Diabetes as Risk Factor for Sick People Hospitalized for Pneumonia during the COVID-19 Period in a Hospital in Abidjan, Ivory Coast

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Abstract: The rate of COVID-19-related mortality among patients with diabetes mellitus (DM) in Ivory Coast is unknown. Diabetes is a risk factor for increased mortality in patients hospitalized for viral pneumonia infection with higher percentage for patients infected by Sars cov-2 virus. This study aims to investigate the association of DM with mortality in this population.
Methods: This is a cohort retrospective study. Electronic medical records from patients admitted from March 2020 to March 2021 were reviewed. Primary outcomes was mortality. Secondary outcomes were health complications and transition to Intensive Care Unit(ICU). These outcomes

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were also studied in a second step after adjustment for covid 19 status, i.e. by including only patients without covid-19 (Covid NEG).

Results: In all 205 patients were part of the study. The overall mortality rate was 21.5% (n =205) with 44 patients. In this group of non-survivor (n =44), 26 (59.1%) patients are diabetics with $P <$ 0.001. That represent 12.7% of global population (n =205) diabetics with $P < 0.001$. Number of Patients admitted to intensive care number was 65 either 31.7% (n =205) with a $P < 0.001$. Among them, 52.3% are diabetic with a $P < 0.001$. The influence of covid-19 on rate of diabetes could not be demonstrated ($P = .44$), however a clear relationship was observed between Diabetes mellitus, age, covid-19 and rate of mortality (**$P =$**1.1895872362833E-5).

For 83 patients without Covid-19, there are only 14 (16.9%) non survivors against 69 (83.1%) survivors with $P = 0.14$. Only 06 persons are diabetics. For second outcome, there are 22 (10.7%) (n =205) patients admitted to intensive care unit with only 08 (3.9%) (n =205) patients diabetics with $P =0.45$.

We note just that we are at the limit of statistical significance in link between diabetes and gender (P = .047).

Conclusions: Diabetes is associated with increased mortality and represent a significant risk factor for health complication and admission to intensive care in ill patients hospitalized for viral pneumonia infection and even higher for patients with COVID-19. However, the presence of sars cov-2 alone is not a factor in increasing the rate of DM. There is no significative link between diabetes and the two outcomes studies for Sick people without covid-19.

The presence of diabetes mellitus in patients treated for Covid-19 therefore has a prognostic value in our environment, and can guide the management of these patients.

1. INTRODUCTION

Regarded as one of the leading causes of hospitalization, morbidity and mortality, pneumonia was the 4th leading cause of death worldwide prior to the COVID-19 pandemic, a disease related to infection with the 2019 novel coronavirus, Sars-Cov-2 [1].

Since 30 January 2020, the World Health Organization (WHO) has designated COVID-19 as a public health emergency. As of 23 September 2021, COVID-19 had infected 229,415,774 people worldwide, resulting in 4,699,359 deaths, with 8,180,555 infections and 206,137 deaths in Africa, corresponding to a fatality rate of 2.5 percent [2].

Throughout the COVID-19 pandemic, several studies have reported a link between diabetic patients with COVID-19 and the duration of hospitalization, admission to the intensive care unit (ICU) [3]. Although it is not known whether people with diabetes are more susceptible to COVID-19, these studies have found a higher risk of severe COVID-19 in patients with diabetes [4,5].

According to WHO estimates in Africa, the prevalence of diabetes is increasing and could reach 47.1 million in adults aged 20 to 79 in 2047 [6]. Interestingly, prior to this pandemic, diabetes was not associated with increased mortality in intensive care patients [7], contrary to what might be expected based on the known complications and risks associated with diabetes in other settings. The risk of developing a serious infection due to SARS cov-2 is higher in diabetics [3].

This vulnerability to infections, including viral infections, is caused by the influence of hyperglycemia on the function of neutrophil polynuclear cells, increased bacterial adhesion, decreased cytokine secretion and bacterial quiescence [8,9].

In general, diabetes is recognized as a chronic disease that predisposes individuals to various health complications, including cardiovascular disease, renal dysfunction, infections, retinopathy, and neuropathy [10]. These complications may contribute to higher morbidity and mortality rates in the general population [11].

Moreover, in people with diabetes with COVID-19, it was also found that many markers, such as C-reactive protein, fibrinogen, and D-dimers, were activated.

Therefore, this condition may worsen COVID-19 cytokine storms and cause more severe disease

[12]. Another mechanism linking diabetes to a more severe outcome in patients with COVID-19 is that diabetic patients are often overweight or obese, which may also contribute to a worse prognosis in case of restrictive lung disease [13].

In Côte d'Ivoire, the prevalence of diabetes among the population aged 20-79 years is 2.1% in 2021 [14]. However, most studies on diabetes have been conducted only in the city of Abidjan [15,9,16]. Very few of these studies have investigated the infectious etiologies of diabetes in other cities in the country [17]. Hence the importance of this work to explore the link between diabetes mellitus and mortality and worsening of the clinical condition of patients hospitalized for viral pneumonia during the COVID-19

2. MATERIALS AND METHODS

2.1 Study Population

This is a retrospective cohort study. The study evaluated all patients aged 17 years and older hospitalized for viral pneumonia from March 2020 to March 2021, during the COVID-19 pandemic. The inclusion criterion was patients hospitalized for viral pneumonia after an evocative chest imaging and/or a positive PCR or antigen test for Sars Cov-2. The exclusion criteria were duration of hospitalization less than 02 days, absence of at least 2 bioavailability reports of interest, absence of COVID-19 status, absence of clinical data. On this basis, a total of 205 patients were included in the study. Clinical and laboratory data were recorded for all patients. The chi two test and survival test of Kaplan Meier was used to assess the mortality rate [18].

2.1.1 The collection of data

Clinical laboratory data were recorded for all patients with only anonymous folders numbers. The Chi 2 test and survival test of Kaplan Meier were used to assess the mortality rate [18]. The data were collected from the examination of electronic medical records, using a pre-established excel file of the survey, containing the study variables: epidemiological data (age, sex, origins), clinical and evolutionary data (history and comorbidities, reason for hospitalization, covid-19 status, diabetic status, change in health status, whether or not to enter intensive care, duration of hospitalization, mode of discharge). Diabetes was defined based on

previous diagnosis, Hyperglycaemia was defined according to the standards of the biology laboratory of the polyclinic as any blood glucose measurement > 1.26 g/L. Patients without a history of diabetes, with HbA1c < 6.5% and blood glucose ≤ 1.10 g/ L were assigned to the normal glucose group. Those with no history of diabetes, HbA1c < 6.5% and blood glucose > 1.26 g/L were classified as stress-induced hyperglycaemia [19]. Hypoglycaemia has been defined as any glycaemic level < 0.70g/ L (N.-S. This is the most common type of diabetes.

2.2 Statistical Analyses

The statistical analysis included the use of the chi-2 test and survival test of Kaplan Meier. The Kaplan-Meier method was also used to perform time to event analyses and outcomes of interest. The size of the delay-to-event effect (hazard P-value) and outcome mortality and variables adjusted for age, presence of diabete and disease severity were estimated by using the survival test and logrank test of Kaplan Meier.

A sample of 205 patients was calculated for this study. Descriptive and statistical analysis of the data was performed using SPSS software version 26 and XLSAT software version 2015. Quantitative variables were expressed as averages with standard deviations and extreme values and qualitative variables were expressed as ratios. The statistical comparisons were based on the khi two test and the Fischer test with a significance threshold of $P \leq 0.05$.

3. RESULTS

A total of 205 patients hospitalized mainly for viral pneumonitis were included in this study. In Table 1, the mean age was 53 ± 15 years with a standard deviation of 15.724 and an age range of 17 to 94 years.

Table 2 shows their main characteristics. There were a total of 44 deaths, representing 21.5% of our study population. We also note that 122 patients (59.5%) (n = 205) had Covid-19. There were 150 men (73.2%) compared with 55 women (26.8%) (n = 205). 68 people (33.2%), including 47 men and 21 women, were diabetics, including 45 people (66.1%) who experienced a worsening of their state of health during hospitalization (n =68). Apart from cough, which was the main visible symptom in our study population of 83 patients (40.5%), 59 patients (28.8%) (n = 205) had a fever on arrival at hospital.

**Table 1. Characteristics linked to the age variable**

Statistics		
AGE		
N	Valid	205
	Missing values	0
Average		53,11
Median		55,00
Standard deviation		15,724
Minimum		17
Maximum		94

Other associated clinical features included dyspnea in 51 patients (25%) and respiratory distress in 24 patients (11.7%) (n = 205).

Table 2 also shows the demographic, clinical and biological characteristics specific to diabetes.

The diabetic status of patients and the coexisting pathologies in each patient were determined on the basis of previous diagnoses, clinical information or observations made on the patient's arrival at hospital.

In this study, 42 patients or 20.5% (n=205) had no other comorbidity apart from diabetes. Among the remaining patients, the most common coexisting pathology (comorbidity) was arterial hypertension (hypertension) in 43 patients, i.e. 21% (n=205) ($P < 0.001$), distributed almost evenly between 21 diabetics and 22 non-diabetics. Apart from high blood pressure (HBP), other co-morbidities such as obesity and chronic renal failure (CRF) were found in very few diabetics (06 and 02 patients respectively).
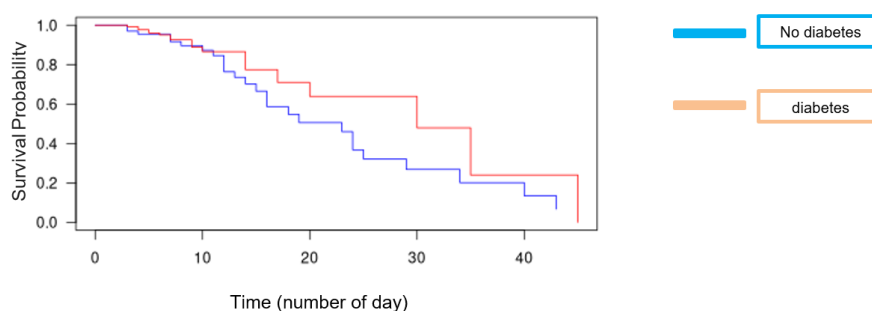
Fig. 1. Probability of survival after adjustment for length of hospital stay only
Log-rank test
- *Test statistic (χ^2): 1.9808002544105*
- *P-value: 0.15930612702109*
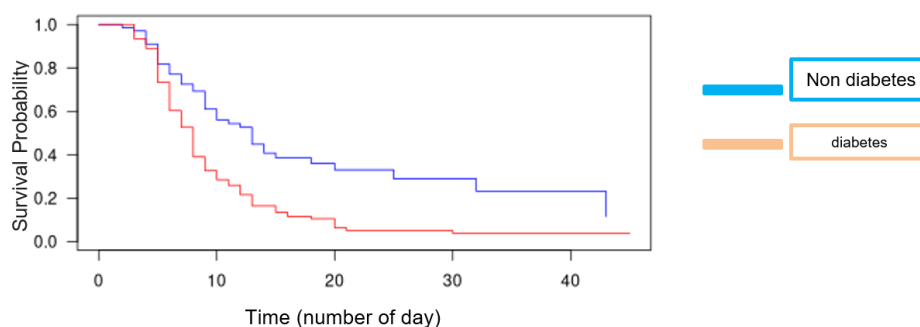
Fig. 2. Probability of survival according to the presence or absence of diabetes mellitus after adjustment for age
- *Test statistic (χ^2): 19.179911099634*
- *P-value: 1.1895872362833E-5*

Table 2. Comparison of demographic variables between diabetic and non-diabetic groups

Comorbidity parameters		diabetes	n-diabetes	Total	Percentage (%)	*P*
	bacterial co-infection	5	5	10	4.8	
Secondary reason for	Respiratory distress	11	13	24	11.7	
hospitalization	shortness of breath	30	22	52	25	
(coexisting symptoms	No secondary reason	13	7	20	9.7	**.69**
At the time of hospitalization)	infectious syndrome	7	10	17	8.3	
	cough + chest pain	25	16	41	20	
	cough + fever + dyspnea + chest pain	23	19	42	20.5	
Total		68	137	205	100	
	Asthma	0	1	1	0,5	
	liver damage	0	2	2	1,0	
	cancer	0	1	1	0,5	
Other antecedents (co-morbidities)	heart disease	0	1	1	0,5	
	heart disease + hypertension	1	2	3	1,5	
	diabetes only	42	0	42	20,5	
	HIGH BLOOD PRESSURE	17	15	32	15,6	**< 0.001**
	HIGH BLOOD PRESSURE + CKD	1	1	2	1,0	
	High blood pressure + obesity	1	4	5	2,4	
	High blood pressure + overweight	1	0	1	0,5	
	immunosuppressed	0	1	1	0,5	
	CRF	1	0	1	0,5	
	obesity	3	3	6	2,9	
	No known history	1	105	106	51,7	
	smoking	0	1	1	0,5	
Total		68	137	205	100	
Demographic characteristics		**diabetes**	**n-diabetes**	**Total**	**Percentage (%)**	*P*
	<50	18 (26.5%)	61	79	38.5	
Age	>50	50 (73.5%)	76	126	61.5	
Total		68	137	205		**.01**
	F	21 (29.9%)	34	55	26,8	
Gender	M	47 (69.1%)	103	150	73,2	**.36**
Total		68	137	205	100	
Disease severity parameters		**diabetes**	**n-diabetes**	**Total**	**Percentage%**	*P*

Whether or not the patient's clinical condition worsened during hospitalization	Complications	45	45	90	43.9	**< 0.001**
	uncomplicated	23	92	115	56.1	
	No	34 (50%)	106	140	**68.3**	**< 0.001**
Transfer to intensive care	Yes	34 (50%)	31	65	31.7	
Total		68	137	205	100	
Patient discharge method (Issue)	Non survivor	26(12.7%)	18(8.7%)	44	21,5	**< 0.001**
	Survivor	42	119	161	78,5	
Total		68	137	205		100,0
Positive or negative covid-19 or antigenic PCR test on admission to hospital	COVID NEG	25 (36.8)	58	83	40,5	**.44**
	COVID POS	43 (63.2%)	79	122	59,5	
Total		68	137	205	100	100,0
Positive or negative covid-19 or antigenic PCR test on admission to hospital	COVID NEG	25 (36.8)	58	83	40,5	**.44**
	COVID POS	43 (63.2%)	79	122	59,5	
Total		68	137	205	100	100,0

Table 3. Relationship between diabetes mellitus with gender in no- covid sick people

		Diabetes	n-diabetes	Total	Percentage (%) (n=205)	P
Gender	F	11	13	24	11.7	.047
	M	14	45	59	28.8	
Total		25	58	83	40.5	

Table 4. Relationship between diabetes and worsening health of patients without covid-19 (no-covid)

		Diabetes	n-diabetes	Total	Percentage (%) (n = 205)	P
Whether or not the patient's clinical condition worsened during hospitalization	Complications	11	16	27	13.2	.14
	uncomplicated	14	42	56	27.3	
Total		25	58	83	40.5	

Table 5. Relationship between diabetes and issue of patients without COVID-19

		Diabetes	n-diabetes	Total	Percentage (%) (n =205)	P
Discharge method (Issue)	Non survivor	6	8	14	6.9	.25
	Survivor	19	50	69	33.6	
Total		25	58	83	40.5	

Table 6. Relationship between diabetes and transfer to intensive care unit of patients without Covid-19

		Diabetes	n-diabetes	Total	Percentage(%) (n =205)	P
Transfer to intensive care	No	17	44	61	29.8	.45
	Yes	8	14	22	10.7	
Total		25	58	83	40.5	

There was also a greater distribution of diabetes among the elderly, where 50 sick people (73.5%) were over 50 years old, compared with the young (<50 years old), where only 18 sick people (26.5%) had diabetes (P = .01). The same predominance of diabetes can be seen in men, with 47 sick people (69.1%) compared with 29.9% of women (21 people), with a P = .36. In the context of the covid-19 pandemic, all patients admitted with pneumonia were tested for Sars-Cov-2. Of the 68 diabetics, 43 were positive for Sars-Cov-2, i.e. 63.2%, compared with 36.8% who were negative. However, the number of people infected with Sars cov-2 was higher among non-diabetics, at 79 (P = .44).

Table 2 shows that 34 diabetics were admitted to an intensive care unit (ICU), i.e. 50% of all diabetics (n = 68) and 16.6% of the total population (n = 205) with a P < 0.001. Of these, 26 died, i.e. 38.2% (n =68) compared with only 18 in the non-diabetic population (P < 0.001).

Unlike Fig. 1, which shows that mortality in our study is not influenced by length of hospitalization, Fig. 2 shows the probability of survival according to the presence or absence of diabetes mellitus after adjustment for age. It shows a close link between age, diabetes status and mortality rate. This is in agreement with the observation made in Table 2, where when patients were separated into diabetic and non-diabetic groups, the mortality rate was 12.7% and 8.7% respectively, with a significant difference in mortality between diabetic and non-diabetic patients (P < 0.001).

3.1 Specifics Characteristics for Sick People Non Infected by Sars cov-2 (Non covid)

We observed in Table 3 that there is 24 females (11.7%) (n =205) against 59 (28.8%) (n =205) males.

The rate of patients diabetics is 30.2% either 25 patients (n = 83) (11 females and 14 males) with $P = .047$ not very significant.

In Table 4, Table 5 and Table 6, we noted an absence of link between diabetes and worsening health ($P = .14$), between diabetes and issues of patients ($P = .25$) and also between diabetes and transfer to intensive care unit $P = .45$.

4. DISCUSSION

In this retrospective cohort study of 205 patients hospitalized for viral pneumonia during the COVID-19 period, diabetes mellitus was associated with a worsening of the patients' state of health, their admission to intensive care and, above all, increased mortality. There was also a close link between diabetes and patient age, as well as comorbidities such as hypertension and obesity. On the other hand, the presence of diabetes in patients is not associated with gender, nor with the covid-19 status of patients, and even less with apparent clinical symptoms (cough, fever, etc.).

In our sample, the prevalence of diabetes mellitus was 33.2% (n=205), almost identical to that of the general population of seriously ill patients [20] and the prevalence of hypertension was 21% (n=205).

We also know that during the Covid-19 pandemic, which is the subject of this study, people with chronic diseases, in particular diabetes mellitus and hypertension, were disproportionately affected, with an increased risk of hospitalization and mortality [21,22].

This is in line with the results of our study, which showed that 65 patients, or 31.7% (n = 205), including 34 diabetics, or 52.3% (n = 65), were admitted to intensive care. With a highly significant $P < 0.001$. This high prevalence confirms that diabetes mellitus and hypertension are risk factors for admission to intensive care during COVID-19 [23],

Similarly, the overall mortality rate in our study of 21.5% (n =205) was significantly higher in patients with diabetes with a $P < 0.001$, as expected. However, more importantly, mortality was higher in patients with diabetes mellitus than in those without, with rates of 12.7% and 8.7% respectively with $P < 0.001$, highly significant.

These data are consistent with a systematic review of 18 studies that reported an elevated risk of severe COVID-19 in patients with diabetes mellitus compared to those without diabetes mellitus [24]. Even after adjusting for age, there is a strong association between diabetes and mortality. This is highlighted in our study by Figs. 1 and 2 using a survival test and a logrank test using the kaplan Meier method with SPSS VERSION 26 software.

In fact, initially, the association of all the patients in our study with their length of hospitalisation showed no significant link with the mortality rate $P = .16$. However, after adjustment for diabetic status and patient age, there was a very strong association with mortality rate with a $P = 1.18958723628 33E\text{-}5$.

In addition, a meta-analysis of 33 studies by Kumar et al. demonstrated that patients with diabetes mellitus faced an increased likelihood of developing a severe form of COVID-19 or death (2.49 [95% CI: 1.98-3.14], $P < 0.01$) [25].

As the results of our study show, 90 people (43.9%) (n = 205) experienced a worsening of their condition. Of these, half (45) were diabetics, with a highly significant $P < 0.001$. Diabetes mellitus is associated with an increased risk of developing complications during severe illness [26], but the presence of diabetes mellitus was not independently associated with an increased risk of death in critically ill patients prior to the COVID-19 pandemic [27]. The "diabetes paradox" [27] suggests that chronic hyperglycaemia prior to acute insult may be associated with favourable outcomes in critical illness [28,29]. Cellular adaptations to chronic hyperglycaemia in diabetes mellitus are thought to "prepare" the cellular antioxidant apparatus to cope with subsequent hyperglycaemia during acute illness [30]. Acute hyperglycaemia would therefore be more deleterious in seriously ill patients without diabetes mellitus, who have no prior cellular conditioning against glucose toxicity.

Also, as described in Table 2, 126 patients or 61.5% (n=205) were over 50 years of age. And 50 people or 73.5% (n=68) of diabetics were over 50, with a significant $P = .01$. The age of patients in this study clearly constitutes a risk of increased prevalence of diabetes mellitus and hence an increased risk of mortality.

This vulnerability in the elderly is often explained by immunosenescence, which is accompanied by a reduction in the production of native T and B cells and a decline in the function of immune cells involved in innate immunity [31,32]. These changes reduce effective viral clearance and increase the likelihood of triggering a dysregulated immune response in which cytokines are largely released by activated immune cells, resulting in a cytokine storm [31,32].

The results of our study provide new insights into the concept of the "diabetes paradox". Traditionally, diabetes mellitus has not been associated with increased mortality rates in critically ill patients. However, our results show that in the context of COVID-19, diabetes mellitus appears to be a significant risk factor not only for mortality but also for worsening the state of health of patients hospitalized with pneumonia. This observation introduces a new hypothesis-generating concept, suggesting that the impact of diabetes mellitus on mortality may vary in different populations of critically ill patients.

5. CONCLUSION

This study has its limitations. Firstly, because of its retrospective nature, some information may have been overlooked, while other information, notably the diabetic status of patients, is collected largely on the basis of information provided by the patient or his or her parents, or on the basis of the history available in the electronic medical record at the time of admission.

However, the results of interest were decided by several researchers and the medical management of the polyclinic. Secondly, the measurement of glycated haemoglobin (HbA1c) was not carried out until later, after high blood sugar levels had been observed from the very first moments of hospitalisation.

In summary, this retrospective cohort study showed that diabetes mellitus was associated with higher rates of mortality, worsening of health status and even admission (transfer) to intensive care than patients without diabetes. The study also showed that older people with diabetes were more likely to die than younger people, but that gender (male or female) had no influence on mortality rates. Although the presence of covid-19 does not increase the risk of becoming diabetic, it does significantly increase the risk of deterioration in health and mortality in diabetics.

However, diabetics patients hospitalized for pneumonia and not infected by Sars cov-2 virus (Covid-19 Negative) are not associated significantly with mortality, worsening health and tranfer to intensive care.

Further studies should also look at the biological parameters disturbed during Covid19, because their assessment upon admission of patients is essential for better management of patients.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

ETHICAL APPROVAL AND CONSENT

The study was approved by the ethics committee and the medical management of the Farah Polyclinic in Côte d'Ivoire and adhered to the Helsinki Declaration. Confidentiality in the disclosure of individual results was respected. The anonymity of the study subjects was guaranteed and data linked to the identities of the subjects were not published under any circumstances. Administrative authorizations to access the clinical and biological data of patients at the Farah Policlinic of Abidjan were granted by the Medical Directorate of this hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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