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Research Article

Electrolytic Disorders in Senegalese SARS-CoV-2 Infected Subjects

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Abstract

Background and Objective: The binding of SARS-CoV-2 to ACE2 inhibits the action of the latter on the RAAS (Renin Angiotensin Aldosterone System), which could increase blood pressure and disturbances in the hydroelectrolyte balance. The objective of this study was to determine the electrolyte profile of patients with COVID-19. **Materials and Methods:** Within that framework, a 3-month retrospective analytical study of patients infected with SARS-CoV-2 was conducted, admitted at Dalal Jamm Hospital and Aristide Le Dantec Hospital. Data were collected from the laboratory records of the said hospitals and included age, sex, clinical information (symptoms, underlying diseases and clinical forms) and blood ionogram results (natraemia and kalaemia). Statistical analysis was performed using SPSS software. **Results:** About 745 patients were recruited. The mean age of the study population was 54.22 ± 18.53 with a sex ratio of 1.15. Ten percent of the population had a severe form. Hypertension was the most frequent comorbidity (14.53%) followed by diabetes (11.73%). The most frequent electrolyte disorders were hyponatremia (13.02%) and hyperkalemia (6.97%). They were more frequent in men, elderly subjects, those with a severe form of the disease and those with comorbidities. **Conclusion:** This data suggested a disturbance of the hydro electrolytic homeostasis in subjects infected by SARS-CoV-2. It appears to be associated with age, gender, disease severity and the presence of comorbidity.

Key words: COVID-19, SARS-CoV-2, electrolyte disorders, comorbidity, blood ionogram, homeostasis, hyperkalemia

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

COVID-19 is an emerging infectious disease caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2). It officially appeared in December 2019 in China in the city of Wuhan and started spreading rapidly plunging the whole world into a health and economic crisis. Thus, WHO¹ qualified it as a health emergency of international concern on January 30, 2020 and then as a pandemic on March 11, 2020.

More than a specific respiratory disease attacking the lungs, COVID-19 is a pathology that is also capable of attacking the heart, kidneys, digestive and nervous systems.

To infect its host, the SARS-CoV-2 virus binds to the ACE2 (Angiotensin-Converting Enzyme 2) receptor, which plays an important role in the Renin-Angiotensin-Aldosterone System (RAAS), a system involved in the maintenance of fluid and electrolyte balance and the regulation of blood pressure. The binding of SARS-CoV-2 to ACE2 inhibits the action of ACE1 on the RAAS, which could increase blood pressure and disturbances in the hydroelectrolyte balance². In addition, patients with COVID-19 often suffer from gastrointestinal symptoms, such as diarrhea and vomiting³.

These signs suggested the possibility of disturbing electrolyte homeostasis in patients infected with SARS-CoV-2. These electrolyte disorders can worsen the prognosis of patients. Studies conducted from the start of the pandemic have revealed disturbances in water and electrolyte homeostasis in patients on admission to treatment centers and which were accentuated in severe forms⁴. In our context, a blood ionogram is frequently requested in patients infected with SARS-CoV-2, however, the nature of the disorders was not documented. Thus in this work a set out to study the electrolyte profile of patients with COVID-19 was studied.

MATERIALS AND METHODS

Study area: A three-month retrospective analytical study (from May 01 to July 31, 2020) on patients with COVID-19 admitted at Dalal Jamm Hospital (Guediawaye, Senegal) and Aristide Le Dantec Hospitals (Dakar, Senegal) was conducted.

Patients: Of the 753 patients hospitalized for COVID-19, 745 were finally selected based on the following criteria: Being tested positive for SARS-CoV-2 on RT-PCR, being hospitalized at the hospitals of Dalal Jamm or Aristide Le Dantec and having a result ionogram available.

Suspected cases with negative PCR and patients who did not have a blood ionogram during their hospitalization were excluded from the study.

Data collection: Current data were collected from the register of laboratories and related to socio-demographic data (age, sex) but also their medical information (clinical signs, underlying diseases, clinical forms and PCR test results) and ionogram results (serum sodium and serum potassium). Mainly hyponatremia, hypernatremia, hypokalemia and hyperkalemia were focused.

Methodology: All patients were classified into mild, moderate and severe groups according to their symptoms: Mild (fever), moderate (fever and respiratory symptoms) and severe (respiratory distress, intensive care unit is needed).

Electrolytes were measured by potentiometric method on the Architect Ci4000 (Abbot, Germany). Data were entered into Excel 2019 (Microsoft, USA) and processed by SPSS version 24 software (IBM, Chicago, IL, USA).

Statistical analysis: The results of quantitative variables were presented as mean \pm standard deviation, minimum and maximum. Those qualitative variables were expressed as frequency and percentage. A Student's t-test was used to compare variables and a type I error equal to 0.05 was considered as the statistical significance threshold.

RESULTS

The mean age of the current study population was 54.22 ± 18.53 (Table 1) with extremes of 02 and 94 years. The majority was older than 60 years (46%) with a sex ratio M/F of 1.15. Ten percent of the population presented a severe form. High blood pressure was the most frequent comorbidity (14.53%) followed by diabetes (11.73%) (Table 1). The most frequent electrolyte disorders were hyponatremia (13.02) and hyperkalemia (5.75). Hyponatremia was more frequent in men

Table 1: Characteristics of the study population

Characteristics	Value
Age (mean \pm SD)	54.22 \pm 18.53
<30 n (%)	87 (11.92)
30-60 n (%)	315 (43.16)
\geq 60 n (%)	343 (46)
Gender	
Female n (%)	345 (46)
Male n (%)	400 (54)
Clinical form	
Mild n (%)	607 (85.01)
Moderate n (%)	34 (4.76)
Severe n (%)	73 (10.22)
Comorbidities	
Hypertension n (%)	78 (14.53)
Diabetes n (%)	63 (11.73)
Hypertension+diabetes n (%)	47 (8.75)
Other n (%)	91 (16.95)

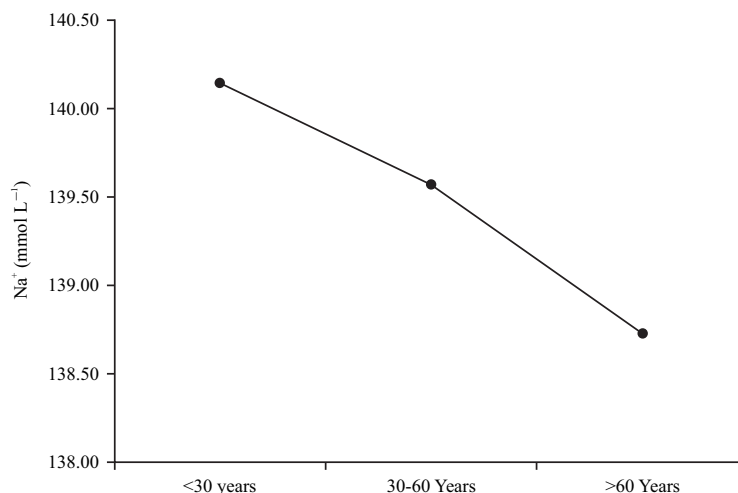


Fig. 1: Variation of sodium according to age

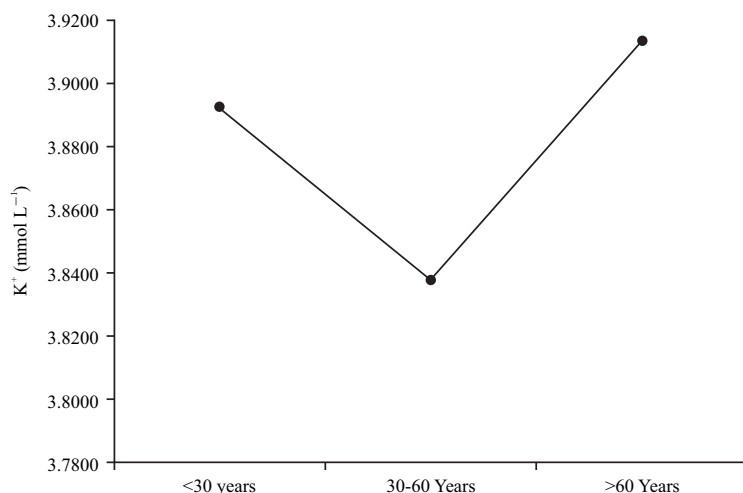


Fig. 2: Variation of potassium according to age

Table 2: Electrolyte profile according to sex

Electrolyte (mEq/L)	Female	Male	Total	P
< 135	30 (8.69%)	67 (16.75%)	97 (13.02)	0.005
135-145	288 (83.47%)	305 (76.25%)	593 (79.59)	
≥145	27 (7.82%)	28 (7%)	55 (7.38)	
<3	12 (3.47%)	15 (3.75%)	28 (3.75)	
3-5	315 (91.30%)	361 (90.25%)	673 (90.73)	
>5	18 (5.21%)	34 (8.5%)	42 (5.75)	

Table 3: Electrolyte profile according to the type of comorbidity

Type	Diabetes N (%)	ATH N (%)	Diabetes/ATH N (%)
Hyponatremia	7 (11.11)	6 (7.69)	14 (29.79)
Hypernatremia	3 (4.74)	9 (11.54)	5 (10.64)
Hypokalemia	4 (8.51)	7 (8.97)	2 (3.17)
Hyperkalemia	0	1 (1.28)	2 (3.17)

(16.75%) compared to women ($p < 0.05$) while hyperkalemia there was no significant difference based on gender (Table 2).

The natremia decreased with age (Fig. 1) whereas the kalemia increased from 60 years onwards (Fig. 2).

Electrolyte disorders were more observed in severe forms (Fig. 3 and 4). Hypertensive and diabetic subjects were more exposed to disorders of natremia (Table 3).

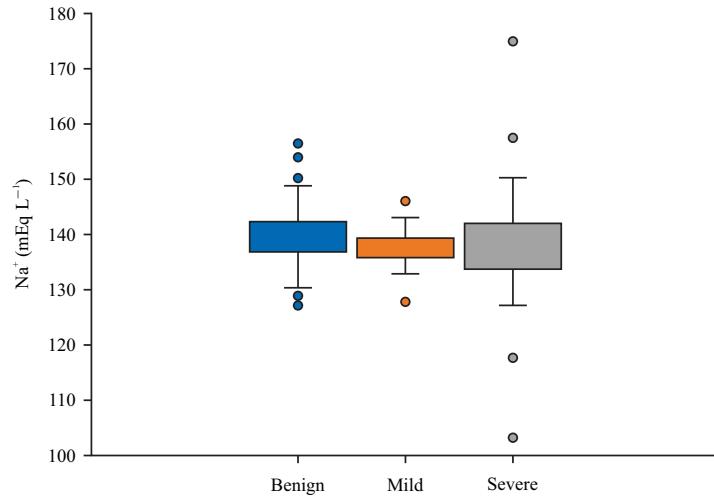


Fig. 3: Distribution of sodium according to the clinical form

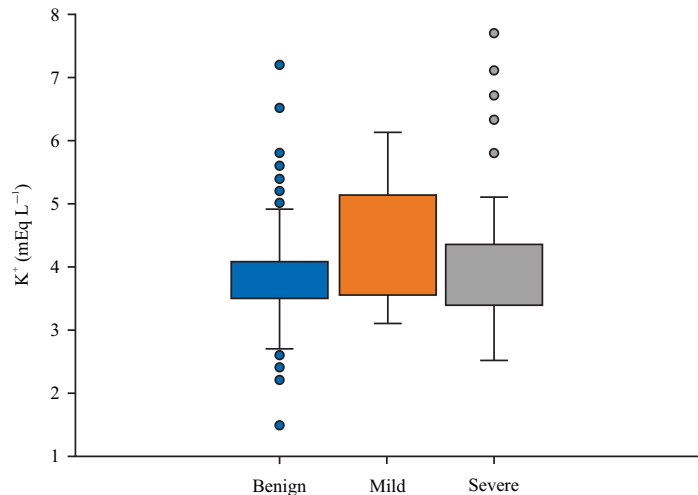


Fig. 4: Variation of potassium according to the clinical form

Electrolyte disorders such as hyponatremia and hyperkalemia were associated with the disease severity and the presence of comorbidities.

DISCUSSION

This study aimed to determine the electrolyte profile of patients with COVID-19 and to investigate the relationship between any imbalances found and clinical characteristics such as age, sex, clinical form and the existence of comorbidity. We have 745 patients aged from 2 to 94 years with an average age of 54.22 years recruited. Subjects over 60 were in the majority (Table 1). These results corroborated those of Shi *et al.*⁵ in China who found a mean age of 56 years.

However, higher mean ages were found in France⁶ and the United States⁷.

This age difference observed between this study and the European and American ones could be related to the aging of their population.

In addition to the advanced age, current results showed that male subjects were likely to be more exposed to the infection (Table 1). This predominance was also reported in several studies^{4,6-8}. According to some authors, this could be explained by female sex hormones that would play an anti-inflammatory and protective role in women. They are potential defensive agents of the immune system because they can influence immune cells, stimulate the production of antibodies, promote the repair of certain respiratory cells and inhibit the ACE2 receptor⁹.

The benign form was noted in most of our population (85.01%). A study conducted in China¹⁰ estimates that asymptomatic infections or infections with moderate clinical signs were by far the most frequent. However, the percentage of severe forms found in this study (10.22%) was not negligible and could be explained by the high proportion of elderly subjects (≥ 60 ans). Indeed, a link has been found between age and severity of the disease, Waechter¹¹, in Algeria found that mortality was 4.5 times higher in the age category of 50 to 60 years. Similarly, Li *et al.*¹² found more than 70% of severe forms in the age group 57-67 years.

The linkage between disease severity and advanced age may be partly due to age-related immune system collapse and increased inflammation that may favour viral replication and prolonged responses to this inflammation¹³. A link between the severity and the presence of comorbidity was also reported¹⁴. The results found showed that almost half of our patients had comorbidity (49.8%) with a predominance of high blood pressure (18.9%). The association between hypertension and diabetes was found in 5.27% of cases.

These data corroborate those of Shi *et al.*⁵ in China whose prevalence far exceeds ours (83.9%). The results of an American study¹⁵ also confirmed these results with a 41.3% hypertension rate. Thus, diabetes and hypertension seem to be the most frequent comorbidities in patients infected with SARS-CoV2. According to Kulkarni *et al.*¹⁶, an alternative explanation is target organ damage in hypertensive patients. Furthermore, ACE2 plays an important role in carbohydrate homeostasis and there is evidence that it also has a protective role in diabetes. Infection with SARS-CoV-2 would induce a reduction in membrane expression of ACE2, resulting in a decrease in insulin secretion and an aggravation of insulin resistance. Direct B-cell involvement was supported by reports of severe ketoacidosis on hospital admission in COVID-19 patients¹⁷.

The binding of SARS-CoV-2 to ACE2 decreases the effects of ACE2 on the renin-angiotensin system, which will lead to an increase in blood pressure and disturbances in electrolyte balance.

Several mechanisms may be involved such as kidney involvement and inappropriate anti-diuretic hormone syndrome¹⁸. Endothelial proximal tubule injury, up-regulated ACE2 in kidney tissue, renal hypoxia and abnormal coagulation could account for electrolyte abnormalities related to kidney injury¹⁹.

These disturbances were also found in this work and were mainly represented by hyponatremia and hyperkalemia. The prevalence of hyponatremia was 13.02% However, prevalences of 50% have been reported in the United States¹⁵.

In this study, hyponatremia was significantly more frequent in men than in women and was more frequent in subjects aged 60 and over. Similarly, hyponatremia was more frequent in the severe forms compared to the moderate forms and was associated with hypertension/diabetes. These results demonstrated the association of hyponatremia with SARS-CoV-2 infection. In addition, a recent study suggested that hyponatremia was associated with the severity of COVID-19 disease^{20,21}.

According to Zhang *et al.*²², COVID-19 patients with hyponatremia tend to have more severe disease and have poor clinical outcomes compared with hypernatremia patients. The severity of COVID-19 has been attributed to lower serum sodium and potassium concentration levels^{6,22,23}. Hypokalemia is the most reported dyskinesia in studies, it was found in 3.75% of our population. This disorder was more observed in male subjects and subjects aged 60 years and was associated with hypertension.

However, in our population, in addition to hyponatremia, a high frequency of hyperkalemia (5.75%) was also found, especially in subjects with a severe form. This hyperkalemia could expose them to cardiac risk. This prevalence of hyperkalemia could be related to underlying renal insufficiency, an important fact that has not been investigated and constitutes a limitation for this work. Hyperkalemia could also be related to the use of medications, such as Renin Angiotensin Aldosterone System (RAAS) inhibitors and potassium-sparing diuretics, which avoid renal potassium excretion. We, therefore, plan to continue the study on a larger population and consider renal function and treatment but also the urinary excretion of these ions.

CONCLUSION

Hyponatremia and hyperkalemia were the main disorders observed in subjects infected with SARS-CoV2. We also found a higher frequency of the disorders described in subjects with comorbidities such as high blood pressure and diabetes. Thus the ionogram could constitute a prognostic and follow-up factor in patients with COVID-19 and could be included more in the monitoring of patients infected with the virus and who suffer from underlying diseases such as diabetes and arterial hypertension.

SIGNIFICANCE STATEMENT

Research on electrolyte abnormalities in SARS-CoV-2 infection is interesting and timely to deepen knowledge and provide the international scientific and health community with

tools for proper treatment and to avoid complications. Thus, our study aimed to research the electrolyte disorders associated with COVID and to seek a link between these disorders and the severity of the disease. Our results show that the most common disorder is hyponatremia and hyperkalemia. This disorder was associated with age, disease severity and the presence of comorbidity (diabetes, hypertension). These data suggest that electrolyte abnormalities such as hyponatremia are a sign of poor prognosis and should be evaluated in all patients with COVID-19 to assess disease severity.

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