

Biological characteristics and mortality in patients with diabetes and COVID-19

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Abstract

The objectives of this study were to determine the biological characteristics of diabetic patients who have been diagnosed with COVID-19 and to estimate the risk of death in these patients. The study included 285 COVID-19 individuals whose diagnosis was confirmed by PCR and/or on the basis of typical signs and radiological findings (CT). Patients admitted to the Infectiology Service of Ali Boushaba Public Hospitalier Khenchela, during the year 2020. The data was collected from 1 January to 30 June 2021. The average age of patients diagnosed with COVID-19 in the enumerated population is 62.53 ± 16.65 years. A male predominance was noted, with a sex ratio of men to women in the range of 1,29. Old diabetic patients account for 48.80 % of our sample patient. The PCR was positive in 87% of diabetic cases, the oxygen desaturation was 64.7%, and the pulmonary affliction was important or critical in 28.8% and 18.7%, respectively. A wide range of biological abnormalities was found in diabetic patients, including high CRP in 95.7% of cases, hyperglycemia in 64%, hyperleucocytose in 26.6% of cases, D-dimer elevation in 56% of cases, and hypoprothrombinemia in 21.6% of cases. A high rate of urea and hypo-creatinemia were found in 36.70% and 12% of patients, respectively. As well as high rates of ASAL and ALAT in 28.80% and 26.60% of patients, respectively. In diabetics a mortality rate of 22.3% was noted. With the exception of glycemia and ALAT, the differences in percentages of these parameters based on the presence of diabetes are statistically insignificant. Furthermore, the diabetic is unrelated to the clinical outcome of the patients. Due to the high number of infections, biological changes, and deaths among diabetics infected with COVID19, it is necessary to consider good care of care of these patients in order to reduce morbidity and mortality rates.

Keywords: biochemical parameters; COVID-19; diabetes; hyperglycemia; mortality

Introduction

SARS-CoV-2 (for severe acute respiratory syndrome coronavirus 2), the virus that causes Coronavirus 2019 (COVID-19), was first reported in Wuhan, China, in December 2019, before spreading worldwide and

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affecting Algeria in March 2020 (Salje *et al.*, 2020; Zhou *et al.*, 2020). This disease is linked to an inflammatory condition, a suffocating respiratory distress syndrome (SDRA), a multi-visceral deficiency, and a state of shock in severe cases (Wu *et al.*, 2020).

According to available epidemiological data, people over the age of 65 and those with chronic diseases such as diabetes, hypertension, coronary artery disease, and cerebrovascular disease are more likely to have a severe COVID-19 infection. In preliminary Chinese data, 12 to 22% of diabetic patients were diagnosed, according to the authors (Yang *et al.*, 2020; Zhang *et al.*, 2020). These findings are consistent with those from the Centers for Disease Control and Prevention in the United States, which found a diabetes prevalence of 6, 24, and 32% among COVID-19 positive people who were not hospitalized, hospitalized without intensive care, and hospitalized with intensive care, respectively (Chow *et al.*, 2020).

Diabetes is one of the most commonly reported comorbidities among COVID-19 patients. Because of the public health emergency, knowledge of this new coronavirus is rapidly advancing. The characteristics of diabetic patients at risk of severe and fatal COVID-19 forms, as well as the diabetic's prognostic impact on infection progression, are currently the subject of research (Orioli *et al.*, 2020).

This is the context in which this study takes place, with the objective of determining the biological characteristics of a group of diabetic patients hospitalized with COVID-19 and estimating the disease's severity and mortality rate among these patients.

Materials and Methods

We conducted a retrospective study including 285 patients with Covid-19 who were admitted to the Ali Boushaba Public Hospitalier Khenchela's Infectiology Service, Algeria, during the year 2020. For the purposes of this study, we used the following criteria for inclusion: Adult patients of both sexes who have been hospitalized for COVID-19 and whose diagnosis has been confirmed by a positive PCR test and/or typical thoracoscopic signs. Diabetic diagnosis is based on the patient's declaration, current treatment, and blood sugar levels. The exclusion criteria were: All patients that tested negative for COVID-19; Patients who have the COVID-19 virus and had incomplete medical information; Patients under the age of 18; All patients with medical history other than diabetes.

The data was collected from 1 January to 30 June 2021 using an exploitation file that included the following information: gender; age; antecedents; hospitalization duration; PCR; TDM; oxygen saturation; glycemia; FNS; hepatic; renal; CRP; D-dimeres; ionogramme. Using of the software "IBM SPSS Statistics 20" and "Microsoft Excel", the submitted data was transformed and analysed.

Results

The sampled population consists of 56.30% (160) male subjects. The resulting sex ratio of men to women is 1.29. The average age recorded is 62.53 ± 16.65 years. Nearly half of the participants in this study (48,80 %) had diabetes. The average hospitalization time for patients is around 30 ± 20 days. The majority of patients were admitted to the hospital for a period of [1-10] days, resulting in a 71.20% hospitalization rate (203). The results of the PCR (Polymérase chain reaction) test revealed that it was positive in 87% of the cases (248) (Table 1).

The distribution of patients according to the severity of COVID-19 at admission by combining oxygen levels and radiological extension of the lesions reveals that the majority of patients 67.40% had oxygen levels (SpO_2) below 90%. Analysis of the results of the chest computed tomography (CT) reveals that 67.70% (193) of the patients presented extensive parenchymal lesions between 25% and 50% (Table 2).

It is observed that the majority of patients have an oxygen saturation below 90%, i.e., 64.70% for diabetics and 69.90% for non-diabetics. However, the statistical difference is not significant ($p = 0,06$).

In term of parenchymal affliction in diabetics and non-diabetics, the study found that the percentage of patients with varying degrees of affliction was nearly the same in both groups. In 28.8% and 18.7% of diabetic individuals, respectively, the disease was important or critical. The observed differences are statistically insignificant ($p=0,922$) (Table 2).

Table 1. Demographics characteristics and PCR results of diabetic and non-diabetic COVID-19 patients

Variable	Available data	n (%) or $\bar{x} \pm SD$			p-value
		Total	Diabetes n= 139	Non diabetes n= 146	
Age (years)	285	62.53±16.65	65.17 ± 15.5	60.03±17.36	0.2
Gender	285				
Male		160 (56.30)	74 (53.2)	86 (58.9)	0.00*
Female		124 (43.70)	65 (46.8)	60 (41.1)	0.00*
Duration of hospital stay (day)	285	8.2 ± 6.24	8 ± 5.71	8,38 ± 6.72	0.605
Positive SARS-CoV-2 PCR	285	248 (87)	123 (88.5)	125 (85.6)	0.473

Table 2. COVID-19 severity and diabetes

Variable	Available data	n (%)		
		Total n=285	Diabetes n=139	Non diabetes n=146
SpO ₂ (%)	285			
< 90		192 (67.4)	90 (64.7)	102 (69.9)
[90-94[83 (29.1)	45 (32.4)	38 (26)
≥ 94		10 (3.5)	4 (2.9)	6 (4.1)
Parenchymal involvement	285			
<25 Minimal		42 (14.7)	20 (14.4)	22 (15.1)
[25-50[Moderate		108 (37.9)	53 (38.1)	55 (37.7)
[50-75[Important		82 (28.8)	40 (28.8)	42 (28.8)
> 75 Critical		53 (18.6)	26 (18.7)	27 (18.5)

In Table 3, there are a variety of biological disturbances that have been noted. Specifically, hyperglycemia is more prevalent among diabetics, there is an increase in CRP and D-dimer, as well as hyponatremia. Table 4 compares the means of the levels of the biochemical parameters between diabetic and non-diabetic patients. The diabetic patients presented hyperglycemia with an average value of 2.83 + 1.34 g / L which is significantly ($p < 0.05$) higher than the value recorded among the non-diabetics. Leukocytosis and hyperkalaemia have also been observed in diabetics. Furthermore, in the two groups of patients, an increase in the mean values of lymphocytes, D-dimers and CRP was noted. The increase in these parameters was greater in diabetics. However, the levels of ALAT and urea were higher in non-diabetics. However, the statistical differences observed for all these parameters, with the exception of ALAT, are not significant ($p > 0.05$) (Table 4).

Table 3. The most common paraclinical disorders of diabetic and non-diabetic COVID-19 patients

Parameters	Diabetes n=139	Non diabetes n=146
SpO ₂ < 90 (%)	64.7	69.9
Parenchymal involvement extensive or critical (%)	47.5	47.3
Hyperglycemia (%)	64	48.6
High hemoglobin count (%)	2.9	10
leukocytosis (%)	26.6	33.6
Lymphocytosis (%)	21.6	17.10

Increase of D-dimer (%)	56.1	54.1
Thrombocytopenia (%)	18	15.8
Hypoprothrombinemia (%)	21.6	22.6
Increase of ASAT (%)	28.8	27.8
Increase of ALAT (%)	26.6	31.5
Increase of CRP (%)	95.7	95.2
Increase of Urea (%)	36.70	40.40
Hypercreatinemia (%)	13.70	13
Hyponatremia (%)	46.80	39.70
Hypokaliemia (%)	7.90	11.60

Table 4. Comparison of laboratory parameters between diabetic and non-diabetic COVID-19 patients

Parameters	Available data	Normal range	$\bar{x} \pm SD$			p-value
			Total	Diabetes n=139	Non diabetes n=146	
Glycemia (g/L)	285	0.7-1.6	2.24±1.26	2.83 ± 1.34	1.67±0.87	0.00 *
Haemoglobin (g/dl)	285	13-18	16.04±25.68	14.51±12.12	17.49±33.88	0.77 NS
White cell count (mm ³)	285	4-10	11.18±22.91	12.81±32.40	9.62±4.90	0.20NS
Lymphocytes (g/l)	285	1.5-4	11.76±76.05	15.15±90.48	8.53±59.29	0.31NS
D-dimer (ng/l)	285	<500	985.79±1508.88	1087.86±1738.32	888.62±1250.54	0.26 NS
Platelet count (mm ³)	285	150-450	242.42±114.7	234.06±106.37	250.38±121.93	0.23NS
TP (%)	285	70-100	82.09±18.21	82.07±18.19	82.11±18.30	0.98NS
ASAT (μ/l)	285	5-40	36.38±41.89	32.97±19.83	39.63±55.15	0.18NS
ALAT (μ/l)	285	5-35	36.89±54.61	29.21±26.66	44.20±71.10	0.02 *
CRP (mg/l)	285	<6	65.81±72.99	70.91±89.62	60.97±52.36	0.25NS
Urea (g/l)	285	0.15-0.45	0.57±2.3	0.56±2.02	0.58±2.54	0.82NS
Plasma creatinine (mg/l)	285	3-13	11.33±9.44	11.42±9.47	11.25±9.45	0.60NS
Na (mEq/l)	285	135-145	134.84±12.39	134.47±12.53	135.18±12.29	0.62NS
K (mEq/l)	285	3.5-5.1	6.41±21.87	7.95±29.32	4.95±10.69	0.60NS

p values are calculated using ANOVA test.

* : p<0,05 : was considered statistically significant.

Relationship of clinical outcome with diabetes

The Chi-square test carried out to study the relationship between diabetes and changes in the state of health of patients reveals that this correlation is statistically insignificant (p = 0.515). A mortality rate of 22.3% was recorded among diabetic patients and 19.2% in the non-diabetic group. However, this difference is statistically insignificant (p = 0.517) (Table 5).

Table 5. Distribution of patients by clinical outcome

Evolution		Healing	Death
Diabetes	n	108	31
	%	77.7%	22.3%
Non diabetes	n	118	28
	%	80.8%	19.2%

Relationship of clinical outcome with the levels of biochemical parameters

The results of the Chi-square test carried out to study the relationship between the clinical outcome of patients on one side and age, oxygen saturation, degree of parenchymal damage and levels of biochemical

parameters on the other side, show a statistically significant correlation of clinical outcome with age ($p = 0,02$), SpO₂ ($p = 0,000$), parenchymal involvement ($p = 0,001$) and creatinine level ($p = 0,02$). While it seems insignificant ($p > 0,05$) for the other biological variables.

Discussion

The SARS (severe acute respiratory syndrome) and MERS (Middle East Respiratory Syndrome) epidemics have shown that diabetic patients and those with comorbidities such as arterial hypertension, cardiovascular disease, and obesity are at a higher risk of serious and deadly coronavirus pneumonia (Hussain *et al.*, 2020). Diabetes appears to be a risk factor for COVID-19 forms that are severe and critical. These are most frequently described in patients over the age of 60 who have one or more chronic sub-jacent diseases (Singh *et al.*, 2020; Guan *et al.*, 2020).

We don't know if the increased risk of serious or fatal infection is linked to the effect of diabetes, the level of chronic hyperglycemia, the associated obesity, the relationship with other comorbidities, and/or the patient's age (Orioli *et al.*, 2020).

The cause of poor prognosis in diabetics is likely multifactorial, reflecting the syndromic character of the disease. Age, gender, ethnicity, and comorbidities such as hypertension, obesity, cardiovascular disease, a pro-inflammatory state, and a pro-coagulant state all likely contribute to an increase in the risk of death. Furthermore, the infection that causes a severe respiratory crisis may be a factor in aggravation for diabetics, since it may predispose to metabolic issues through direct negative effects on cell function. These cellular effects might cause diabetic ketoacidosis, hyperglycemia during hospitalization in people with undiagnosed diabetes, or even lead to the development of a new diabetes (Apicella *et al.*, 2020).

The average age of the patients in our study was 62.53 ± 16.65 years. The [64-74] year age group is the most prevalent, which is similar to other studies' findings. In an Italian study, it was reported that 78.5 years old is the average age (Luigi *et al.*, 2020). However, Guan *et al.* (2020) reported an average age of 47 years, as did Zhou *et al.* (2020) and Wang *et al.* (2020), who reported an average age of 56 years. In addition, a Wuhan study found that the average age was 55.5 years old (Chen *et al.*, 2019).

In this group of patients, the percentage of male subjects is around 56.30%. Other studies have shown a similar frequency: 58.1% (Guan *et al.*, 2020); 54.3% (Wang *et al.*, 2020) and 62% (Zhou *et al.*, 2020). However, in an Italian series, a percentage of 70.06% was recorded (Luigi *et al.*, 2020).

The study's first objective was to describe the biological profile of diabetic patients infected with COVID-19 and compare it to that of non-diabetic patients. In comparison to non-diabetic individuals, we found a variety of biochemical aberrations in diabetic patients.

There was a significant increase in hyperglycemia among diabetics compared to non-diabetics. A glycemia value of around 2.83 ± 1.34 g/L was found in the diabetic group. Our findings are comparable to those of Lounici *et al.* (2021) who found a glycemia of 2.23 ± 1 g/L in a sample of diabetic patients. This stress hyperglycemia appears to be linked to the tenacity of the inflammatory response.

Based on the literature to date, it is clear that hyperglycemia is an independent risk factor that disrupts immune responses and stimulates inflammatory and pro-coagulant states (Lounici *et al.*, 2021). However, there has yet to be a randomized trial that has demonstrated the benefit of tight glycemia control throughout the septic (Van *et al.*, 2001).

In addition to glycemia, diabetics have been shown to have hyperleucocytosis and hyperkalemia. On the other hand, there was an increase in the average D-dimers and CRP values, an increase in the values of ALAT and ASAT, and hyperlymphocytosis in both groups of patients. The increase in these last parameters was more expressed among diabetics. Our findings are consistent with previous research that has shown an increase in

CRP, lymphopenia, and a rise in hepatic transaminases in diabetics who have been diagnosed with COVID-19 (Malik *et al.*, 2020).

According to studies conducted in China among COVID-19 patients, an increase in CRP level was observed in around 60% of those admitted to the hospital (Rodriguez-Morales *et al.*, 2020; Fu *et al.*, 2020; Zhou *et al.*, 2020). When compared to the findings of another study based on the data of 175 patients, the percentage of diabetics with elevated CRP was 32.8%, while the percentage of non-diabetics with elevated CRP was 16.3% (Guo *et al.*, 2020). A high CRP level is associated to a negative progression of the disease as well as a higher mortality rate (Luo *et al.*, 2020; Ruan *et al.*, 2020).

In terms of ALAT, the average was $29.21 \pm 26.66 \mu /L$ in diabetics and $44.20 \pm 71.10 \mu /L$ in non-diabetics. Similarly, in a previous study, the authors found that diabetics had an average of $45.6 \pm 44 \mu /L$ (Lounici *et al.*, 2021). According to the findings of studies conducted in China, lymphopenia was discovered in around 50% of hospitalized patients out of a total of 511 individuals (Rodriguez *et al.*, 2020). Another study by Alzaid *et al.* (2020) used a cohort of 45 COVID-19 patients, 30 of whom were diabetics. Lymphopenia was associated to severe COVID-19 in patients with type 2 diabetes who needed intensive care, according to the authors of this research.

The immunological response, particularly lymphocytes T, appears to be highly involved in the pathological process associated with COVID-19 (Qin *et al.*, 2020). In fact, the SARS-CoV-2 virus appears to target lymphocytes directly, causing their destruction or dysfunction with a rapid decline (Gao *et al.*, 2020; Tan *et al.*, 2020). Furthermore, lymphocytes express the ACE2 receptor, making them a direct target of the virus; hence, their alteration (Xu *et al.*, 2020) would be a significant factor in the aggravation of infection symptoms (Diao *et al.*, 2020).

In our research, we recorded an increase in D-dimer. This percentage was higher among diabetic individuals. However, this result is statistically insignificant. According to the literature, patients with COVID-19 and coagulopathy often experience an increase in D-dimères, a slight decrease plate numeration, and a lengthening of Quick time (Levi *et al.*, 2020).

According to cohort studies, the incidence of thromboembolic events in COVID-19 patients ranges from 11% to 35% (Levi *et al.*, 2020). Coagulation problems (such as thromboembolism of the veins, cerebral vascular accidents, syndrome coronarien aigu - SCA or myocardial infarction) and intravascular coagulation are relatively common among COVID-19 patients, particularly in critical cases with high D-dimer levels that require constant monitoring and prompt intervention. As a result, patients infected with COVID-19 are at a higher risk of thromboembolic events. Notably, Tang *et al.* (2020) recently pointed out that the vast majority of COVID-19 patients die during their hospital stay despite meeting all of the diagnostic criteria for intravascular coagulation (71.6% vs. 0.6% among survivors).

A Chinese study compared the clinical presentation of COVID-19 in diabetic and non-diabetic individuals (Guo *et al.*, 2020). This research reveals a number of intriguing aspects. First, the COVID-19's early symptomatology appears to be more frustrating in diabetic patients. In fact, the presence of fever is reduced, which may result in a diagnostic lag. Secondly, the use of thoracoscopic scanners reveals that diabetics have more severe pneumonias. Thirdly, diabetes is associated with numerous of biological abnormalities, including the elevation of inflammatory biomarkers (such as C-reactive protein (CRP) and interleukin 6 (IL-6)), the elevation of tissue enzymes, and coagulation abnormalities (such as D-dimer). These abnormalities, according to the authors, indicate a severe, multi-organ affliction with a proclivity for thrombo-embolic events as well as "cytokine orage," which is described as a COVID-19 aggravating factor. Finally, lymphopenia, which is frequently cited as a predictor of poor prognosis, is more common and severe in diabetics (Orioli *et al.*, 2020).

A meta-analysis of 17 687 participants observed at the relationship between diabetic phenotypes and COVID-19 severity. With a few exceptions, the risk factors identified in the diabetic community are similar to those seen in the general population, according to this study. Clinical variables include advanced age, male

gender, obesity, hypertension, chronic lung diseases, MCV, and recurrent cancer (Schlesinger *et al.*, 2020), as well as biological variables such as lymphopoiesis, elevated CRP, and hepatic transaminases (Malik *et al.*, 2020).

Increased expression of the angiotensin-converting enzyme 2 (ACE 2) in diabetic patients, both type 1 and type 2, is one of the physiopathological hypotheses (Wan *et al.*, 2020). This enzyme, which is found in the salivary glands, the intestine, the kidneys, and the blood vessels, is thought to be linked to the SARS-CoV-2 virus and might explain why some individuals have a more severe infection. Furthermore, hyperglycemia, whether acute or chronic, is known to alter the immune system's response, leading to an exaggerated pro-inflammatory response that has been observed in individuals with severe COVID-19 disease (Geerlings *et al.*, 1999; Tan *et al.*, 2020).

Beyond determining the biological characteristics of diabetic patients, the second objective of this research was to estimate and evaluate the COVID-19's severity and mortality rates in diabetic and non-diabetic individuals. In terms of the COVID-19's severity, which is based on oxygen saturation and the extent of pulmonary involvement, there was no significant difference between diabetics and non-diabetics. In addition, diabetics have a mortality rate of 22.3%, whereas non-diabetics have a rate of 19.2%. The statistical analysis reveals a significant correlation between the clinical issue, age, SpO₂, parenchymal involvement, and creatinine level. However, it is not significant for other biological factors.

The COVID-19-related mortality rate varies from study to study, ranging from 2% to 15% in severe forms to more than 20% and even 50% in critical forms (Singh *et al.*, 2020). According to Chinese data based on more than 70,000 cases, the overall mortality rate associated with COVID-19 was 2.3%, whereas it was 7.3% in diabetic patients (Epidemiology Working Group for Ncip, 2020). However, the subject of diabetes as a prognostic factor "per se" has resurfaced, with the most severely affected individuals frequently having other comorbidities. According to the study of Guo *et al.* (2020) mentioned above, diabetic patients died more frequently than non-diabetic individuals (10.8% against 3.6%). Despite the fact that diabetes appears to be a poor prognostic factor for COVID-19, it also has a negative influence on diabetic disease. The first element is the glycemic imbalance induced by infection and, as a result, the risk of complications such as ketoacidosis and hyperosmolar coma (Orioli *et al.*, 2020).

CORONADO, a French observational study whose primary objective was to identify clinical and biological characteristics associated to disease severity and mortality in diabetic patients hospitalized for COVID-19 (Cariou *et al.*, 2020). According to this study, certain biological variables (admission glycemia, elevation of hepatic transaminases and the inflammatory marker CRP, decline in renal function, and reduction in plate numeration at admission) are all independently associated with a higher risk of early mortality in diabetic patients hospitalized for COVID-19 (Scheen *et al.*, 2020). In the CORONADO study, high blood sugar at admission was associated to the need for mechanical ventilation and/or death within the first seven days (Cariou *et al.*, 2020).

The literature revealed a correlation between hyperglycemia and admission to a severe COVID-19 prognosis. A study in Guangzhou (China) found that a high glycemia at admission was a significant risk factor for COVID-19 severe form, with a glycemia at admission of >1.13 g/L being an optimal threshold for a poor prognosis in the 30 days after admission (Zhang *et al.*, 2020). Another retrospective study conducted in Wuhan on 605 patients admitted to the hospital without a prior diagnosis of diabetes found that a glycemia level of >1.27g/L predicted mortality at 28 days in an independent manner (Wang *et al.*, 2020). In 271 patients hospitalized with COVID-19, the Italian study Pisa COVID-19 showed that hyperglycemia at admission is an independent factor associated with a severe prognosis (Coppelli *et al.*, 2020).

Conclusions

In our series of diabetic patients infected with Covid-19, there are mainly elderly male patients. They have high blood sugar on admission. We noted a high rate of these patients presenting severe forms with a high frequency of hospital mortality which confirms that in association with diabetes, the disease progression becomes more severe and unfavorable, this is due to the variations mostly organic. Indeed, the biological characteristics of our series of diabetic patients with COVID-19 are mainly hyperglycemia, an increase in CRP, a decrease in hemoglobin, hyperleukocytosis, lymphopenia, an increase in D-dimers, hypoprothrombinemia, hyperglycemia alone constitutes a risk factor that hinders immune responses and stimulates inflammatory and procoagulant states. Optimizing blood glucose control on admission makes clear clinical sense. Managing diabetes is essential to reduce morbidity and mortality rates.

Authors' Contributions

NA took the lead in methodology, oversight, statistical analysis, interpretation and discussion of results. AZ and SM participated in carrying out the survey; in the design and also provided critical feedback on the manuscript. SG and LR assisted in its revision and editing. All authors read and approved the final manuscript.

Ethical approval (for researches involving animals or humans)

Informed consent was obtained from all parents of participants to complete the questionnaire.

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Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

References

- Alzaid F, Julla JB, Diedisheim M (2020). Monocytopenia, monocyte morphological anomalies and hyperinflammation characterize severe COVID-19 in type 2 diabetes. *EMBO Molecular Medicine* 12:e13038. <https://doi.org/10.15252/emmm.202013038>
- Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S (2020). COVID-19 in people with diabetes: understanding the reasons for worse outcomes. *The Lancet Diabetes & Endocrinology* 8(9):782-792. [https://doi.org/10.1016/S2213-8587\(20\)30238-2](https://doi.org/10.1016/S2213-8587(20)30238-2)
- 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* 63:1500-1515. <https://doi.org/10.1007/s00125-020-05180-x>
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet* 395(10223):507-513. [https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)

- Covid C, Team R, COVID C, Team R, Chow N, Fleming-Dutra K, ... Ussery E (2020). Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019-United States, February 12–March 28, 2020. *Morbidity and Mortality Weekly Report* 69(13):382. <https://doi.org/10.15585/mmwr.mm6913e2>
- Coppelli A, Giannarelli R, Aragona M, Penno G, Falcone M, Tiseo G, ... Del Prato S (2020). Hyperglycemia at hospital admission is associated with severity of the prognosis in patients hospitalized for COVID-19: the Pisa COVID-19 study. *Diabetes Care* 43(10):2345-2348. <https://doi.org/10.2337/dc20-1380>
- Diao B, Wang C, Tan Y, Chen X, Liu Y, Ning L, ... Chen Y (2020). Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). *Frontiers in Immunology* 11:827. <https://doi.org/10.3389/fimmu.2020.00827>
- Epidemiology Working Group for Ncip Epidemic Response (2020). The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Chinese Journal of Epidemiology* 41(2):145-51.
- Fu L, Wang B, Yuan T, Chen X, Ao Y, Fitzpatrick T, ... Zou H (2020). Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and meta-analysis. *Journal of Infection* 80(6):656-665. <https://doi.org/10.1016/j.jinf.2020.03.041>
- Gao Y, Li T, Han M, Li X, Wu D, Xu Y, ... Wang L (2020). Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *Journal of Medical Virology* 92(7):791-796. <https://doi.org/10.1002/jmv.25770>
- Geerlings SE, Hoepelman AI (1999). Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunology & Medical Microbiology* 26(3-4):259-265. <https://doi.org/10.1111/j.1574-695X.1999.tb01397.x>
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, ... Zhong NS (2020). Clinical characteristics of coronavirus disease 2019 in China. *New England Journal of Medicine* 382(18):1708-1720. <https://doi.org/10.1056/NEJMoa2002032>
- Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, ... He JX (2020). Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *European Respiratory Journal* 55(5). <https://doi.org/10.1183/13993003.00547-2020>
- Guo L, Shi Z, Zhang Y, Wang C, Moreira NCDV, Zuo H, Hussain A (2020). Comorbid diabetes and the risk of disease severity or death among 8807 COVID-19 patients in China: a meta-analysis. *Diabetes Research and Clinical Practice* 166:108346. <https://doi.org/10.1016/j.diabres.2020.108346>
- Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, ... Hu D (2020). Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes/metabolism Research and Reviews* 36(7):e3319. <https://doi.org/10.1002/dmrr.3319>
- Hussain A, Bhowmik B, do Vale Moreira NC (2020). COVID-19 and diabetes: Knowledge in progress. *Diabetes Research and Clinical Practice* 162:108142. <https://doi.org/10.1016/j.diabres.2020.108142>
- Levi M, Thachil J, Iba T, Levy JH (2020). Coagulation abnormalities and thrombosis in patients with COVID-19. *The Lancet Haematology* 7(6):e438-e440. [https://doi.org/10.1016/S2352-3026\(20\)30145-9](https://doi.org/10.1016/S2352-3026(20)30145-9)
- Lounici A, Benmekki A, Ghenou A, Tahir S, Belmimoune A, Zini S, ... Nigassa NB (2021). Particularités cliniques des patients diabétiques hospitalisés pour Covid-19 sur une période d'une année. *Revue Algérienne d'Allergologie et d'Immunologie Clinique* 6:2543-3555.
- Luo X, Zhou W, Yan X, Guo T, Wang B, Xia H, ... Yang W (2020). Prognostic value of C-reactive protein in patients with coronavirus 2019. *Clinical Infectious Diseases* 71(16):2174-2179. <https://doi.org/10.1093/cid/ciaa641>
- Malik P, Patel U, Mehra D, Patel N, Kelkar R, Akrmah M, ... Sacks H (2021). Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis. *BMJ Evidence-Based Medicine* 26(3):107-108. <https://doi.org/10.1136/bmjebm-2020-111536>
- Orioli L, Hermans MP, Preumont V, Loumaye A, Thissen J-P, Alexopoulou O, Furnica R, Burlacu M-C, Maiter D, Yombi C-J, Vandeleene B (2020). COVID-19 et diabète. *Louvain Medicine* 139(05-06):252-257.
- Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y (2020). Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis*. 28;71(15):762-768. <https://doi.org/10.1093/cid/ciaa248>
- Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, ... Sah R (2020). Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Medicine and Infectious Disease* 34:101623. <https://doi.org/10.1016/j.tmaid.2020.101623>

- Ruan Qk Yang K, Wang W, Jiang L, Song J (2020). Clinical predictors of mortality due to COVID-19 based on an analysis data of 150 patients from Wuhan, China. *Intensive Care Medicine* 1-3. <https://doi.org/10.1007/s00134-020-05991-x>
- Salje H, Tran Kiem C, Lefrancq N, Courtejoie N, Bosetti P, Paireau J, ... Cauchemez S (2020). Estimating the burden of SARS-CoV-2 in France. *Science* 369(6500):208-211. <https://doi.org/10.1126/science.abc3517>
- Scheen AJ, Marre M, Thivolet C (2020). Prognostic factors in patients with diabetes hospitalized for COVID-19: findings from the CORONADO study and other recent reports. *Diabetes and Metabolism* 46(4):265-271. <https://doi.org/10.1016/j.diabet.05.008>
- Schlesinger S, Neuenschwander M, Lang A, Pafili K, Kuss O, Herder C, Roden M (2021). Risk phenotypes of diabetes and association with COVID-19 severity and death: a living systematic review and meta-analysis. *Diabetologia* 64(7):1480-1491. <https://doi.org/10.1007/s00125-021-05458-8>
- Singh AK, Gupta R, Ghosh A, Misra A (2020). Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 14(4):303-310. <https://doi.org/10.1016/j.dsx.2020.04.004>
- Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, ... Miao H (2020). Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduction and Targeted Therapy* 5(1):1-3. <https://doi.org/10.1038/s41392-020-0148-4>
- Tang N, Li D, Wang X, Sun Z (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis*, 18(4):844-847. <https://doi.org/10.1111/jth.14768>
- Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, ... Bouillon R (2001). Intensive insulin therapy in critically ill patients. *New England Journal of Medicine* 345(19):1359-1367. <https://doi.org/10.1056/NEJMoa011300>
- Wan Y, Shang J, Graham R, Baric RS, Li F (2020). Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus. *Journal of Virology* 94(7):e00127-20. <https://doi.org/10.1128/JVI.00127-20>
- Wang D, Hu B, Hu C (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 323(11):1061. <https://doi.org/10.1001/jama.2020.1585>
- Wang S, Ma P, Zhang S, Song S, Wang Z, Ma Y, ... Jin Y (2020). Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study. *Diabetologia* 63(10):2102-2111. <https://doi.org/10.1007/s00125-020-05209-1>
- Wu Z, McGoogan JM (2020). Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 323:1239-1242. <https://doi.org/10.1001/jama.2020.2648>
- Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, ... Chen Q (2020). High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *International Journal of Oral Science* 12(1):1-5. <https://doi.org/10.1038/s41368-020-0074-x>
- Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, ... Shang Y (2020). Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine* 8(5) :475-481. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5)
- Zhang B, Liu S, Zhang L, Dong Y, Zhang S (2020). Admission fasting blood glucose predicts 30-day poor outcome in patients hospitalized for COVID-19 pneumonia. Vol. 22, *Diabetes, Obesity and Metabolism*. Blackwell Publishing Ltd. pp 1955-1957. <https://doi.org/10.1111/dom.14132>
- 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. <https://doi.org/10.1111/all.14238>
- 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. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)



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