Diabetes and COVID-19 in a Moroccan Hospital

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Abstract		Original Research Article

SARS-CoV-2 infection named COVID-19 is an infectious disease that emerged in December 2019 in Wuhan, Hubei Province, China. The infection has spread rapidly internationally and has had devastating consequences by producing large numbers of infected people and deaths as well as a negative socioeconomic impact. As for diabetes, it is a chronic, insidious, multi-factorial disease. In Morocco it is a major public health problem. This pandemic has raised questions about the risk of chronic diseases. Among them, diabetes; one of the most frequently reported comorbidities in patients with COVID-19. Our work consisted of a retrospective descriptive and analytical study of 72 cases of COVID-19 associating Diabetes and COVID-19, collected at the Military Hospital Avicenne of Marrakech, during a period of 4 months between June 2021 and September 2021. The aim of this work was to define the clinical, paraclinical, therapeutic and evolutionary profile of the association between diabetes and COVID19, to identify the risk factors associated with the death of these patients through an analytical study and to propose recommendations for the management of diabetic patients with COVID-19. Hypertension was the most frequent comorbidity 44.4% followed by heart disease in 18.1%. The average age of our patients was 67 ±10 years with a male predominance (62.5%). The majority of our patients were vaccinated (70.8%). The presence of fever, as a clinical sign of Covid19 infection, was observed in the majority of patients (56 patients or 77.8%) followed by dyspnea in 56 patients or 77.8%. RT-PCR was positive in 68.1%, CRP was increased in 97.6%. Ferritinemia was increased in 83.3%. Blood glucose was increased in 89.7%. The extension of the lesions on thoracic CT of 25-50% was predominant in 48.4% of cases. In our study, the parameters of evolution, whose statistical variation was significantly associated with an unfavorable evolution were age>60 years, presence of digestive signs, hypertension, vaccination status, high CRP, high ferritinemia. Treatment in our series was mostly corticosteroid therapy in 97.2% of patients, anticoagulants in 91.7% with a favorable outcome in 76.4% of patients. In order to control this association between COVID-19 and diabetes, it is necessary to ensure glycemic control during the infection, to detect (pre)diabetes in all patients with COVID-19 and to respect preventive measures: hygiene measures, physical distancing as well as to encourage an effective vaccination.
Keywords: Covid-19, diabetes, morbidity, mortality, Morocco.

INTRODUCTION

COVID-19 is a global health emergency. The course of the disease is unpredictable with catastrophic socioeconomic consequences.

Diabetes is one of the comorbidities that clearly worsen the prognosis of Covid-19. Type 2 diabetes is by far the most represented. Although it is not certain that diabetes increases susceptibility to infection by SARS-CoV-2, many studies have highlighted its frequent association with the most severe forms of Covid-19 with atypical clinical and radiological presentations and with their mortality. Therefore, a particular management will be necessary.

The objectives of this work are: To define the clinical, paraclinical, therapeutic and evolutionary profile in diabetic patients with COVID-19 at the Avicenna hospital and to highlight the risk factors associated with the mortality of these patients.

MATERIALS AND METHODS

This is a retrospective descriptive and analytical study of a series of 72 patients associating diabetes and COVID-19 among 192 cases of COVID-19 infection carried out at the Avicenna hospital in Marrakech, over a period of 4 months (between June and September 2021). Corresponding to the 2nd wave of COVID-19. All patients with a primary diagnosis of SARS-COV-2 infection associated with old or newly

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discovered diabetes at the time of infection were included in our study. The diagnosis was confirmed by detection of the SARS-COV-2 viral genome in the upper airways (nasopharynx or oropharynx) by RT-PCR and/or radiological images suggestive of COVID-19 infection.

The data were collected through clinical observations, results of paraclinical explorations and follow-up noted on the medical record using a completed pre-established exploitation form. Statistical analysis of the data was performed using SPSS version 21 software with univariate analysis using the Chi-square and Student's t tests. The significance level was set at 5% (<0.05).

RESULTS

The average age of our patients was 67 ±10 years [35 to 88 years], with a male predominance (62.5%). The average prevalence of pre-existing diabetes was 37.5%. Diabetes was old and known in 64 patients (88.9%). Hypertension was the most common comorbidity in 44.4% of cases (Table 1).

Table 1: Distribution of diabetic patients with COVID-19 by history

History	Number	Percentage (%)
Hypertension	32	44,4%
Heart diseases	13	18,1%
Obesity	11	15,3%
Cancer	4	5,6%
Nephropathy	3	4,2%
Old COVID-19 episod	2	2,8%.

The majority of our patients (70.8%) were vaccinated. Among them, 74.5% were vaccinated with AstraZeneca vaccine, while 25.5% received Sinopharm vaccine.

Almost 1/3 of the patients (26 or 36.1%) had an oxygen saturation, on room air, between 85 and 89%, while 19 or 26.4% had a saturation between 80 and 84%. Eleven patients (15.3%) had a saturation between 70 and 79%.

The most frequent functional signs included: Tachycardia (84.7%), dyspnea (77.8%), fever (77.8%), anosmia (31.9%), polypnea (13.9%), runny nose (12.5%), digestive signs (5.6%), cough (4.2%), chest pain (2.8%) were the predominant symptoms on admission.

The main biological abnormalities observed were: elevated CRP and Procalcitonin in the majority of patients. Ferritinemia was elevated in the majority of patients tested. Renal and liver function tests were normal in the majority of patients. Blood glucose and HbA1C were elevated in 89.7% and 90.9% respectively (Table 2).

Table 2: Data from the biological assessment of patients during their hospitalization

	Number of tested patients	average±standard deviation	Minimum	Maximum	N (%) of patients with values above baseline
CRP (mg/l)	41	140,33 ± 84,50	4,00	320,00	40 (97,6%)
LDH	18	436,09 ± 124,50	264,22	639,00	18 (100%)
Procalcitonin	15	1,57 ± 5,08	0,05	19,90	12 (80%)
Ferritin ng/ml	12	719,87 ± 505,79	143,00	1650,00	10 (83,3%)
Na+	55	138,07 ± 6,82	122,80	159,00	4 (7,3%)
K+	32	4,22 ± 0,74	2,90	5,73	5 (15,6%)
UREA (mg/l)	35	8,46 ± 5,75	2,68	34,76	15 (42,9%)
CREAT (mg/l)	41	118,81 ± 115,78	55,39	712,17	18 (43,9%)
AST (UI/L)	22	31,98 ± 20,84	2,10	102,70	5 (22,7%)
ALT (UI/L)	19	31,16 ± 19,80	8,76	82,35	2 (10,5%)
Glycemia (g/l)	39	2,77 ± 1,53	0,76	8,51	35 (89,7%)
Hba1C (%)	11	9,37 ± 2,30	6,40	14,00	(90,9%)

Confirmation of the diagnosis of COVID-19 was made by PCR in 68.1% of cases. In our series, all the patients hospitalized had type 2 diabetes, known for 1 to 20 years in 64 patients (88.9%). Diabetes on insulin: 52 cases (81.2%), diabetes not treated with insulin: 12 cases (18.7%). Diabetes was newly discovered at the time of COVID infection in 8 patients (11.1%).

Chest CT scan was performed in 60 patients of the series (83.3%). It was found to be abnormal in all of these patients. Almost half (30 or 48.4%) had lung involvement between 25 and 50%, while 20 (32.2%) had involvement between 50 and 75%.

In the univariate analysis, advanced age, female gender, non-vaccination against COVID-19, presence of digestive signs, high CRP level, extent of lesions on CT greater than 50%, need for non-invasive ventilation, and administration of certain antibiotics other than azithromycin were mortality factors (Table 3).

Table 3: Prognostic factors associated with adverse patient outcomes

Prognosis factors	Evolution		P-Value
	Death	**Favorable**	
Age:	$70,5 \pm 10,2$	$46,5 \pm 10,4$	0,031
Gender:			
Women	37,0%	63,0%	0,048
Man	15,6%	84,4%	
Hypertension:			
No	17,5%	82,5%	0,035
Yes	76%	24%	
Vaccinal status:			
No	47,6%	52,4%	0.004
Yes	13,7%	86,3%	
CRP	$190,2 \pm 80,8$	$100 \pm 54,4$	0,033
Ferritin	$779,3 \pm 537,7$	$322,5 \pm 12,0$	0,045
Extent of lesion on the CT scan:			
≤50 %	14,5%	85,5%	0,003
>50%	71,0%	29,0%	
Other ATB than azithromycin:			
No	14,3%	85,7%	0.047
Yes	36,7%	63,3%	

Regarding the treatment protocol of our diabetic patients with Covid19, in addition to insulin therapy, 70 or 97.2% were put on Corticosteroid therapy, while 66 (91.7%) were put on Low Molecular Weight Heparin. Vitamin therapy was administered in 42 (58.3%) patients. For antibiotic treatment, 48.6% of patients were put on azithromycin while 30 (41.7%) were put on an antibiotic other than azithromycin (protected amoxicillin - ciprofloxacin - C3G). Plaquenil was prescribed in 9 (12.5%) patients. Only one patient received anti-interleukin6 biotherapy (Tocilizumab). Twelve of our patients (16.7%), required non-invasive ventilation during their hospitalization. Emergency intubation in the department was necessary in only one patient.

DISCUSSION

Diabetes is one of the most frequently reported comorbidities in patients with COVID-19 and this has been demonstrated in several studies such as the study by Bhatraju *et al.,* [1] and Seiglie *et al.,* [2]. In our study the prevalence of the association of COVID-19 and diabetes was 37.5%. For the majority of studies: Guo *et al.,* [3] in China, Goyal *et al.,* [4] in America, Coronado in France [5], the male sex is the most affected by SARS-CoV-2, which is consistent with our study where we note a male predominance. 45 men or 62.5%, against 27 women or 37.5% with a sex ratio of 1,7. The median age of the patients was 67.5, which is close to the results of the different studies conducted by Cariou *et al.,* [5], Wargny *et al.,* [6], and Seiglie *et al.,* [7]. Obesity was present in 15.3% of cases in our series, which is similar to the data of the study conducted by Escobedo [7] with a percentage of 16% of obese patients.

Clinically, our study is in agreement with the studies carried out by Zhang [8] and Bertrand Cariou, which revealed that the circumstances of discovery were dominated by fever and dyspnea. Digestive signs were less frequent in our series than in other studies.

Hematological abnormalities were dominated by lymphopenia in the different studies [9-11]. Regarding the inflammatory balance: in our study CRP was increased in 97% of our patients. This is consistent with the study of Zhang and the study of Wu [12], who reported an increase in CRP in 91.9% and 85.6% of cases respectively. In the study by Guo *et al.,* 26.5% of patients had hepatic cytolysis. A similar result was reported in the study by Wu. These data are in agreement with the results of our study where cytolysis was noted in 22.7% of cases. According to Wu's series the LDH level was increased in 98% of the cases, which is close to the results of our study where an increase of the LDH level was found in 100% of the patients tested. Renal involvement has been reported in several studies [13, 14] and varies from simple proteinuria to acute renal failure. In our series, 43% of patients had renal function tests above normal values.

On imaging, the results of our study as well as those of V. Rangankar *et al.,* [15] showed that extensive, severe and critical involvement on the thoracic CT scan are the most frequent in diabetic patients with COVID-19. This may be explained by the frequency of severe forms of Covid19 in diabetic patients.

The use of corticosteroid therapy in diabetic patients with COVID-19 varies considerably between

studies, ranging from 18.6% to 97.2% in our study. These differences can be explained by the balance observed between the advantages and disadvantages of the use of corticosteroid therapy in this type of patient. Concerning anticoagulation, and given that the national protocol insists on systematic anti-coagulant treatment, with prophylactic dose for all patients hospitalized for COVID-19, and with curative dose for patients who have a higher risk of having a thrombo-embolic event, 91.7% of our patients were under anticoagulant treatment.

For antiviral treatment: antivirals were used in 35.8% and 68.3% of the patients included in the studies of Guan *et al.,* [16] and Zhu *et al.,* [17] successively. While they were not used in our study and in the studies of Wu *et al.,* and Liu *et al.,* [11]. These differences are explained by the lack of a clear consensus for the use of antivirals in the treatment of COVID-19 in all patients in general and in diabetic patients in particular. The use of antibiotics in our study was 48% which is discordant with the different studies conducted. This can be explained mainly by the use of Azithromycin which is still a controversial subject. Our study is the only one that used Hydroxychloroquine in the treatment of diabetic patients with COVID-19. This is explained by the great debate and international disagreement that accompanies the use of this molecule, in the treatment of patients with COVID-19.

From the analysis of our results and in the light of the current literature, we can conclude that the prognosis of COVID-19 infection in diabetic patients depends mainly on: The advanced age of the patients (> 60 years) which was a statistically significant risk factor associated with unfavorable progression during hospitalization. This is in good agreement with the data in the literature. For gender, according to the study of Wu *et al.,* female gender is a risk factor for mortality; this is consistent with our study. However, in many studies it is rather the male sex that is associated with the unfavorable evolution of the patients. For clinical prognosis factors: Vaccination in our study decreased the risk of death in patients. This was confirmed in a retrospective cohort study from the Russian Federation [18]. A similar result was revealed in a study by Dispinseri *et al.,* [19]. In the same sense, the Office for National Statistics [20] in England reported that the age-standardized mortality rate for COVID-19-related deaths is 32 times higher for unvaccinated persons than for those who received the second dose.

In our study, hypertension was associated with a poor prognosis, which is consistent with the study by Mandana *et al.,* [21].

According to comparative studies undertaken in the ICU, a percentage of death of more than 50% was found in diabetic and hypertensive patients, notably in the study by Al Mutair *et al.,* [22], with mortality percentages of 75% and 81% respectively, and also in the study by Grasseli *et al.,* [23] with 63.8% and 58.5% respectively. Some studies like ours have reported a more severe disease profile with more severe pneumonia in the presence of gastrointestinal manifestations [24, 25]. The outcome was favorable in 76.4% of our patients. The results of our study are in agreement with those of the literature.

In our series, the patients who died had a higher CRP and hyperferritinemia, which was also demonstrated in Guo's study, which revealed an increased risk of severe pneumonia in diabetics with uncontrolled inflammatory response.

According to the studies of Rush Y *et al.,* [26] and Lanza *et al.,* [27], the extent of lesions on the initial CT scan was associated with prognosis, with a higher number of deaths among patients with > 50% lung involvement. This is in agreement with our results.

In our study the use of an antibiotic other than azithromycin was significantly associated with the risk of death. This is consistent with a multicenter cohort that showed that antibiotic use was associated with higher mortality, but only in the subgroup of patients who did not have criteria for antibiotic prescription [28, 29].

According to the different studies, the factors associated with increased mortality in patients with COVID-19 treated with non-invasive ventilation are the presence of moderate and severe ARDS, hypoxemia, high tidal volumes, the presence of bilateral pneumonia as well as progressive worsening of the chest CT [30-32].

CONCLUSION

SARS COV-2 infection is a complex pathology with intertwined infectious and inflammatory mechanisms. Diabetes is among the most frequently reported comorbidities in patients with COVID-19 and is a risk factor for progression to the more severe and critical forms of this disease. Diabetic patients need special surveillance, hence the need for preventive measures, strict control of diabetes and vaccination against COVID-19, especially in elderly subjects who are more vulnerable, in order to improve the prognosis and to limit the risk of hospitalization and death.

Conflict of Interest: None.

REFERENCES

1. Bhatraju, P. K., Ghassemieh, B. J., Nichols, M., Kim, R., Jerome, K. R., Nalla, A. K., ... & Mikacenic, C. (2020). Covid-19 in critically ill patients in the Seattle region—case series. *New England Journal of Medicine*, *382*(21), 2012-2022.
2. Seiglie, J., Platt, J., Cromer, S. J., Bunda, B., Foulkes, A. S., Bassett, I. V., ... & Manne-Goehler, J. (2020). Diabetes as a risk factor for poor early

outcomes in patients hospitalized with COVID-19. *Diabetes care*, *43*(12), 2938-2944.

3. Wei, X. B., Wang, Z. H., Liao, X. L., Guo, W. X., Wen, J. Y., Qin, T. H., & Wang, S. H. (2020). Efficacy of vitamin C in patients with sepsis: An updated meta-analysis. *European journal of pharmacology*, *868*, 172889.

4. Goyal, P., Choi, J. J., Pinheiro, L. C., Schenck, E. J., Chen, R., Jabri, A., ... & Safford, M. M. (2020). Clinical characteristics of Covid-19 in New York city. *New England Journal of Medicine*, *382*(24), 2372-2374.

5. Cariou, B., Hadjadj, S., Wargny, M., Pichelin, M., Al-Salameh, A., Allix, I., ... & Gourdy, P. (2020). Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. *Diabetologia*, *63*(8), 1500-1515.

6. Wargny, M., Gourdy, P., Ludwig, L., Seret-Bégué, D., Bourron, O., Darmon, P., ... & Cariou, B. (2020). Type 1 diabetes in people hospitalized for COVID-19: new insights from the CORONADO study. *Diabetes Care*, *43*(11), e174-7.

7. BRAZIL. orientacoes-manuseio-medicamentoso-covid19-pdf.pdf [Internet]. [cité 7 déc 2022]. Disponible sur: https://www.gov.br/saude/pt-br/centrais-de-conteudo/arquivos/orientacoes-manuseio-medicamentoso-covid19-pdf

8. Zhang, J. J., Dong, X., Cao, Y. Y., Yuan, Y. D., Yang, Y. B., Yan, Y. Q., ... & Gao, Y. D. (2020). Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy*, *75*(7), 1730-1741.

9. Wu, C., Chen, X., Cai, Y., Zhou, X., Xu, S., Huang, H., ... & Song, Y. (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA internal medicine*, *180*(7), 934-943.

10. Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., ... & Feng, Z. (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England journal of medicine*.

11. Liu, W., Tao, Z. W., Wang, L., Yuan, M. L., Liu, K., Zhou, L., ... & Hu, Y. (2020). Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chinese medical journal*, *133*(09), 1032-1038.

12. Sheleme, T., Bekele, F., & Ayela, T. (2020). Clinical presentation of patients infected with coronavirus disease 19: a systematic review. *Infectious Diseases: Research and Treatment*, *13*, 1178633720952076.

13. Pan, X. W., Xu, D., Zhang, H., Zhou, W., Wang, L. H., & Cui, X. G. (2020). Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis. *Intensive care medicine*, *46*, 1114-1116.

14. Darrivere, L., Fieux, F., & de la Jonquière, C. (2020). COVID-19 and acute renal failure in intensive care. *The Anesthesia Resuscitation Practitioner,* 24(4), 207-211.

15. Rangankar, V., Koganti, D. V., Lamghare, P., Prabhu, A., Dhulipala, S., Patil, P., & Yadav, P. (2021). Correlation between ct severity scoring and diabetes mellitus in patients with covid-19 infection. *Cureus*, *13*(12).

16. Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., ... & Feng, Z. (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England journal of medicine*.

17. Zhu, L., She, Z. G., Cheng, X., Qin, J. J., Zhang, X. J., Cai, J., ... & Li, H. (2020). Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. *Cell metabolism*, *31*(6), 1068-1077.

18. Shestakova, M. V., Vikulova, O. K., Elfimova, A. R., Deviatkin, A. A., Dedov, I. I., & Mokrysheva, N. G. (2022). Risk factors for COVID-19 case fatality rate in people with type 1 and type 2 diabetes mellitus: A nationwide retrospective cohort study of 235,248 patients in the Russian Federation. *Frontiers in Endocrinology*, *13*. https://www.frontiersin.org/articles/10.3389/fendo.2022.909874 (2022, accessed 7 December 2022).

19. Dispinseri, S. (2021). Robust Neutralizing Antibodies to SARS-CoV-2 Develop and Persist in Subjects with Diabetes and COVID-19 Pneumonia. *J Clin Endocrinol Metab,* 106(5), 1472-1481.| MEDLINE [Internet]. [cité 7 déc 2022]. Disponible sur: https://pesquisa.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/resource/fr/covidwho-1054860

20. Office for National Statistics. Deaths involving COVID-19 by vaccination status, England [Internet]. [cité 7 déc 2022]. Disponible sur: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingcovid19byvaccinationstatusengland/deathsoccurringbetween1january2021and31may2022

21. Hasanzad, M., Larijani, B., & Aghaei Meybodi, H. R. (2022). Diabetes and COVID-19: a bitter nightmare. *J Diabetes Metab Disord*, 21(1), 1191-3.

22. Al Mutair, A., Al Mutairi, A., Zaidi, A. R. Z., Salih, S., Alhumaid, S., Rabaan, A. A., & Al-Omari, A. (2021). Clinical predictors of COVID-19 mortality among patients in intensive care units: a retrospective study. *International journal of general medicine*, 14, 3719-3728.

23. Grasselli, G., Greco, M., Zanella, A., Albano, G., Antonelli, M., Bellani, G., ... & Zoia, E. (2020). Risk factors associated with mortality among patients with COVID-19 in intensive care units in

Lombardy, Italy. *JAMA internal medicine*, *180*(10), 1345-1355.

24. 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.

25. Zhang, H., Liao, Y. S., Gong, J., Liu, J., Xia, X., & Zhang, H. (2020). Clinical characteristics of coronavirus disease (COVID-19) patients with gastrointestinal symptoms: A report of 164 cases. *Digestive and Liver Disease*, *52*(10), 1076-1079.

26. Ruch, Y., Kaeuffer, C., Ohana, M., Labani, A., Fabacher, T., Bilbault, P., ... & Danion, F. (2020). CT lung lesions as predictors of early death or ICU admission in COVID-19 patients. *Clinical Microbiology and Infection*, *26*(10), 1417-e5.

27. Lanza, E., Muglia, R., Bolengo, I., Santonocito, O. G., Lisi, C., Angelotti, G., ... & Balzarini, L. (2020). Quantitative chest CT analysis in COVID-19 to predict the need for oxygenation support and intubation. *European radiology*, *30*, 6770-6778.

28. Rosca, A., Balcaen, T., Lanoix, J. P., Michaud, A., Moyet, J., Marcq, I., ... & Deschasse, G. (2022). Mortality risk and antibiotic use for COVID-19 in hospitalized patients over 80. *Biomedicine & Pharmacotherapy*, *146*, 112481.

29. Pinte, L., Ceasovschih, A., Niculae, C. M., Stoichitoiu, L. E., Ionescu, R. A., Balea, M. I., ... & Baicus, C. (2022). Antibiotic Prescription and In-Hospital Mortality in COVID-19: A Prospective Multicentre Cohort Study. *Journal of Personalized Medicine*, *12*(6), 877.

30. Radovanovic, D., Coppola, S., Franceschi, E., Gervasoni, F., Duscio, E., Chiumello, D. A., & Santus, P. (2021). Mortality and clinical outcomes in patients with COVID-19 pneumonia treated with non-invasive respiratory support: a rapid review. *Journal of critical care*, *65*, 1-8.

31. Du, Y., Tu, L., Zhu, P., Mu, M., Wang, R., Yang, P., ... & Xu, G. (2020). Clinical features of 85 fatal cases of COVID-19 from Wuhan. A retrospective observational study. *American journal of respiratory and critical care medicine*, *201*(11), 1372-1379.

32. Mina, B., Newton, A., & Hadda, V. (2022). Noninvasive ventilation in treatment of respiratory failure-related COVID-19 infection: review of the literature. *Canadian Respiratory Journal*, *2022*, 9914081.