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Research Article

Some Hepatic and Renal Biochemical Markers Associated with *Salmonella* Infections in Patients Consulting at the Bafoussam Regional Hospital and the Mifi District Hospital, West-Cameroon: Cross-sectional Study

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ABSTRACT

Introduction: *Salmonella* is a bacterium that can cause illness in humans, ranging from gastroenteritis to serious systemic infections. However, its diagnosis remains a challenge for developing countries. Delayed or incorrect diagnosis of *Salmonella* infections can have negative consequences on the vital prognosis of patients and significant medical costs for the healthcare system. The aim of this study was to evaluate selected hepatic and renal biochemical markers that can be used to optimise monitoring and manage this disease.

Methods: This was a cross-sectional study conducted between April and June 2024 in 166 volunteer who gave their consent in Bafoussam Regional Hospital and Mifi District Hospital. A questionnaire was given to each participant on admission, followed by stool and blood sampling. Following stool culture and biochemical tests, the participants were seperated into positive and negative groups. Hepatic and renal biochemical markers were evaluated using standard methods from commercial kits and automated biochemical analysers. Statistical analyses were performed using SPSS version 22 software.

Results: At the end of this study, 18/166 cases of *Salmonella* infections were observed, representing a prevalence of 10.8%. Clinical manifestations such as fever, vomiting, abdominal pain, headache and loss of appetite were strongly associated with the disease (95% CI>1). Student's test showed that alanine aminotransferase, aspartate aminotransferase, C-reactive protein, direct and total bilirubin were significantly elevated in the infected patients, particularly the elders ($P<0.003$), indicating liver damage.

Conclusion: The results of this study highlight the burden of *Salmonella* infections and the need to reinforce prevention and epidemiological surveillance measures in this region. Analyses of hepatic biochemical markers showed the severity of these infections, highlighting the fact that, it is important to carefully monitor these parameters in order to optimize the management of infected patients.

Keywords: Infection; *Salmonella*; Hepatic markers; Renal markers

INTRODUCTION

Salmonella infection is a condition caused by a gram-negative bacteria called *Salmonella*. This bacterium causes gastrointestinal infection through contaminated food and water [1]. When it occurs in humans, it can take two main forms, namely gastroenteritis (or non-typhoid salmonellosis) and enteritis fever (or typhoid salmonellosis), which is the most severe form of the disease [2]. They represent a public health challenge and have a significant impact on the global economy [3]. Symptoms typically include fever, vomiting, diarrhoea/constipation, abdominal pain, nausea, asthenia and headache [4].

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According to the WHO, between 11 and 20 million people suffer from typhoid fever per year in developing countries, due to precarious hygiene and sanitation conditions, with limited access to good drinking water and appropriate advanced treatments. It causes 128 to 161 thousand deaths, 70% of which are children [1,5]. In addition, there are an estimated 93.8 million cases of gastroenteritis worldwide each year, with around 155,000 deaths per year [3].

The management of salmonellosis is increasingly complex in countries with limited resources, such as Cameroon. Reference tests for diagnosing the disease, such as blood culture and stool culture, are often outdated in some of the country's clinics and hospitals. The widal serological test, although used in almost all health facilities for the sole diagnosis of typhoid serotype, excluding all other potentially diagnosable serovars, remains not very sensitive or specific for the diagnosis of this disease [6]. Faced with these challenges, the diagnosis of the disease when it is present may be delayed or erroneous, leading to severe complications in the organism. This is why it is necessary to explore alternative methods of managing these Salmonella infections.

Systemic infection caused by *Salmonella* can have harmful consequences within the body's functional organs such as the liver and kidney, among others [7]. In view of this particularity of the bacterium, the search of the biochemical parameters of the liver and kidneys released into the blood when the bacterium passes through the blood will serve as a witness of the damage caused by the latter and can therefore be used to optimize the follow-up and management of affected patients.

The present study was carried out to determine the prevalence of *Salmonella* infections in patients who came for consultation either in the Bafoussam Regional Hospital or the Mifi District Hospital, furthermore characterize the clinical signs of infected patients, and evaluate certain hepatic and renal biochemical markers in *Salmonella*-infected patients.

MATERIALS AND METHODS

Design and study population

This was a cross-sectional study conducted in two health facilities in the town of Bafoussam in Cameroon, namely the Bafoussam Regional Hospital (HRB) and the Mifi District Hospital (HDM). Participants, regardless of sex or age, coming for a medical visit to one of these health structures, were solicited for the study. Participants with or without clinical signs of the disease were included in the study. The following clinical signs were considered: Fever, diarrhoea/constipation, vomiting, abdominal pain, fatigue and loss of appetite. The non-inclusion criteria concerned individuals with malaria, diabetes, viral hepatitis, a history of chronic disease, including liver or kidney disease, alcohol addiction and medication that may interfere with biochemical markers. Eligible participants gave their consent by signing the consent form and afterward received a questionnaire which they answered. A stool and blood sample were collected from each patient after the questionnaire was answered. A total of 166 participants were enrolled in this study and patients who had a negative stool culture result were considered a control group.

Data and sample collection procedure

Data were first collected using a questionnaire administered to the participants. Variables collected included sociodemographic characteristics, medical history and clinical manifestations. A quantity of stool sample was collected with a sterile spatula and deposited in a wide mouth sterile jar from each participant for stool culture in search of *Salmonella*. To assess the biochemical parameters, approximately 5 ml of venous blood was collected from all study participants by venipuncture at the elbow crease using a needle adapted to a vacutainer body. The blood collected was placed in anticoagulant-free tubes which were protected from light and centrifuged after 30 minutes at 3000 rpm for 5 minutes. The serum obtained was separated from the clot in Eppendorf tubes and stored at -20°C until biochemical analysis.

Isolation and identification of the bacterium

Stool analysis was performed within 2 hours of collection. A quantity of stool was homogenized with 10 ml of enrichment broth (Selenite F Borth broth) and incubated aerobically at 37°C for 18 to 24 hours for enrichment. After the enrichment step, aliquots of the stool suspensions were inoculated on SS agar selective culture medium and incubated at 37°C for 18-24 hrs. After 24 h of incubation, suspect colonies (colorless with black centers) were identified using the API 20E gallery.

Evaluation of some hepatic and renal biochemical markers

Biochemical parameters were analyzed such as Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), direct bilirubin, total bilirubin, urea and creatinine were analyzed on the Rayto-Chemary 120 automaton using standard commercial chemical analysis kits (Monlab Test®). C-reactive Protein (CRP) was quantified on a fluorecare reader using the commercial fluorerare® kit.

Statistical analysis

Data were entered and analyzed using SPSS version 22 software application. Descriptive analyses were used to determine the prevalence of *Salmonella* infections among patients at the two healthcare facilities. A binary logistic regression test was used to establish an association between *Salmonella* infection and clinical manifestations. ANOVA test followed by the student's t test were used to compare the difference in mean hepatic and renal biochemical markers between *Salmonella*-positive and *Salmonella*-negative patients. The biochemical marker values were expressed as a mean ± standard deviation. A significance level of 5% ($p<0.05$) and a confidence interval (95% CI) were used to interpret the results.

RESULTS

Sociodemographic characteristics of the study population

The study sample comprised a total of 166 participants. The mean age (± standard deviation) of the respondents was 35.81 ± 22.99 years, with extremes of 2 and 90 years. Bacteriological analysis of stool identified 18 cases of *Salmonella* infection, representing a prevalence of 10.8%, all female with 7.2% of patients aged 46 years and over. The Mifi district hospital was the most represented with 18 (10.8%) cases (Table 1).

Table 1: Distribution of patients socio-demographic characteristics.

Characteristics	Frequency (n=166)	Salmonellosis n (%)	
		Negative 148 (89.2)	Positives 18(10.8)
Age (35.81 ± 22.99)			
0-15 years	36	30 (18.1)	6 (3.6)
16-45 years old	72	72 (43.4)	0 (0.0)
46 years and older	58	46 (27.7)	12 (7.2)
Gender			
Female	120	102 (61.4)	18 (10.8)
Male	46	66 (27.7)	0 (0.0)
Place of residence			
Bafoussam	134	122 (73.5)	12 (7.2)
Foumbot	2	0 (0.0)	2 (1.2)
Mbouda	22	18 (10.8)	4 (2.4)
Foumban	4	4 (2.4)	0 (0.0)
Buea	4	4 (2.4)	0 (0.0)
Occupation			
Farmer	22	18 (10.8)	4 (2.4)
Pupil	40	32 (19.3)	8 (4.8)
Student	36	36 (21.7)	0 (0.0)
Housewife	36	30 (18.1)	6 (3.6)
Laboratory technician	4	4 (2.4)	0 (0.0)
Saleswoman	2	2 (1.2)	0 (0.0)
Driver	8	8 (4.8)	0 (0.0)
Electrician	2	2 (1.2)	0 (0.0)
Teacher	6	6 (3.6)	0 (0.0)
Mason	2	2 (1.2)	0 (0.0)
Pastor	2	2 (1.2)	0 (0.0)

Nurse	2	2 (1.2)	0 (0.0)
Carpenter	2	2 (1.2)	0 (0.0)
Health facility			
HRB	80	80 (48.2)	0 (0.0)
HDM	86	68 (41.0)	18 (10.8)

Note: n=Frequency, %=Percentage, HRB=Bafoussam Regional Hospital, HDM=Mifi District Hospital

Clinical manifestations associated with Salmonellosis

Statistical analysis using binary logistic regression showed a positive association between *Salmonella* infection and clinical manifestations such as fever 16 (9.6%), vomiting 12 (7.2%), abdominal pain 16 (9.6%), headache 14 (8.6%) and loss of appetite 8 (4.8%) (P<0.05), at a 95% confidence interval (Table 2).

Table 2: Clinical manifestations associated with Salmonellosis.

Clinical manifestations		Frequency (n=166)	Salmonellosis n (%)		OR	P-value	IC 95%
			Negative 148 (82.2)	Positive 18 (10.8)			
Fever	With	72	56 (33.7)	16 (9.6)	13.43	0.018	1.56-110.73
	Without	94	92 (55.4)	2 (1.2)			
Diarrhoea	With	60	48 (28.9)	12 (7.2)	4.16	0.057	0.95-18.10
	Without	106	100 (60.2)	6 (3.6)			
Constipation	With	46	42 (25.3)	4 (2.4)	0.72	0.698	0.13-3.75
	Without	120	106 (63.9)	14 (8.4)			
Vomiting	With	34	22 (13.3)	12 (7.2)	11.45	0.002	2.48-52.72
	Without	132	126 (75.9)	6 (3.6)			
Abdominal pain	With	70	54 (32.5)	16 (9.6)	13.92	0.015	1.65-117.42
	Without	96	94 (56.6)	2 (1.2)			
Asthenia	With	48	40 (24.1)	8 (4.8)	2.16	0.285	0.52-8.85
	Without	59	54 (65.1)	5 (6.0)			
Headache	With	34	20 (12.0)	14 (8.4)	22.4	0	1.56-110.73
	Without	132	128 (77.1)	4 (2.4)			
Loss of appetite	With	26	18 (10.8)	8 (4.8)	5.77	0.021	0.95-18.10
	Without	140	130 (78.3)	10 (6.0)			

Note: n=Frequency, P-value=Significance threshold, CI=Confidence Interval, OR=Odds Ratio

Comparison of the means of biochemical abnormalities between sick and healthy patients according to age group

Analysis of biochemical markers showed that *Salmonella*-infected patients had an average, significantly elevated level of C-reactive Proteins (CRP), Alanine Aminotransferase (ALT) in the 0-15 age group. In addition, Aspartate Aminotransferase (AST), direct bilirubin and total bilirubin were significantly higher in the elderly group (46 and over), compared to non-infected participants (P<0.003). However, there was a moderate elevation of CRP, AST and direct bilirubin in the elderly group (46 and over) compared to the reference value. Furthermore, creatinine and urea levels in both groups were normal and the difference in mean was not statistically significant (p-value>0.05) (Table 3).

Table 3: Comparisons of means biochemical abnormalities between sick and healthy patients.

Biochemical markers	Age range	Reference values	Salmonellosis (n=166)		P-value
			Negative (n=148)	Positive (n=18)	
CRP (mg/L)	0-15 years	<6	5.93 ± 3.10	80.05 ± 56.24	0
	16-45 years old		5.10 ± 3.04	...	
	46 year over		6.41 ± 3.05	72.40 ± 54.33	0
AST (UI/L)	0-15 years	F: <31	30.14 ± 14.18	42.59 ± 17.63	0.198
	16-45 years old	M: <35	30.31 ± 14.50	...	
	46 and over		34.87 ± 10.78	59.92 ± 30.46	0.003
ALT (UI/L)	0-15 years	<42	8.47 ± 6.94	44.36 ± 7.34	0
	16-45 years old		8.62 ± 7.60	...	
	46 and over		11.24 ± 9.34	47.27 ± 12.71	0
Bilirubin D (mg/dL)	0-15 years	<0.3	0.32 ± 0.24	0.24 ± 0.08	0.121
	16-45 years old		0.34 ± 0.20	...	
	46 and over		0.33 ± 0.15	0.84 ± 0.35	0
Bilirubin T (mg/dL)	0-15 years	<1.0	0.77 ± 0.28	0.68 ± 0.07	0.595
	16-45 years old		0.76 ± 0.28	...	
	46 and over		0.71 ± 0.33	1.42 ± 0.83	0.003
Urea (g/L)	0-15 years	(0.10-0.50)	0.18 ± 0.13	0.26 ± 0.02	0.32
	16-45 years old		0.19 ± 0.15	...	
	46 and over		0.17 ± 0.08	0.22 ± 0.05	0.19
Creatinine (mg/L)	0-15 years	(5-13)	5.70 ± 1.50	5.79 ± 0.88	0.996
	16-45 years old		8.13 ± 2.29	...	
	46 and over		8.36 ± 2.04	9.64 ± 2.50	0.205

Note: n=Frequency, CRP=C-Reactive Protein, AST=Aspartate Aminotransferases, ALT=Alanine Aminotransferase, T=Total, D=Direct, M=Male, F=Female

DISCUSSION

The aim of this study, carried out at the Bafoussam Regional Hospital and the Mifi District Hospital, was to evaluate some hepatic and renal biochemical markers in patients with *Salmonella* infection in order to identify biomarkers that are potentially predictive of the disease and that can be used to optimize the follow-up and management of patients with this infection.

The results of the present study indicate that the prevalence of *Salmonella* infections among these patients is 10.8%, showing that enteric *Salmonella* infections are also common in the town of Bafoussam. This rate is close to that of Awung et al. [8] who in a study in the Bamenda district health zone in Cameroon, noted a prevalence of 8.70% of *Salmonella* infections. This relatively high prevalence underscores the high burden of this bacterial infection in our region.

Clinical data revealed that fever, vomiting, abdominal pain, headache and loss of appetite were closely associated with *Salmonella* infection in this study with a P-value of less than 5%. These clinical signs are characteristic of systemic *Salmonella* infection. These results are close to that of Lefebvre et al. [9] in Senegal, who showed that fever, vomiting, abdominal pain, headache were predictive signs of *Salmonella* serovar Typhi; and that of Kashosi et al. [10] who noted an association between *Salmonella* and the appearance of symptoms such as fever, vomiting, abdominal pain.

The results of the Analysis of Variance (ANOVA) confirmed by the student's t test showed that *Salmonella* infection in these patients led to significant disturbances in hepatic markers, particularly in elderly subjects. There was a marked increase in transaminases (ALT, AST), a significant rise in CRP and an increase in total and direct bilirubin. These results are close to those of Etouke et al. [6] who noted hyperalanine aminotransferase, total hyperbilirubinemia, direct hyperbilirubinemia and C-reactive hyperprotein in the case of typhoid salmonellosis and to that of Ndukaku et al. [11] who showed that transaminases (ALT, AST) were very high in people with *Salmonella serovar typhi*. Also, Albayrak et al. [12] noted elevations in ALT, AST, CRP, total bilirubin and direct bilirubin in patients with typhoidal salmonellosis. Increased Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) clearly indicate liver damage. In addition, the significant rise in CRP underlines the presence of an important systemic inflammatory process. Increase direct bilirubin is the result of biliary tract involvement, which may translate into cholestatic jaundice. Increase total bilirubin suggests hemolysis and accumulation of direct bilirubin in the blood. Also, the moderate elevation of CRP, AST and direct bilirubin levels observed in elderly *Salmonella* negative elderly patients may be the result of another pathological condition or of their deficienct immune status.

The markers (urea and creatinine) of renal function in this study were within the reference range. This indicates the renal function is preserved in this context. This result is not the first, since a previous study showed that creatinine and urea levels remain within physiological norms in cases of *Salmonella ser. typhi* [13]. However Etouke et al. [6] and Ndukaku et al. [11] reported high levels of these markers in their studies.

This study was conducted over a limited period. It focused on the detection of *Salmonella* spp. in stool samples, without further characterization of the serotypes. The small sample size in the various study variables limited the scope of statistical analysis. Other markers of liver function were not measured.

CONCLUSION

This study contributed to a better understanding of the prevalence of *Salmonella* infections in patients who came for consultation at the Bafoussam Regional Hospital and the Mifi District Hospital, the associated clinical symptoms and their influence on biochemical markers in the liver and kidneys. The results of this study showed that 10.8% of patients were affected by this disease cases, with clinical symptoms such as fever, vomiting, abdominal pain, headache and loss of appetite. In addition, these infections disrupt certain hepatic biochemical markers by causing significant elevations of alanine aminotransferase, aspartate aminotransferase, C-reactive protein, direct bilirubin and total bilirubin, mostly in elderly patients. These results underline the burden of this disease and biochemical markers related to liver function, should be used to reinforce monitoring and optimize the management of this disease in case of severe infection.

ETHICS STATEMENT AND CONSENT

Ethical approval for this study was obtained from the Western Region Human Health Research Ethics committee (CRERSH-Ouest) (ref: N°/436/27/03/2024/CE/CRERSH-OU/VP). Written informed consent was obtained from each participant for voluntary participation and for the publication of all their data.

CONFLICTS OF INTEREST

The authors do not have any conflicts of interest.

AUTHOR CONTRIBUTIONS

Y.N.J.D. was the field investigator, developed data collection tools; collected, analyzed, and interpreted data; drafted and reviewed the manuscript. G.S.S.N. designed and supervised the study, conceptualized the protocol and reviewed the manuscript.

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SUPPORTING INFORMATION

Additional supporting information can be obtained upon demand from authors.

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