Digestive manifestations of SARS-COV2 infection in Togo

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ABSTRACT

Objective: to identify the main digestive manifestations related to SARS-CoV-2 in Togo and to determine their impact on the prognosis of the disease. **Patients and method:** This was a cross-sectional study with retrospective and prospective collection, with descriptive and analytical aims, conducted from May 1, 2020 to April 30, 2021 at the national center for the management of infectious diseases of Lome. Patients of both sexes and of any age, tested positive for SARS-CoV-2 by PCR on nasopharyngeal and oropharyngeal samples and hospitalized at the national center for infectious disease management of Lome were included in this study. Digestive manifestations were divided into gastrointestinal manifestations and hepatobiliary manifestations. The threshold of significance of the tests was retained for a p value less than or equal to 0.05. **Results:** out of 876 patients hospitalized during the study period, 215 presented with digestive manifestations, corresponding to a prevalence of 24.54%. the predominance was male, with a male/female sex ratio of 1.74. the mean age was 46.07+/-16.14 [02 months - 82 years]. gastrointestinal manifestations were found in 11.98% of cases. abdominal pain was the most frequent digestive symptom (15.35%). hepatobiliary manifestations were represented by cytolysis syndrome (44.19%) and cholestasis syndrome (36.28%). digestive manifestations were associated with renal failure (p=0.03) and thrombocytosis (p<0.01). The occurrence of death was associated with a decrease in HDL-cholesterol (p<0.001) and the presence of renal failure (p=0.027). The cure rate in our study was 83.72% with a lethality of 16.27%. **Conclusion:** the digestive manifestations constitute a not negligible form of revelation of the disease with coronavirus 2019. The best prevention is the vaccination and the respect of the measures of social distanciation.

Keywords: digestive manifestations, COVID-19, SARS-COV 2, prognosis, death, Lome, Togo

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1. Introduction

In December 2019, a new coronavirus, named SARS-CoV-2, responsible for unexplained severe pneumonia was identified in Wuhan, China [1, 2]. After SARS-CoV-1 in 2002 in China and MERS-CoV (Middle East Respiratory Syndrome) in 2012 in the Arabian Peninsula, responsible for often fatal respiratory distress syndromes, this is the third coronavirus-related global health threat in less than 20 years [3]. This virus, enveloped with single-stranded RNA, was quickly responsible for a pandemic of the Coronavirus 2019 or Covid-19 disease declared on March 11, 2020 by the WHO. In its latest report, dated September 28, 2021, WHO states that SARS-CoV-2 has infected more than 231 million people and caused the death of more than 4.7 million people worldwide. In Togo, according to the same report, 25218 people have tested positive for this new coronavirus with 226 deaths. Although the initial manifestations of Covid-19 disease are respiratory, ranging from mild upper respiratory involvement to severe pneumonia with acute respiratory distress syndrome (ARDS), the digestive system appears to be involved in the clinical expression, transmission, and possibly pathogenesis of the disease. Digestive manifestations related to SARS-CoV-2 have been reported, raising the hypothesis of a digestive tropism of the virus [4]. In addition, the detection of viral RNA in the stools of infected patients led to the hypothesis of a possible fecal-oral transmission of the virus [5, 6].

In view of the poor documentation of digestive manifestations related to SARS-CoV-2, manifestations that may be indicative of the infection, it seemed necessary to conduct this study with the objective of identifying the main digestive manifestations related to SARS-CoV-2 in Togo and determining their impact on the prognosis of the disease.

2. Patients and Method

This was a cross-sectional study with retrospective and prospective collection, with descriptive and analytical aims, conducted from May 1, 2020 to April 30, 2021 at the national center for the management of infectious diseases of Lome.

Patients of both sexes and of any age, tested positive for SARS-CoV-2 by PCR on nasopharyngeal and oropharyngeal samples and hospitalized at the national center for infectious disease management of Lome were included in this study.

Digestive manifestations were divided into gastrointestinal manifestations, represented by diarrhea, vomiting, abdominal pain and digestive hemorrhage, and hepatobiliary manifestations represented by hepatic cytolysis and hepatic cholestasis. Diarrhea was defined as the emission of more than three episodes of liquid stools per 24 hours. Hepatic cytolysis was defined as an elevation of transaminases (ASAT or ALAT) to more than twice the upper limit of the normal value. Hepatic cholestasis was defined as a concomitant increase in Gamma Glutamyl Transferase (GGT), Alkaline Phosphatase (ALP) activity and bilirubin. Patients with Covid-19 were classified according to WHO into four stages based on severity: Mild, Moderate, Severe and Critical [7].

The collected data were entered into a data entry mask designed in EPIDATA 3.1. The statistical audit and analysis had been done with STATA 2013 software; and included a descriptive and an analytical component. Quantitative variables were presented in the form of numbers, means, standard deviations and intervals; qualitative variables in the form of numbers and percentages of tables or figures. Statistical tests used were Fischer's exact test and Chi-square test for categorical variables; and Student's t-test for quantitative variables. The univariate analysis compared patients with digestive manifestations with patients without digestive manifestations and patients who died in hospital with patients who were cured. Variables showing a significant difference between the two groups were inserted into a logistic regression model for multivariate analysis. The threshold of significance of the tests was retained for a p value less than or equal to 0.05.

3. Results

Epidemiological data

A total of 876 patients were hospitalized at the national center for the management of infectious

diseases of Lome for Coronavirus 2019 disease from May 1, 2020 to April 30, 2021. Of these 876 patients, 215 had presented with digestive manifestations, which corresponds to a prevalence of 24.54%. The average age of the patients was 46 ±16 years. Seventy-eight (78) patients were female and 137 were male, corresponding to a male/female sex ratio of 1.74. Demographic and clinical data are detailed in Table I.

Table I: Demographic and epidemiological characteristics of   patients

	Digestives manifestations	No digestives manifestations	p-value
Mean age (years)	24,55	75,45	<0,001
Gender			
Male	137 (63,72%)	406 (61,42%)	0,56
Female	78 (36,28%)	254 (38,43%)	
BMI>25	37 (17,21%)	46 (6,96%)	0,98
Comorbidities			
Diabetes	44 (34,11)	85 (29,11)	<0,001
High blood pressure	75 (58,14)	123 (42,12)	<0,001
Asthma	10 (7,75)	21 (7,19)	0,31
Chronic renal failure	2 (1,55)	1 (0,34)	0,09
HIV	8 (6,20)	14 (4,79)	0,19
Symptoms			
Fever	84 (39,07)	144 (21,78)	<0,001
Dyspnea	73 (33,95)	130 (19,67)	<0,001
Chest pain	20 (9,30)	30 (4,54)	<0,001
Headache	50 (23,25)	116 (17,55)	0,06
Severe and critical form	53 (24,65)	78 (11,80)	<0,001
Intensive care	88 (40,93)	111 (16,79)	<0,001
Oxygenation	60 (27,91)	89 (13,46)	0,03
Death	35 (17,28)	62 (9,38)	<0,001

BMI : Body Mass Index

Table II: Biological data of patients

	Digestive manifestations		No digestive manifestations		p-value
	Mean+/-SD	Eff (%)	Mean+/-SD	n (%)	
Hemoglobin rate	12,36±2,7		12,79±2,20		0,04
Anemia		91 (50,56)		89 (20,75)	0,98
White blood cells	9009±6358		7108±4757		<0,001
Leucopenia		19 (10,55)		159 (37,06)	<0,001
Hyperleukocytosis		50 (27,77)		128 (29,84)	<0,001
Platelets	249219±120285		238050±92185		0,23
Thrombopenia		40 (22,22)		135 (31,46)	<0,001
Thrombocytosis		23 (12,77		152 (35,43)	<0,001
C-reactive protein	87,17±122,69		31,46±67,77		<0,001
CRP>6 mg/L		41 (80,39)		10 (10,75)	<0,001
Creatininemia	16,77±20,22		13,36±20,53		0,07
Kidney failure		49 (28,99)		120 (31,01)	<0,001
Ions Na+	138,5±7,5		140±5,2		0,08
Hyponatremia		15 (17,65)		70 (52,63)	0,09
Ions K+	4,29±0,8		4,41±0,8		0,26
Hypokaliemia		13 (15,29)		71 (53,78)	0,21
Hyperkaliemia		36 (42,35)		48 (36,09)	0,15
Total Cholesterol	1,79±1,70		8,19±4,54		0,52
Hypercholesterolemia		45 (37,19)		76 (25,42)	<0,001
HDL-cholesterol	0,42±0,19		0,86±4,91		0,47
Hypo HDL		19 (30,65)		11 (6,79)	<0,001

SD : Standard deviation ; Na : sodium ; K : potassium ; HDL :High Density Lipoprotein ; CRP : C reactive protein

Table III: Comparison of data for deceased and cured patients

	Dead patients n(%)	Healed patients n(%)	p-value
HIV	3 (8,57)	5 (2,77)	0,09
Diabetes	12 (34,28)	32 (17,77)	0,02
High blood pressure	17 (48,57	58 (32,22)	0,06
Chronic kidney failure	2 (5,51)	0 (0)	<0,001
Fever	19 (54,28	65 (36,11)	0,04
Dyspnea	27 (77,14)	46 (25,55)	<0,001
Headache	2 (5,71)	48 (26,66)	<0,001
Critical form	4 (11,42)	2 (1,11)	<0,001
Anemia	20 (71,42)	71 (46,71)	0,01
Leukocytosis	18 (64,28)	32 (21,33)	<0,001
Thrombopenia	10 (37,03)	30 (20,27)	0,05
Acute kidney failure	23 (74,19)	26 (18,44)	<0,001
Hyperkaliemia	16 (61,53)	20 (34,48)	0,02
Hypokaliemia	1 (3,84)	12 (20,68)	0,04
Hyponatremie	8 (30,76)	7 (11,86)	0,03
Hypo-HDL	13 (81,25)	3 (13,04)	<0,001

HDL : High Density Lipoprotein

Table IV : Factors associated with digestive events in multivariate analysis

	Initial model			Final model		
	OR	CI95%	p-value	ORa	CIa95%	p-value
High blood pressure	0,97	[0,33-2,83]	0,96	-	-	-
Diabetes	0,87	[0,30-2,51]	0,79	-	-	-
Fever	3,04	[1,19-7,74]	0,01	**1,69**	**[1,12-2,54]**	**0,01**
Dyspnea	0,29	[0,06-1,28]	0,10	-	-	-
BMI≥25 kg/m2	1,29	[0,13-12,65]	0,82	-	-	-
Intensive care	9,41	[2,02-43,66]	0,004	**2,36**	**[1,49-3,74]**	**<0,001**
Hypo HDL-Chol	1,10	[0,33-3,65]	0,87	-	-	-
Hyper LDL-Chol	1,46	[0,45-4,79]	0,52	-	-	-
Acute kidney failure	3,33	[1,15-9,58]	0,02	-	-	-
Anemia	1,04	[0,46-2,35]	0,90	-	-	-
Hyperleucocytosis	2,63	[0,85-8,11]	0,09	**2,10**	**[1,22-3,62]**	**0,007**

OR : Odds ratio ; ORa : adjusted Odds ratio ; CI :confidence interval ; CIa :adjusted confidence interval   BMI : Body Mass Index ; HDL : Hign Density Lipoprotein ; LDL : Low Density Lipoprotein

Table V: Factors associated with death

	Modèle Initial			Modèle Final		
	OR	IC95%	P	ORa	ICa95%	p
High blood pressure	1,01	[0,02-46,11]	0,57	-	-	-
Diabetes	24,59	[0,39-1550,29]	0,99	-	-	-
Fever	6,85	[0,25-186,17]	0,13	-	-	-
Hyponatremia	2,66	[0,11-60,39]	0,53	-	-	-
Hyperkaliemia	3,91	[0,21-70,46]	0,35	-	-	-
Hypo HDL-Chol	110,61	[3,43-3559,96]	**0,008**	23,58	[4,62-120,10]	**<0,001**
Kidney failure	59,45	[0,62-5678,56]	**0,013**	6,29	[1,23-31,99]	**0,027**

OR : Odds ratio ; ORa : adjusted Odds ratio ; CI :confidence interval ; CIa :adjusted confidence interval ; HDL : Hign Density Lipoprotein

Clinical Data

Abdominal pain (15.35%), vomiting (14.42%) and diarrhea (13.95%) were the most common gastrointestinal manifestations. Apart from the gastrointestinal manifestations, these patients also presented extra-digestive symptoms such as fever, dyspnea and pain. The presence of certain comorbidities such as arterial hypertension

and diabetes mellitus were unequally distributed in the two groups with a statistically significant difference. The severity assessment classified 104 patients (48.37%) as Mild while 47 patients (21.86%) were Severe and 6 (2.79%) as Critical. Eighty-eight (40.93%) patients with digestive manifestations had required hospitalization in intensive care unit, compared to 111 (16.79%) in patients without digestive manifestations (p <0.001).

Statistical analysis noted that the presence of fever (ORa=1.69; CIa95%: [1.12-2.54] and hospitalization in intensive care unit (ORa=2.36; CIa95%: [1.49-3.74]; p <0.001) were statistically associated with digestive events during Covid-19 infection.

Biological Data

Liver enzymology found liver cytolysis in 95 patients (44.19%) and cholestasis in 78 patients (36.28%). The blood count data showed a statistical difference between the two groups in some variables such as hemoglobin and white blood cell count. There was also an increase in C-reactive protein in 80.39% (p<0.001). Decreased plasma HDL cholesterol levels were found in 30.65% of cases (p<0.001). Hyperleukocytosis was statistically associated with digestive manifestations in multivariate analysis (ORa=2.10; CIa95%: [1.22-3.62]; p=0.007).

Evolution

A high case fatality was found in patients with digestive manifestations (16.27%; p<0.001). Statistical analysis revealed that the risk factors for death in patients with digestive events were lower plasma HDL cholesterol levels as a risk factor for death (ORa= 23.5; 95% CI [4.62-120.10], p<0.00) and the presence of renal insufficiency (ORa= 6.29; 95% CI [1.23-31.99], p=0.02)

4. Discussion

The prevalence of gastrointestinal manifestations during Covid-19 was 24.54%, similar to the Ramachadran et al data [8].

There was a male predominance with a male/female sex ratio of 1.74. This male predominance was also found in the series of Papa et al in Italy [9], of Elmunzer et al in North America [10], of Ramachadran in New York [8] and of Nobel et al in New York [11]. This low prevalence of digestive manifestations during Covid is related with the lower prevalence of Covid-19 in women and that could be explained by the role of innate immunity, steroid hormones and factors related to the X sex chromosomes [12]. Indeed, the presence of two X chromosomes in women enhances the action of the immune system. The immune regulatory genes encoded by the X chromosome in women are thought to be related to lower viremia and moderate inflammation compared to men [12].

The mean age of our patients was 46.07±16.14 years. Ramachadran et al in New York [8] and Chen et al in China [13] had reported a mean age of 57.6 years and 60 years respectively. These results show that the manifestations are more frequent in young adults.

The gastrointestinal manifestations found in our study were essentially abdominal pain (15.35%), diarrhea (13.95%) and vomiting (14.14%). These data are consistent with those reported in the literature [8, 10, 13] and confirm the high expression of CEA2 in the gastrointestinal tract and thus the digestive tropism of SARS-Cov-2 [14-16]. The evaluation of the severity of the disease found a moderate form in 26.98% of cases, a severe form in 21.86% of cases and a critical form in 2.79% of cases. Statistical analysis showed that the presence of digestive manifestations during Covid-19 was associated with hospitalization in an intensive care unit (ORa=2.36; CIa95%: [1.49-3.74]; p<0.001). This result is not consistent with those of Chen et al [13]. This discordance could be explained by the lack of standardization of admission criteria in intensive care unit.

Biologically, hepatic cytolysis syndrome was found in 44.19% of cases, while cholestasis was reported in 36.28% of cases. These results are consistent with the literature [10, 17]. These results confirm the theory of hepatic lesions related to the systemic inflammatory reaction of the organism as evidenced by the elevation of biological markers of inflammation including CRP found in 80.39% of cases.

The CRP measurement had a mean value of 87.17mg/L in patients with digestive manifestations (p<0.001). CRP was elevated to more than 6 mg/L in 80.39% of cases (p<0.001). These results are in line with those of Chen et al in China [13], who found a mean CRP of 30.8 mg/L in patients with digestive manifestations (p<0.001). This statistically significant elevation of CRP could be explained by the fact that the digestive involvement during Coronavirus 2019 disease would be related to the systemic inflammation of the body in response to the presence of SARS-CoV-2.

This study found an estimated case fatality of 16.27%. This result is much higher than those reported in the literature [11, 13]. This high case fatality observed in our study could be explained by the inadequacy of the technical platform, which does not allow for optimal management of patients at the severe or critical stage.

In this study, the presence of digestive manifestations was statistically associated with the occurrence of death (p<0.001) contrary to Chen et al [13] who did not find a significant difference (p=0.17). The cure rate was nevertheless high in our study (83.72%) as in the study of Chen et al [13] (70.75%). This discrepancy could be explained by the presence of factors associated with death in patients with digestive manifestations. The digestive events taken in isolation would therefore not be associated with the occurrence of death.

Multivariate analysis of factors associated with death in our study population found that low HDL cholesterol (p<0.001; OR=110) was associated with death in patients with GI events. This association between low HDL-Cholesterol and the occurrence of death could be explained by the decreased antioxidant, anti-inflammatory and anti-infectious properties of HDL-Cholesterol [18].

Conclusion

Digestive manifestations are frequent in Coronavirus 2019 disease. They are generally more frequent in young subjects, with a predominance for the male subject. Gastrointestinal involvement, represented by symptoms such as diarrhea, vomiting, and abdominal pain, is the most frequently encountered presentation, sometimes without associated respiratory symptomatology. Hepatobiliary involvement, which is less common, is related to the tropism of SARS-CoV-2 for hepatocytes and cholangiocytes and is manifested by a cytolysis syndrome and/or a cholestasis syndrome. Digestive symptoms may be associated to varying degrees with classic symptoms of Coronavirus-2019 disease such as fever, cough, dyspnea. Factors associated with the occurrence of digestive manifestations are mainly impaired renal function and thrombocytosis. This digestive involvement is generally responsible for mild or moderate forms of covid-19 with an evolution towards recovery in the vast majority of cases

Aknowlegment : none

Conflicts of interest : none

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