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SARS-CoV-2 infection associated with hemopathies: An experience of a clinical hematology center in sub-Saharan Africa, Senegal

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Abstract:

INTRODUCTION: Many studies have reported the association of SARS-CoV-2 with benign and malignant hemopathies. Data from African series are scarce. This work was conducted in sub-Saharan Africa and aimed to study the clinical, biological, and evolutionary features of hemopathies associated with this infection.

MATERIALS AND METHODS: It was a retrospective, cross-sectional study carried out over 32 months including 86 patients with benign or malignant hemopathies who underwent coronavirus disease-2019 (COVID-19) confirmed by the real-time reverse transcriptase-polymerase chain reaction or presenting with atypical clinical signs associated with highly suggestive computed tomography (CT) scan signs.

RESULTS: The mean age of patients was 48.3 ± 18.7 years with a sex ratio of 0.75. The main benign hemopathies were sickle cell trait (SCT) (n = 51), sickle cell disease SS (n = 8), and sickle cell disease SC (n = 1), while malignant hemopathies were represented by multiple myeloma (n = 5), non-Hodgkin lymphoma (n = 5), and chronic lymphocytic leukemia (n = 4). The clinical symptoms mainly featured anemic syndrome (16.3%) and a vaso-occlusive crisis was found in 9.3% of homozygous sickle-cell patients. The infection was moderate in 48% of cases and severe in 19.7%. The severe forms were commonly found in patients with malignant hemopathies (47.6%) and the benign forms were noted in benign hemopathies (38.4%). Full blood count outlined anemia in 32.5% and lymphopenia in 23.2% of cases. On imaging, the CT scan reported severe lesions in 41.3% of cases. The outcome resulted in full recovery in 76.7% of cases, and mortality occurred in 23.3%. In univariate analysis, death was mainly noted in patients with lymphoid hemopathies (15%). Comorbidities (P < 0.0001), lymphoid hemopathies (P < 0.0001), and the severity of COVID-19 (P < 0.0001) had a positive impact on death occurrence in univariate analysis.

CONCLUSION: The association between SARS-CoV-2 and hemopathy is not uncommon and is dominated by benign hemopathies. Malignant hemopathies are at-risk underlying conditions justifying a hospital follow-up of mild forms, allowing better survival. Particular attention must be paid to SCT with comorbidities and those with sickle cell disease of disease.

Keywords:

Benign hemopathy, malignant hemopathy, SARS-CoV-2, Senegal

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Introduction

Coronavirus disease-2019 (COVID-19) is a viral infection due to SARS-CoV-2 belonging to the *Coronaviridae* family. It is a likely life-threatening disease of hefty global public health concern. Since December 2019, many countries in the world have been affected by the COVID-19 pandemic with around 5.5 million related deaths.[1] Regarding management strategies for patients with COVID-19, epidemic points-of-care was set in hospital facilities for systematic hospitalization of symptomatic. Therefore, algorithms were used for clinical forms classification and therapeutic indications. Data from the literature report a high mortality risk from COVID-19 in patients undergoing a significantly high mortality rate.[2]

Epidemiological data from the first wave outlined that the mortality rate in patients with malignant hemopathies ranged from 13.8% to 37% compared to 0.5% to 2% in the general population.[3] Compared to the general population, besides the comorbidities and thromboembolic complications, this risk is related to their immunocompromised status, which can be secondary to malignancy, immune deficiency, chemotherapy, and age. The clinical course is also worsened by comorbidities.[4] Other studies conducted on patients with hemoglobinopathies reported an increased risk for hospital admission and death related to COVID-19 in sickle cell patients and also suggest that such risk might be increased, even in those with sickle cell trait (SCT).[5] This association, commonly reported in Western studies, is not well documented in sub-Saharan Africa. It is against this backdrop that we take stock of SARS-CoV-2 infection in our patients followed for hemopathy. This work aimed to study the clinical, biological, and evolutionary features of SARS-CoV-2 infection among patients with an underlying hemopathy condition.

Materials and Methods

Study design and inclusion criteria

We conducted this retrospective, cross-sectional, and analytical study in the largest epidemic point-of-care in Senegal and clinical hematology service of reference for the management of benign and malignant hemopathies, located in Dalal Jamm Teaching Hospital Center (Senegal). We recruited all patients, adults who underwent SARS-CoV-2 infection on the basis of real-time reverse transcriptase-polymerase chain reaction or typical computed tomography (CT) scan signs,[6] and associated with a benign or malignant hemopathy defined by the WHO and followed in the Clinical Hematology Department of the Aforementioned Hospital. The study was approved by review ethical committee of Dalal Jamm Teaching Hospital, and being dealing with file records of patients as retrospective study design, so no consent needed to be obtained.

Disease severity

COVID-19 infection could be symptomatic or not and was classified into critical, severe, moderate, and minimal forms. Severe COVID-19 was defined by the constellation of dyspnea, blood oxygen saturation ≤93%, PaO_2/FiO_2 <300, and progression of lung infiltrates >50% within 24–48 h. Critical COVID-19 was defined by the presence of respiratory failure, septic shock, and/or multiple organ dysfunction.[7]

Statistical analysis

Data were entered and processed by the SPSS software version 24.0. Qualitative data are considered by frequencies and quantitative data by mean and standard deviation. We used Fischer's extract test for statistical analysis and a $P < 0.05$ was considered statistically significant.

Results

During the study period ranging from 2020 to 2022 (32 months), 86 cases were collected, 37 men, and 49 women with a sex ratio of 0.75. The mean age was 48.3 ± 18.7 years old. Hemoglobinopathies including SCT (59%), SS form (9.3%), and SC form (1.2%) mainly constituted benign hemopathies [Table 1]. Other benign hemopathies include bone marrow aplasia (2.3%), Biermer's disease (2.3%), and immune thrombocytopenic purpura (ITP) (1.2%). Malignant hemopathies were mostly represented by multiple myeloma (5.8%), non-Hodgkin's lymphoma (5.8%), chronic lymphocytic

Table 1: Distribution of hemopathies in patients followed up for COVID and hemopathies at Dalal Jamm Hospital from 2020 to 2022

Types of hemopathy	Workforce, *n* (%)
Benign hemopathies	
Sickle cell trait	51 (59)
Sickle cell disease SS	8 (9.3)
Biermer	2 (2.3)
Sickle cell disease SC	1 (1.2)
ITP	1 (1.2)
Bone marrow aplasia	2 (2.3)
Malignant hemopathies	
Multiple myeloma	5 (5.8)
CLL	4 (4.7)
NHL	5 (5.8)
CML	2 (2.3)
HL	3 (3.5)
MDS	1 (1.2)
AML	1 (1.2)

ITP=Immunologic thrombocytopenia, CLL=Chronic lymphocytic leukemia, HL=Hodgkin lymphoma, NHL=Non-HL, CML=Chronic myeloide leukemia, MDS=Myelodysplastic syndrome

leukemia (CLL) (4.7%), Hodgkin's lymphoma (2.3%), and chronic myeloid leukemia in 2.3%. Acute myeloblastic leukemia and myelodysplastic syndrome were noted in one patient for each.

Comorbidities were represented by hypertension (8 patients), hypertensive cardiomyopathy (1 patient), and diabetes (2 patients). Symptoms on admission were variable [Table 2] and the most prominent features were headache (65%), rhinitis (11.6%), and cough (59%). Clinical signs were dominated, respectively, by the anemic syndrome in 16.3% of cases and the vaso-occlusive pain crises in 9.3% of cases in sickle cell patients [Table 2]. The distribution of the severity according to the type of hemopathy showed that the severe form was mainly found in subjects with malignant hemopathies (47.6%) whereas the benign form was predominant in patients with benign hemopathy (38.4%) [Table 3]. Regarding full blood count, anemia was found in 32.5% of cases, lymphopenia in 23.2%, neutrophilia in 20.9%, and thrombocytopenia in 12.8% of cases. The hemostasis assessment revealed biologically disseminated intravascular coagulation in 9.3% of cases. The nonspecific biological inflammatory syndrome was observed in 40.6% of cases with a mean C-reactive protein of 84.5 ± 78.7 mg/L and acute renal failure in 2.3% of cases [Table 4]. On imaging, chest CT scans were performed in 33.7% of patients which revealed ground-glass images with peripheral predominance suggestive of SARS-CoV-2 infection. The lesions were severe in 41.3% of cases, moderate in 34.4%, extensive in 20.6%, and critical in 3.4%. Regarding the outcome, recovery was noted in 76.7% of cases with functional signs regression within an average time limit of 6 days. The mortality rate was 23%. In univariate analysis [Table 5], the clinical severity of COVID-19, the correlation between comorbidities and the type of hemopathy with death occurrence was statistically significant ($P < 0.0001$). Death due to acute respiratory distress in 38.1%, hydrolytic disorders in 9.5%, clinical disseminated intravascular coagulation (DIC) complicated by a stroke in 4.76%, and hepatocellular failure in 4.76%. In nine patients (42.8%), the cause of death is not found.

Table 2: Frequency of symptoms on admission among patients followed for COVID and hematological diseases at Dalal Jamm Hospital from 2020 to 2022

Parameters	Workforce, *n* (%)
Headache	56 (65)
Cough	51 (59)
Fever	36 (41)
Rhinitis	10 (11.6)
Chest pain	12 (14)
Dysphagia	5 (5.8)
Anosmia/agueusia	15 (17.4)
Dyspnea	9 (10.5)
Anemic syndrome	14 (16.3)
Adénopathy	5 (5.8)
Splenomegaly	5 (5.8)
Hepatomegaly	4 (4.7)
Pain vaso-occlusive crises	8 (9.3)

Table 3: Severity according to etiology

	Workforce, *n* (%)
Benign hemopathies	
Benign	25 (38.4)
Moderate	34 (12.3)
Severe	6 (9.2)
Critique	0
Malignant hemopathies	
Benign	2 (9.5)
Moderate	8 (38.1)
Severe	10 (47.6)
Critique	1 (4.8)

Table 4: Distribution by biological anomalies

Parameters	Workforce, *n* (%)
Anemia	28 (32.5)
Thrombopenia	11 (12.8)
Lymphopenia	20 (23.2)
Neutrophilia	18 (20.9)
Hepatic cytolysis	3 (3.5)
Nonspecific biological inflammatory	35 (40.6)
D-dimer ≥500 mg/mL	16 (18.6)
Acute renal failure	2 (2.3)

Discussion

To our knowledge, our series is the first large-scale population-based study in Africa of COVID-19 patients with hemopathies, of which 65 patients underwent benign hemopathy. A series was reported in France on hemoglobinopathies at the pandemic onset.[8] In our study, benign hemopathies were mostly represented by the SCT. This finding is related to the high prevalence of this form in Senegal[9] on the one hand and to the benign feature of this condition on the other hand; SCT carriers generally remain asymptomatic.[5] Mortality in this patient group was low (5.9%) compared to the report of Clift *et al*.[5] where mortality was higher (19%) with an increased risk of hospital admission related to COVID-19. The results on the impact of SCT during COVID-19 are inconsistent.

Clift AK *et al*.[5] reported a 1.38-fold increased risk of hospitalization related to COVID-19 and a 1.51-fold increased risk of death related to COVID-19 in patients with SCT compared to the general population[10] while other studies did not find a significant difference between those with SCT and those without SCT.[11,12] In all cases, the presence of underlying comorbidities such as

Table 5: Univariate analysis of the evolution of patients followed for COVID and hemopathies at the Dalal Jamm Hospital from 2020 to 2022

Types	Healing, *n* (%)	Deaths, *n* (%)
Sickle cell trait (*N*=51)	48 (94.1)	3 (5.9)
Sickle cell disease (N=8)	7 (87.5)	1 (12.5)
Bone marrow aplasia (*N*=2)	1 (50)	1 (50)
Biermer disease (*N*=2)	1 (50)	1 (50)
ITP (*N*=1)	1 (100)	0
Sickle cell disease SC (*N*=1)	1 (100)	0
MM (*N*=5)	1 (20)	4 (80)
CLL (*N*=4)	1 (25)	3 (75)
NHL (*N*=5)	1 (25)	4 (75)
LH (*N*=3)	1 (33.3)	3 (66.7)
CML (*N*=2)	1 (50)	1 (50)
MDS (*N*=1)	1 (100)	0
AML (*N*=1)	1 (100)	0

N=Total population, *n*=Population concerned, ITP=Immunologic thrombocytopenia, CLL=Chronic lymphocytic leukemia, HL=Hodgkin lymphoma, NHL=Non-HL, CML=Chronic myeloide leukemia, MDS=Myelodysplastic syndrome, MM=Myeloma multiple

chronic kidney disease or those on whom kidney injury occurred during the course of their COVID-19 disease may influence the COVID-19 results for people with SCT. Unlike the SCT, SS sickle cell is a condition with a risk of bacterial superinfection due to the functional asplenia induced by the disease.

Even though acute situations are life-threatening in SS sickle cell disease, only one death was reported in our cohort. Besides the low prevalence of this form in our series, this could be explained by its occurrence in adults. In our series, the SC form represented 1.2% of cases, and death was not observed. As per Arlet *et al*.[7] in France, this form was independently associated with an increased risk of needing mechanical ventilation or dying and with a higher thromboembolic risk. The worsening of ITP was not observed in our series as only benign clinical forms were noted. SARS-CoV-2 infection was unlikely causes thrombocytopenia aggravation and/or relapse. Most of the studies reported in the literature focus on the association between SARS-CoV-2 and malignant hemopathies and outline a high clinical severity and mortality.[3,13,14] In our study, among all malignant hemopathies, we reported a mortality rate of 61.9%. Regarding these malignant hemopathies, patients with lymphoid hemopathies were more affected than other subtypes. This corroborates with the data reported in other published series.[3]

The high frequency of lymphoid hemopathies could be a consequence of adaptive immune failure in these cancers.[15] The outcome of patients with lymphoma (Hodgkin's and non-Hodgkin's) was poor with a mortality rate of 23.8%. As for Lamure S *et al*.,[15] this rate represented 34% of patients with lymphoma and COVID-19. CLL is a disease of the elderly characterized by immune deficiency. Therefore, patients with CLL could be considered more susceptible to develop severe complications of COVID-19 with high mortality. In our cohort, the population size was small, but mortality was high (75%). The mortality rate was 32.5% (55/169) and 33% in the studies reported by Scarfò *et al*.[16] and the Mato *et al*.,[17] respectively. The outcome of patients undergoing multiple myeloma complicated by SARS-CoV-2 infection remains poor in most cases with a mortality rate of 34% in 185 patients in France[18] and 24% in 58 patients in the USA.[19] In our cohort, it represented 80% of patients with multiple myeloma. We identified in our patients death-related risk factors. Besides the severity of the clinical course on admission, we noted advanced age and high-risk disease (Salmon Diurie stage III). Therefore, malignant hemopathies are an underlying risk factor condition for developing a severe form of COVID-19 and high mortality. The presence of comorbidity increases this risk.

Conclusion

Our study is consistent with other studies and showed that patients undergoing hemopathies have an increased risk of severe COVID-19 with high mortality, especially those with lymphoid hemopathies. SCT carriers with comorbidity as well as a major form may experience an increased risk of morbidity and mortality.

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Conflicts of interest
There are no conflicts of interest.

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