 whose diagnosis was confirmed by a positive Polymerase Chain Reaction (PCR) COVID-19 or retained on clinico-biological and radiological arguments within the Avicenne Military Hospital of Marrakech. Patients treated as outpatients were excluded. Data were collected retrospectively from the records of patients hospitalized for COVID-19 infection using a pre-established data sheet. We studied demographic, clinical, biological, therapeutic and evolutionary parameters. A total of 192 patients were included. The collected data were entered and analyzed by Word, Excel 2016, SPSS version 26.0 software and chi2 statistical tests (p<0.05) were used.

RESULTS

There were 192 patients, 124 men (64.6%) with a sex ratio of 1,82. The median age at diagnosis

was 65 years [54-72], the predominant age range was 60-70 years. The most predominant history was diabetes in 37.5% of cases, followed by hypertension in 28.1% (Table 1).

Table 1: Distribution of Covid 19 patients by history (in order of frequency)

Medical History	Number	Percentage (%)
Diabetes	72	37.5
Hypertension	54	28.1
Heart disease	21	10.9
Neoplasia	17	8.9
Obesity	16	8.3
Pulmonary pathology	15	7.8
Surgical	11	5.7
Nephropathy	10	5.2
Neurological	9	4.7
Immunodepression	6	3.1
Thyroïd pathology	6	3.1
Covid 19	5	2.6
Systemic disease	3	1.6
Hepathopathy	2	1.0
Psychiatric	1	0.5
Autres (HIV, Dyslipidemia)	2	1.0

In this cohort, 119 patients (62%) were vaccinated; of which 41.7% were vaccinated with AstraZeneca's COV-2 SARS vaccine. 39 patients (20.3%) were vaccinated with Sinopharm COV-2 SARS vaccine. In our study 97.9% were symptomatic; the signs revealing the disease were dominated by fever (74.0%), dyspnea (65.6%), anosmia (29.2%), nasal discharge (13.5%) and digestive signs (diarrhea, abdominal pain) in 9.9%. Cough was found in 8.9%, 3.6% had anorexia, headache and chest pain in 1.6% and 2.1% of cases respectively. Other signs (agueusia, myalgia, ...) in 14 patients, 76.6% of the patients had an oxygen saturation below 95%. RT-PCR was positive in 131 patients (68.2%). The biological workup revealed an increase in CRP in 97.9%, LDH was increased in 96.1% the rest of the biological abnormalities are summarized in Table 2.

Table 2: Summary of biological results

Biological tests	Patients (n)	Reference values	Number of patients with a deviation from the reference value
Biochemical:			
LDH (UI/L)	78	<225	75(96.1%)
Natremia (mmol/l)	141	136-145	45(31.9%)
Kalemia (mmol/l)	137	3.5-4.6	48(35%)
Urea (mmol/l)	140	2.5-7.50	50(35.7%)
Creatinine (µmol/l)	123	60-120	17(13.8%)
AST (UI/l)	80	<50	18(22.5%)
ALT (UI/l)	74	<65	7(9.5%)
Glycemia (g/l)	72	<1.1	53(73.6%)
Infectious :			
CRP (mg/l)	140	<5	137(97.9%)
Procalcitonin (µg/l)	44	<0.5	11(75%)
Ferritinemia (ng/ml)	32	30-400	19(59.4%)

Chest CT was performed in 157 patients in our series, i.e. 81.25%. It revealed CT lesions suggestive of COVID- 19 in 156 patients and pulmonary embolism in one patient. The extension of the lesions of less than 25% was found in 14.1%, 25-50% in 34.4% of cases, 50-75% in 25.5% of patients, and more than 75% in 6.8% of cases. Of the 192 patients, 167 (86.9%) required in-hospital oxygen support; non-invasive ventilation (NIV) was required in 7 (3.64%) patients. Hydroxychloroquine was administered in 27 patients (14.1%), azithromycin was administered in 99 patients (51.6%) in our series, at a dose of 500 mg on the first day and 250 mg from the second day to the seventh day. The combination of azithromycin and hydroxychloroquine was prescribed in 14.1% of cases. A dual antibiotic therapy was administered in 18 patients (9.37% of cases) based on C3G (ceftriaxone at a dose of 2 g/day). 181 (94.3%) of our patients received

corticosteroid therapy based on: either methylprednisolone injection at a dose of 40mg × 2 per day for 5 days and then 40 mg per day for 5 days, or hydrocortisone hemisuccinate (HSHC) injection at a dose of 100mg × 2 per day for 5 days. 173 patients (90.1%) had received Enoxaparin throughout their hospitalization at prophylactic and curative doses of 0.4 IU/day subcutaneously and 0.6 IU ×2/day respectively. Three patients received Anti-IL 6 Tocilizumab-based biotherapy (slow intravenous infusion / 400 mg (adult) / single dose) Vitamin therapy was prescribed in 129(67.2%) patients: Vitamin C 1g ×2/ Day and Zinc 45 mg/Day for 10 days. The evolution of our patients was favorable in 161(83.9%) patients, 47(24.5%) were transferred to the intensive care unit, 31 patients (16.1%) died. The majority of the deceased patients were male, the unvaccinated patient was 19, 28 patients had saturation<90%, diabetes and hypertension were in 16 and 11 patients respectively. The risk factors associated with an unfavorable outcome in our series are summarized in Table 3.

Table 3: Risk factors associated with an unfavorable outcome

	OR	**IC (95%)**	***p value***
Age: >60 y <60 y	2.805	(1.308-7.826)	0.036
Gender: Man Women	0.613	(0.281-1.336)	0.215
Diabetes: Yes No	2.340	(1.074-5.099)	0.029
Hypertension: Yes No	1.789	(0.801-3.998)	0.152
Vaccinal status : Vaccinated Non Vaccinated	0.319	(0.144-0.705)	0.004
SpO_2: <92% >92%	3.924	(0.952-11.401)	0.034
CRP>100mg/l : Yes No	3.929	(1.254-12.311)	0.013
LDH>500 UI/l : Yes No	5.333	(1.429-19.901)	0.008
Ferritin>100ng/ml : Yes No	0.789	(0.626-0.996)	0.077
PCT>0.5µ/l : Yes No	2.571	(0.566-11.685)	0.213
Glycemia>1.1g/l : Yes No	5.512	(1.075-24.685)	0.027
Scan Lesions>75% : Yes No	3.678	(1.116-12.116)	0.024
Azithromycin alone Yes No	0.537	0.247-1.179	0.86
Azithromycin+HCQ Yes No	2.056	0.785-5.389	0.116
Other antibiotics Yes No	2.438	1.117-5.320	0.021

	OR	IC (95%)	*p value*
Corticosteroids Yes No	0.829	0.776-0.885	0.136
Anticoagulant Yes No	3.776	0.485-29.385	0.150
Vitamin therapy Yes No	0.624	0.284-1.371	0.165
Non invasive Ventilation Yes No	7.802	1.653-36.820	0.003

DISCUSSION

This study describes the clinical characteristics and outcomes of patients hospitalized with COVID-19 during the second wave. For the majority of studies, the male sex is the most affected by SARS-CoV-2, which is consistent with our study. This can be explained by the nature of the sample; indeed, the majority of the patients hospitalized in our services are military personnel, or members of their families. Our study is close to that of Egoryan *et al.*, [4] and Mathew *et al.*, [5] who found a male predominance of 58.8% and 60.1%, the median age was 69.5 years and 54.4 years respectively, which is consistent with our study. Comorbidities are possible risk factors for increasing the severity of COVID-19. Diabetes and hypertension were the predominant in 37.5% and 28.1% of cases, which is consistent with the study by Mathew *et al.*, Diabetes and hypertension were present in 44.7% and 41.5% respectively. 62% of our patients were vaccinated against 38% not vaccinated. According to the study of Bhakta *et al.*, [6], 28.7% were vaccinated while in the study of Mathew *et al.*, only 10% were vaccinated. The presenting signs of the disease in our series were mainly fever, dyspnea and anosmia which were present in 74.0%, 65.6% and 29.2% of the cases respectively which is in agreement with the studies of Iftimie *et al.*, where fever was 64.3%, dyspnea in 50. 7% of cases and Mathew *et al.*, where fever was 71.9%, dyspnea in 74.6%, discordant with the results of the study of El Madkouri where only 1.9% was dyspneic and 6.3% had fever. This can be explained by the severe nature of the second wave of Covid 19. The study of Sharma *et al.*, [7] showed an increase in CRP in 78.7% of the patients, CRP was elevated in 64% of the cases in the study of Chen *et al.*, [8], which is consistent with our study where CRP was elevated in 97.9%. The LDH level in our study was increased in 96.1% of patients. Our result is consistent with Sim *et al.*, (99.61%), higher than that reported by Richardson *et al.*, [9] and El Madkouri which is 70.3% and 66.7% respectively. In our study hyperferritinemia was found in 59.4% of cases. Other studies have more frequently recorded hyperferritinemia; Richardson *et al.*, found hyperferritinemia in 76% of patients, Sharma *et al.*, [7] in 28.7% of cases. However, the study by El Madkouri found hyperferritinemia in 15.9% of cases during the first wave. The median procalcitonin in the study of Egoryan *et al.*, [4] was 0.24ng/ml, while in the study of Bakhta *et al.*, [6] the median was 0.1ng/ml which is close to our study. This high number is explained by the small number of patients in whom MDT was performed.

The WHO recommends that in all suspected cases, samples (nasopharyngeal and pharyngeal) from the upper respiratory tract (URT) should be collected for RT-PCR and, if clinical suspicion persists and URT samples are negative, samples from the lower respiratory tract (LRT) should be collected when readily available [10]. In our study, RT-PCR was positive in 131 patients (68.2%) and negative in 61 patients (31.8%), which is explained by the delay of patients who consulted after 7 days of symptoms, the diagnosis being made on clinical and radiological grounds. In the United States, the American College of Radiology (ACR) recommends that chest CT should not be used for screening or diagnosis of COVID-19 and should be reserved for hospitalized patients when necessary for management [11]. Chest CT scans of patients with COVID-19 most commonly show ground-glass opacification with or without consolidation abnormalities, consistent with viral pneumonia. In a systematic review [12], studies evaluating chest CT findings in more than 2700 patients with COVID-19, noted: ground glass opacifications (83%), ground glass opacifications with mixed consolidation (58%), adjacent pleural thickening (52%), interlobular septal thickening (48%), air bronchograms (46%). In our study series, CT was predominantly extended to more than half of the lung field in 32.3% of cases. Our results were close to those of Han *et al.*, [13] where half of the lung field was affected in 33% of cases. In our series, corticosteroid therapy was prescribed in 94.3% of the patients either by dexamethasone or methylprednisolone; our patients had recourse to antibiotic therapy for 51.6% for azithromycin alone and 14.1% in association with hydroxychloroquine, oxygen therapy in 90.1% of the patients. Most of our patients received anticoagulant 90.1% according to the national protocol established by the Ministry of Health,

tocilizumab in 3 patients, vitamin therapy (Zinc, Vit C, Vit D) was prescribed in 67.2% of cases. Hydroxychloroquine was not recommended at the time of the second wave in several studies due to lack of evidence, in an open-label, multicenter, randomized, controlled trial of hospitalized patients with confirmed mild to moderate Covid-19, 7-day treatment with hydroxychloroquine plus azithromycin or alone did not result in better clinical outcomes, as measured by a seven-level ordinal scale at 15 days. There was also no effect on any of the secondary outcomes [14]. Several clinical reports have demonstrated that the use of corticosteroids in severe COVID-19 has multiple clinical benefits, including a reduction in the need for and duration of invasive ventilation. Cano *et al.*, performed a meta-analysis of 73 available clinical studies of corticosteroid use in 21,350 patients with COVID-19 infection and concluded that mortality benefits were seen in severely ill patients [15]. According to a cohort of Mathew *et al.*, [5], dexamethasone-based corticosteroid therapy was used in 91.7% of cases and methylprednisolone in 6.3% of patients, 53.2% had azithromycin, oxygen therapy (by non-invasive and non-invasive means) was needed in 90.1% of patients. Zinc-based vitamin therapy and vitamin C were used in 92.1% and 88.8% respectively in pre-hospital care.

In our series, 31 patients (16.1%) died. Our results are close to those of Egoryan *et al.*, where 14.3% died. Mortality was 14.7% in the study by Bakhta *et al.*, [6]. The study by El Madkouri [16] showed a mortality of 0.9% in the first wave. The high case fatality rate in our study could be explained by the following reasons: first, due to the rapid influx of cases and the lack of adequate intensive care facilities, a large proportion of the cases were managed in the emergency room, creating a backlog and a disaster-like situation; second, at the time the second wave hit Morocco, the vaccination program had just begun, and thus a large proportion of the patients were not yet vaccinated. Various studies have shown that vaccination prevented serious illness in patients compared with those who were not vaccinated.

Numerous analytical studies on COVID-19 have shown that advanced age and male gender are factors associated with severe forms of the disease. In our study, no patient under 30 years of age had an unfavorable outcome. Whereas 70.9% of the patients with unfavorable evolution were older than 50 years. In our study, age >60 years is a DRF for unfavorable disease progression. In an American study, 83.3% of the patients who required invasive mechanical ventilation were men. Among them, a significantly large portion who was successfully weaned from mechanical ventilation was young people [17]. In our series, diabetes is a risk factor for an unfavorable outcome. Diabetes is a common comorbidity in COVID-19 patients. It is suggested to be a risk factor for severe and fatal cases of COVID-19 [18]. A meta-analysis showed that diabetic patients with COVID-19 had a higher risk (OR: 2.96; 95% CI: 2.31-3.79) of severe disease or death [8], and a higher rate of ICU admission [19].

In a cohort study of COVID-19 patients in New York City (USA), those with diabetes had an increased risk of hospitalization (OR: 2.24; 95% CI: 1.84-2.73) and of developing severe forms (OR: 1.24; 95% CI: 1.03-1.50) [20]. Other comorbidities have been described as being associated with unfavorable outcome, Wang *et al.*, reported that the prevalence of hypertension was significantly higher in COVID-19 patients requiring ICU care [21]. However, the prevalence of hypertension is high in the elderly, so this confounding factor should be excluded. Huang *et al.*, [22] showed that the OR for hypertension was 1.562 (P = 0.092) and 1.262 (P = 0.458) in the multivariate analysis of severity and mortality, respectively. According to the study by Muller *et al.*, [19], lung disease was among the most common comorbidities leading to adverse outcomes. According to the study by Williamson *et al.*, [20], patients followed for chronic kidney disease have a higher risk of developing severe COVID-19 disease. The severity of COVID-19 disease, according to the same study, is inversely related to glomerular filtration rate.

Vaccination status was statistically associated with an unfavorable patient outcome. The study by Sezen *et al.*, [23] also showed that non-vaccination was a significant factor associated with high mortality. Stepanova *et al.*, [24] found that vaccination was associated with an approximate halving of inpatient mortality. In our study, all patients with an unfavorable outcome had an elevated CRP level. Statistical variations in CRP were significant (p=0.013 OR=3.929 CI95% 1.254-12.311). Thus, CRP is an independent risk factor for adverse disease progression. According to the literature, elevated serum CRP levels are key markers of disease progression and an important risk factor for severe COVID-19 disease. Its increased level is also indicative of a developing cytokine storm in COVID-19 patients [25, 26]. In the study by Soraya *et al.*, [27], it was reported that a CRP cut-off value of 34.67 mg/L (sensitivity 82.3%, specificity 73%) can discriminate severe COVID-19 disease from other clinical forms of the disease. In most of our patients with an unfavorable course, the LDH level was increased and the LDH level >500 was significantly related to an unfavorable course. Elevated serum LDH levels have been widely reported in COVID 19 and were mainly higher in severe patients [28].

According to the study by Zeng *et al.*, an early decline in LDH may be related to a better disease course [29]. Thus by measuring it at admission it will have a greater predictive value for patients' risk rather than during the complication of the disease. Therefore,

LDH is reasonably considered a valuable biomarker for severe and critical COVID-19 patients. Although in our cohort, static variations were not significant (p=0.077). As well as it is not a risk factor for poor disease progression (OR= 0.789). The study of Gandini *et al.*, [30], reported that hyperferritinemia was observed in all severe patients on admission, and mild cases had normal mean serum ferritin levels; moreover, severe and intensive care patients had higher ferritin levels than mild patients.

CONCLUSION

Covid-19 is a major public health problem in Morocco and worldwide. The clinical presentation is very polymorphic, it can give an influenza syndrome, a digestive presentation with diarrhea and vomiting, an acute respiratory syndrome, however, it can be asymptomatic. To date, the therapeutic management is better known and better codified. Preventive measures are essential to reduce the spread of the virus and vaccination remains the key to long-term immunization.

Conflict of Interest: none

REFERENCES

1. CDC. COVID-19 and Your Health. Centers for Disease Control and Prevention. Published February 11, 2020. https://www.cdc.gov/coronavirus/2019-ncov/your-health/about-covid-19/basics-covid-19.html
2. COVID-19 – Chronologie de l'action de l'OMS. https://www.who.int/fr/news/item/27-04-2020-who-timeline---covid-19
3. Sohrabi, C., Alsafi, Z., O'neill, N., Khan, M., Kerwan, A., Al-Jabir, A., ... & Agha, R. (2020). World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International journal of surgery*, *76*, 71-76. doi:10.1016/j.ijsu.2020.02.034
4. Egoryan, G., Yanez-Bello, M. A., Ozcekirdek, E. C., Zhang, Q., Poudel, B., Ozen, E., ... & Rodriguez-Nava, G. (2022). Clinical characteristics and outcomes of the first two waves of the COVID-19 pandemic in a community hospital: a retrospective cohort study. *IJID Regions*, *3*, 1-7. doi:10.1016/j.ijregi.2022.02.001
5. Mathew, R., Bhaskararayuni, J., Kumar, A., Rai, R., Imran, M., Roshan, P. K., ... & Ranjan, P. (2022). Clinical characteristics and outcome of patients presenting to emergency department during the second wave of COVID-19. *Journal of Family Medicine and Primary Care*, *11*(6), 2723-2728. doi:10.4103/jfmpc.jfmpc_1726_21
6. Bhakta, S., Sanghavi, D. K., Johnson, P. W., Kunze, K. L., Neville, M. R., Wadei, H. M., ... & Cowart, J. B. (2022). Clinical and laboratory profiles of the SARS-CoV-2 Delta variant compared with pre-Delta variants. *International Journal of Infectious Diseases*, *120*, 88-95. doi:10.1016/j.ijid.2022.04.050
7. Sharma, S., Aggarwal, A., Sharma, R. K., Patras, E., & Singhal, A. (2022). Correlation of chest CT severity score with clinical parameters in COVID-19 pulmonary disease in a tertiary care hospital in Delhi during the pandemic period. *Egyptian Journal of Radiology and Nuclear Medicine*, *53*(1), 1-8. doi:10.1186/s43055-022-00832-x
8. Chen, T., Wu, D. I., Chen, H., Yan, W., Yang, D., Chen, G., ... & Ning, Q. (2020). Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *bmj*, *368*, m1091. doi:10.1136/bmj.m1091
9. Richardson, S., Hirsch, J. S., Narasimhan, M., Crawford, J. M., McGinn, T., Davidson, K. W., ... & Northwell COVID-19 Research Consortium. (2020). Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *Jama*, *323*(20), 2052-2059. doi:10.1001/jama.2020.6775
10. Haut Conseil de la santé Publique. Rapport relatif à l'actualisation de la prise en charge des patients atteints de Covid-19.
11. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. https://psnet.ahrq.gov/issue/acr-recommendations-use-chest-radiography-and-computed-tomography-ct-suspected-covid-19
12. Bao, C., Liu, X., Zhang, H., Li, Y., & Liu, J. (2020). COVID-19 computed tomography findings: a systematic review and meta-analysis. *J Am Coll Radiol*, *17*(6), 701-709. doi:10.1016/j.jacr.2020.03.006
13. Han, X., Fan, Y., Alwalid, O., Li, N., Jia, X., Yuan, M., ... & Shi, H. (2021). Six-month follow-up chest CT findings after severe COVID-19 pneumonia. *Radiology*, *299*(1), E177-E186. doi:10.1148/radiol.2021203153
14. Cavalcanti, A. B., Zampieri, F. G., Rosa, R. G., Azevedo, L. C., Veiga, V. C., Avezum, A., ... & Berwanger, O. (2020). Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19. *New England Journal of Medicine*, *383*(21), 2041-2052. Published online July 23, 2020:NEJMoa2019014. doi:10.1056/NEJMoa2019014
15. Cano, E. J., Fuentes, X. F., Campioli, C. C., O'Horo, J. C., Saleh, O. A., Odeyemi, Y., ... & Temesgen, Z. (2021). Impact of corticosteroids in coronavirus disease 2019 outcomes: systematic review and meta-analysis. *Chest*, *159*(3), 1019-1040. doi:10.1016/j.chest.2020.10.054
16. Houda ELMADKOURI. Covid 19 à l'hôpital Militaire Avicenne de Marrakech Maroc Bases virologiques, épidémiologiques, cliniques et évolutives. Accessed October 28, 2021.

http://wd.fmpm.uca.ma/biblio/theses/annee-htm/FT/2021/these06-21.pdf

17. Deng, Y., Liu, W., Liu, K., Fang, Y. Y., Shang, J., Zhou, L., ... & Liu, H. G. (2020). Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 in Wuhan, China: a retrospective study. *Chinese medical journal*, *133*(11), 1261-1267. doi:10.1097/CM9.0000000000000824
18. Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*, *395*(10229), 1054-1062. doi:10.1016/S0140-6736(20)30566-3
19. Muller, M., Bulubas, I., & Vogel, T. (2021). Les facteurs pronostiques dans la Covid-19. *NPG Neurologie-Psychiatrie-Gériatrie*, *21*(125), 304-312. doi:10.1016/j.npg.2021.06.002
20. Williamson, E. J., Walker, A. J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C. E., ... & Goldacre, B. (2020). Factors associated with COVID-19-related death using OpenSAFELY. *Nature*, *584*(7821), 430-436. doi:10.1038/s41586-020-2521-4
21. Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., ... & Peng, Z. (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *jama*, *323*(11), 1061-1069. doi:10.1001/jama.2020.1585
22. Huang, S., Wang, J., Liu, F., Liu, J., Cao, G., Yang, C., ... & Xiong, B. (2020). COVID-19 patients with hypertension have more severe disease: a multicenter retrospective observational study. *Hypertension Research*, *43*(8), 824-831. doi:10.1038/s41440-020-0485-2
23. Sezen, Y. I., Senoglu, S., Karabela, S. N., Yesilbag, Z., Borcak, D., Unlu, E. C., ... & Yasar, K. K. (2022). Risk factors and the impact of vaccination on mortality in COVID-19 patients. *Bratislavske lekarske listy*, *123*(6), 440-443. doi:10.4149/BLL_2022_068
24. Stepanova, M., Lam, B., Younossi, E., Felix, S., Ziayee, M., Price, J., ... & Younossi, Z. M. (2022). The impact of variants and vaccination on the mortality and resource utilization of hospitalized patients with COVID-19. *BMC Infectious Diseases*, *22*(1), 1-11. doi:10.1186/s12879-022-07657-z
25. Zhang, J. J., Cao, Y. Y., Tan, G., Dong, X., Wang, B. C., Lin, J., ... & Gao, Y. D. (2021). Clinical, radiological, and laboratory characteristics and risk factors for severity and mortality of 289 hospitalized COVID-19 patients. *Allergy*, *76*(2), 533-550. doi:10.1111/all.14496
26. Azkur, A. K., Akdis, M., Azkur, D., Sokolowska, M., van de Veen, W., Brüggen, M. C., ... & Akdis, C. A. (2020). Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. *Allergy*, *75*(7), 1564-1581. doi:10.1111/all.14364
27. Gu, S. X., Tyagi, T., Jain, K., Gu, V. W., Lee, S. H., Hwa, J. M., ... & Hwa, J. (2021). Thrombocytopathy and endotheliopathy: crucial contributors to COVID-19 thromboinflammation. *Nature Reviews Cardiology*, *18*(3), 194-209. doi:10.1038/s41569-020-00469-1
28. Mori, S., Ai, T., & Otomo, Y. (2020). Characteristics, laboratories, and prognosis of severe COVID-19 in the Tokyo metropolitan area: a retrospective case series. *PloS one*, *15*(9), e0239644. doi:10.1371/journal.pone.0239644
29. Zeng, Z., Yu, H., Chen, H., Qi, W., Chen, L., Chen, G., ... & Wu, D. (2020). Longitudinal changes of inflammatory parameters and their correlation with disease severity and outcomes in patients with COVID-19 from Wuhan, China. *Critical Care*, *24*, 1-12. doi:10.1186/s13054-020-03255-0
30. Gandini, O., Criniti, A., Ballesio, L., Giglio, S., Galardo, G., Gianni, W., ... & Lubrano, C. (2020). Serum Ferritin is an independent risk factor for Acute Respiratory Distress Syndrome in COVID-19. *Journal of Infection*, *81*(6), 979-997. doi:10.1016/j.jinf.2020.09.006