African Journal of Environment and Natural Science Research
ISSN: 2689-9434
Volume 8, Issue 3, 2025 (pp. 54-68)
www.abjournals.org

PESTICIDE EXPOSURE CONTRIBUTES TO THE PATHOPHYSIOLOGY OF *SALMONELLA TYPHI* AND *SALMONELLA PARATYPHI*A IN INFECTED PATIENTS

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Cite this article:

Promise Penn Muluh, Edith Lem, Wilfred A. Abia, Leona Akwese, Christian Suh Fusi, Etienne Yuh Jam, Faustin Pascal Tsague Manfo, Edouard Akono Nantia (2025), Pesticide Exposure Contributes to the Pathophysiology of Salmonella Typhi and Salmonella Paratyphia in Infected Patients. African Journal of Environment and Natural Science Research 8(3), 54-68. DOI: 10.52589/AJENSR-BNDRFCVN

Manuscript History

Received: 30 Jun 2025

Accepted: 11 Aug 2025

Published: 23 Oct 2025

ABSTRACT: *The increasing prevalence and burden of Salmonella infections is a major public health concern, with pesticide exposure potentially playing a substantial role in its development and severity. This study assessed the implication of pesticides on the pathophysiology of Salmonella typhi and Salmonella paratyphi in patients. This study included 159 participants suffering from Salmonella infection attending the Bamenda District Hospital in Cameroon. The participants' socio-demographic information, clinical and biochemical parameters as well as pesticide exposure biomarkers were investigated. The most represented participants were females (62.3%) and people between 5 and 44 years old. Drugs commonly used to manage typhoid showed variable pharmacological patterns with more resistance reported with Cefixime (40.9%) and Ciprofloxacin (30.8%). About 40% of the participants used pesticides and showed significantly increased (p = 0.015) levels of oxidative stress biomarker, the tiobarbituric acid reactive substances (TBARS), as compared to patients not using the pesticides. The biomarkers of pesticides exposure (acetylcholinesterase, butyrylcholinesterase) were not significantly altered when compared to the non-users of the pesticides. However, these biomarkers were significantly associated with oxidative stress biomarkers levels, TBARS and glutathione (GSH). This study suggests a potential contribution of pesticides to the pathophysiology of Salmonella in patients mainly through exacerbating the oxidative stress.*

KEYWORDS: Salmonella infection, drug resistance, pesticide exposure, oxidative stress.

Article DOI: 10.52589/AJENSR-BNDRFCVN
DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN

African Journal of Environment and Natural Science Research
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Volume 8, Issue 3, 2025 (pp. 54-68)

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INTRODUCTION

Typhoid fever is a systemic infection caused by Gram-negative bacilli *Salmonella enteric* serovars*typhi* and *paratyphi* in humans and animals with severe morbidity and mortality in all areas of the world [1]. In sub-Saharan African countries, especially in Cameroon, the prevalence of typhoid fever is considerably high, ranging from 30% to 40%, particularly affecting children, with more than 90% cases caused by *Salmonella typhi* [2,3]. Typhoid fever is commonly managed in clinical settings using antibiotics such as fluoroquinolone, cephalosporins and macrolides [4]. However, successful therapeutic outcomes of these different antibiotics vary considerably and this is constantly challenged by the disease resurgences. In fact, antibiotics used in the treatment of typhoid infection, either administered individually or in combination, have demonstrated variable therapeutic efficacy [5]. Salmonellahas developed various survival strategies against antibiotics, includingenzymatic inactivation, expelling drugs from cells using efflux pumps, and altering drug target structures, changing or hiding of drug targets in the system [6], and immune evasion. Similarly, resistance to Salmonella can be exacerbated by environmental factors, such as pesticides, that biochemically or molecularly enhance the microbe pathogenicity.

Pesticides are chemicals applied in agriculture and public hygiene to control, prevent, or eliminate harmful organisms [7]. Direct or indirect exposure of humans to pesticides disrupts cellular mechanisms, leading to various health dysfunctions such as reproductive toxicity, neurotoxicity, immunotoxicity, carcinogenicity and haematological alterations [8-11]. Pesticides can disrupt cellular signaling, impair immune cell function, and induce oxidative stress and inflammation [12-14], which are key pathways in typhoid infection. The latter is induced by *Salmonella typhi*, which triggers intestinal inflammation while exacerbating systemic oxidative stress in affected patients. This overlap in pathogenic mechanisms suggests that pesticide exposure may potentially worsen typhoid outcomes by amplifying these shared cellular disruptions [15,16]. Both drug-resistant bacteria and pesticide exposure independently exert negative effects on human health, and their mechanisms of toxicity may interact, potentially leading to additive or synergistic effects [17]. Simultaneous exposures to these two stressors may amplify harm to the human system, posing greater risk than either factor alone. However, the mechanistic interplay between these two high-burden threats remains poorly understood, limiting the information available between Salmonella infection and pesticide toxicity, despite their high burden on Cameroonian population. This article reports on the contribution of pesticides to the pathophysiology status of typhoid patients attending the Nkwen District Hospital in Bamenda (NDHB), North-West Region of Cameroon.

Article DOI: 10.52589/AJENSR-BNDRFCVN
DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN

MATERIALS AND METHODS

Study Type and Population

This cross-sectional study was hospital-based, conducted at the NDHB, from April to June 2024. The NDHB is one of the referral hospitals of the North-West region of Cameroon.

The research included 159 male and female participantsof ages between 5 and 60 years, clinically diagnosed and confirmed to be suffering from Salmonella infection. Patients vaccinated against typhoid, those on antibiotic treatment, and individuals who did not sign the consent form were excluded from the study.

An ethical clearance (Ref No: 2024/0156H/UBa/IRB) was obtained from the Ethical Committee Review Board of the University of Bamenda, Cameroon. Additionally, administrative clearances were issued by the authorities of the Nkwen District Hospital, Bamenda (Ref.N^{o}.I.1/MPH/RDPH/NDH/177) and The Regional Delegation of Public Health (Ref No: 003/ATT/NWR/RDPH/BRIGAD).

Questionnaire Administration and Sample Collection

Data was collected during patients' clinical visit to the hospital using an interviewer-administered questionnaire, in which patients were asked questions and their responses were recorded in a pre-designed form. After the objectives, confidentiality clause, advantages and disadvantages of the study were thoroughly explained to the patients who were interviewed individually on the demographic data (gender, age, education, etc.) and potential exposure to pesticides. Freshly passed faeces were collected in a sterile wide mouthed container—a measure taken to avoid contamination. Likewise, 10 mL of venous blood from participants were collected into sterile dry tubes by vein puncture and allowed to coagulate. Sera obtained from coagulated blood were used for different biochemical analyses (TBARS, GSH, AChE, BuChE and PON 1 activities).

Microbiological Analysis Using the Stool Culture

Salmonella-Shigella Agar (SSA) was used in the analysis. Briefly, faeces were inoculated onto SSA and the plates were incubated at 37^{o} C for 24 hrs. Presence of growth attesting the positivity of the test was followed by a biochemical test using Kligler Iron Agar (KIA) to confirm acid production of the slant, gas and H_2S. The presence of a red slant, yellow butt, weak H_2S reaction (black colony centers), and no gas indicated a positive KIA [18].

Determination of Pesticide Exposure Biomarkers

Acetylcholinesterase (AChE) activity was evaluated according to the method described earlier [19]. Briefly, serum was diluted 100 times by adding 3 µL serum in 297 µL 0.1M phosphate buffer pH 7.4). 50 µL 2mM Ellman's reagent (5, 5'-dithiobis-2-nitrobenzoic acid) (DTNB) was added to 50 µL of diluted serum sample and incubated for 10 min at room temperature. Then 100 µL of freshly prepared 10 mM substrate (acetylcholine thioiodide (ACTI)) was added and the absorbance was immediately read at 1 min interval for 20 min at 405 nm using a microplate reader. The serum activity of AChE was calculated as the change in absorbance per minute and expressed in units per litre (U/L).

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Butyrylcholinesterase (BChE) activity was evaluated using the same method described for AChE activity with the substrate butyrylcholinethioiodide (BCTI) replaced by ACTI.

Serum Paraoxonase 1 (PON1) aryleterase activity was determined according to methods described by Haagen et al. [20], with modifications. Briefly, 28 µL of a 1:3 diluted serum in TrisHCl buffer (50 mM, pH 8.0, containing 1 mM $CaCl_2.2H_2O$) was pipetted into 400 µL of the buffer, and the reaction was initiated by adding 100 µL of 4-phenylacetate as the substrate. Increase in absorbance was measured using a spectrophotometer at 405 nm every 10 second interval for 150 seconds. PON1 activity was expressed in U/L.

Quantification of Oxidative Stress Parameters

The glutathione levels were determined using the method of Ellman [21]. Summarily, 20 µL of the participant's serum was mixed with 750 µL of phosphate buffer (0.1 M phosphate buffer, pH 6.5) and 750 µL of 1.2 mM DNTB was added. The mixture was incubated in the dark at room temperature for 60 minutes and the absorbance was read at 405 nm using an ELISA Microplate reader. The serum thiobarbituric acid reactive substance(TBARS) levels were evaluated as reported elsewhere [19]. One hundred (100 µL) of serum was mixed with 1 mL of a working solution containing 15% (w/v) trichloroacetic acid, 0.38% (w/v) thiobarbituric acid and 0.25 N of hydrochloric acid; then the mixture was heated at 100°C for 30 min, and centrifuged (2500 xg, 5 min). The absorbance was measured at 532 nm, and TBARS levels were calculated using a molar extinction coefficient of $1.56 \times 10^5\ M^{-1}\ cm^{-1}$.

Statistical Analysis

Data obtained was entered into Microsoft Excel 2010 sheets. Descriptive analysis was used to describe the qualitative data from the questionnaire while quantitative variables were analyzed by the one-way analysis of variance (ANOVA), with the Chi-square, paired sample T, and Fisher's exact tests as post hoc tests when appropriate. Logistic regressions using Odd ratios were carried among t variables, generated at 95% confidence interval using the Stata MP Software (version 14.0), and differences were considered significant at $p < 0.05$.

RESULTS

Socio-demographic Characteristics of the Study Population

Salmonella typhi was the most common ($p< 0.001$) species (94.3%) as compared to *Salmonella paratyphi* A among the population, with more females (57.8%) affected compared to males (36.4%). The disease was similarly distributed among the different patient age ranges with the highest being between 5 and 44 years old. In terms of education level, the *Salmonella typhi* infection rate was more prevalent among people who attended secondary and higher educations. Tap water (60.4%) and well water (32.2%) were the main water sources. The vast majority of the population relied on roadside food whereas almost 40% of the participants acknowledged being exposed to pesticides (Table 1).

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ISSN: 2689-9434
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www.abjournals.org

Table 1: Salmonella species with socio-demographic information of the participants, sanitary conditions, and pesticide use.

Characteristic of population	Category	*Salmonella typhi*(%)	*Salmonella paratyphi* A (%)	Total (%)	*P* value
Gender	Male	58 (36.4)	2 (1.3)	60 (37.7)	< 0.001
	Female	92 (57.8)	7 (4.4)	99 (62.3)	
	Total population	150 (94.3)	9 (5.7)	159 (100)	
Age group (Years)	5-14	31 (19.5)	1 (0.6)	32 (20.1)	< 0.001
	15-24	31 (19.5)	2 (1.3)	33 (20.8)	
	25-34	31 (19.5)	2 (1.3)	33 (20.8)	
	35-44	31 (19.5)	3 (1.9)	34 (21.4)	
	45-54	11 (6.9)	1 (0.6)	12 (7.5)	
	> 54	15 (9.4)	0 (0.0)	15 (9.4)	
	Total	150 (94.3)	9 (5.7)	159 (100)	
Marital status	Single	78 (49)	4 (2.5)	82 (51.5)	< 0.001
	Married	69 (43.4)	5 (3.1)	74 (46.5)	
	Widow(er)	3 (1.9)	0 (0.0)	3 (1.9)	
	Total population	150 (94.3)	9 (5.7)	159 (100)	
Educational status	No education	4 (2.5)	0 (0.0)	4 (2.5)	< 0.001
	Primary education	42 (26.4)	2 (1.3)	44 (27.7)	
	Secondary education	57 (35.8)	1 (0.6)	58 (36.4)	
	Higher education	47 (29.6)	6 (3.8)	53 (33.4)	
	Total population	150 (94.3)	9 (5.7)	159 (100)	
Source of drinking water	Tap water	90 (56.6)	6 (3.8)	96 (60.4)	< 0.001
	Borehole	5 (3.1)	1 (0.6)	6 (3.8)	
	Well	49 (30.8)	2 (1.3)	51 (32.2)	
	Others	6 (3.8)	0 (0.0)	6 (3.8)	
	Total population	150 (94.3)	9 (5.7)	159 (100)	
Consumption of foods and drinks from street vendor	No	18 (11.3)	1 (0.6)	19 (11.9)	< 0.001
	Yes	132 (83)	8 (5.1)	140 (88.1)	
	Total population	150 (94.3)	9 (5.7)	159 (100)	
Use of pesticides	No	90 (56.6)	6 (3.8)	96 (60.4)	< 0.001

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	Yes	60 (37.7)	3 (1.9)	63 (39.6)
	Total population	150 (94.3)	9 (5.7)	159 (100)

Data represent the frequency (%) of the socio-demographic data of *Salmonella typhi* and *Salmonella paratyphi* in the study population. The difference between the groups is statistically significant at $p < 0.05$ (paired sample T-Test)

Distribution of Clinical Symptoms in the Study Population

Globally, up to four-fifths of the population experienced the disease symptoms, including headache, nausea, diarrhea and abdominal pains (Table 2). Notably, pesticide users were more likely experiencing these symptoms than the non-users, though the differences were not significant ($p > 0.05$).

Table 2: Clinical symptoms inpesticide users and non users.

Parameters	**Category**	**Pesticide users (Frequency, %)**	**Non-pesticide users (Frequency, %)**	**Total (Frequency , %)**	***P* value**
Headache	No	12 (7.6)	13 (8.2)	25(15.8)	0.170
	Yes	84 (52.8)	50 (31.4)	134(84.2)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Nausea	No	18 (11.3)	16 (10)	34 (21.3)	0.320
	Yes	78 (49.1)	47 (29.6)	125 (78.7)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Vomiting	No	57 (35.8)	37 (23.3)	94 (59.1)	0.936
	Yes	39 (24.5)	26 (16.4)	65 (40.9)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Diarrhea	No	14 (8.8)	13 (8.2)	27 (17)	0.323
	Yes	82 (51.6)	50 (31.4)	132 (83)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Fever	No	0 (0.0)	0 (0.0)	0 (0.0	<0.001
	Yes	96 (60.4)	63 (39.6)	159 (100)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Abdominal pain	No	18 (11.3)	15 (9.4)	33 (20.7)	0.445
	Yes	78 (49.1)	48 (30.2)	126 (79.3)	
	Total	96 (60.4)	63 (39.6)	159 (100)	

Data represent the frequency (%) of the clinical symptoms in pesticide users and nonusers in the study population. The difference between the groups is statistically significant at $p < 0.05$ (paired sample T-Test).

Pesticide Use and Antibiotic Susceptibility

Article DOI: 10.52589/AJENSR-BNDRFCVN
DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN

African Journal of Environment and Natural Science Research
ISSN: 2689-9434
Volume 8, Issue 3, 2025 (pp. 54-68)
www.abjournals.org

The highest resistance against Salmonella was recorded for the antibiotics Cefixime (40.9%) and Ciprofloxacin (30.8%). Comparatively, patients who used pesticides exhibited higher drug resistance than their non-user counterparts (Table 3).

Table 3: Comparison of antibiotics susceptibility among participants based on pesticide use.

Parameters		Pesticide users (Frequency, %)	Non-pesticide users (Frequency, %)	Total (Frequency, %)	P value
Ciprofloxacin	Sensitive	50 (31.4)	30 (18.9)	80 (50.3)	0.212
	Intermediate	21 (13.2)	9 (5.6)	30 (18.9)	
	Resistant	25 (15.7)	24 (15.1)	49 (30.8)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Ceftraxone	Sensitive	58 (36.5)	30 (18.9)	88 (55.3)	0.278
	Intermediate	17 (10.7)	14 (8.8)	31 (19.5)	
	Resistant	21 (13.2)	19 (11.9)	40 (25.2)	
	Total	96 (60.4)	63 (39.6)	159 (100)	
Cefixime	Sensitive	5 (3.1)	1 (0.6)	6 (3.7)	0.371
	Intermediate	50 (31.5)	38 (23.9)	88 (55.3)	
	Resistant	41 (25.8)	24 (15.1)	65 (40.9)	
	Total	96 (60.4)	63 (39.6)	159 (100)	

Data represent the frequency (%) of antibiotic susceptibility in pesticide users and non-users in the study population, with $P > 0.05$ χ^2 (chi square) test.

Pesticide Exposure Biomarkers

No significant difference was observed in the serum activities of butyrylcholinesterase (BuChE), acetyl cholinesterase (AChE), and paraoxonase (PON1) between pesticide users and their non-user counterparts. However, the enzyme displayed a low trend of being lower in the users of pesticide compared to nonusers. The percentage decrease in the activities in pesticide users infected by Salmonella was 12.27 for AChE, 11.63 for BuChE and 0.19% for PON1 respectively (Table 4).

Table 4: Pesticide exposure biomarkers among pesticide users and non-users.

Parameters	**Pesticide users**	**Non- pesticide use**	**% Decrease**	**P value**
AChE (U/L)	1557.46 ±694.93[a]	1775.30 ±675.03 [a]	12.27	0.052
BuChE (U/L)	2252.52± 941.00 [a]	2549.00 ±1129.45 [a]	11.63	0.075
PON1 activity (U/L)	221.58 ±153.55 [a]	221.16 ±158.29 [a]	0.19	0.987

Data expresses mean ± SD of a given parameter. AChE = Acetylcholinesterase, BuChE = Butyrylcholinesterase, PON1 = Paraoxonases1 enzyme activity. The values with the same superscript are not statistically different at $p < 0.05$ (Fisher's Exact Test).

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African Journal of Environment and Natural Science Research
ISSN: 2689-9434
Volume 8, Issue 3, 2025 (pp. 54-68)
www.abjournals.org

Oxidative Stress Biomarkers

The levels of the oxidative stress biomarker TBARS were significantly higher (p = 0.015) in patients who used pesticides compared to those who did not, whereas Glutathione levels were similar in both (Figure 1).

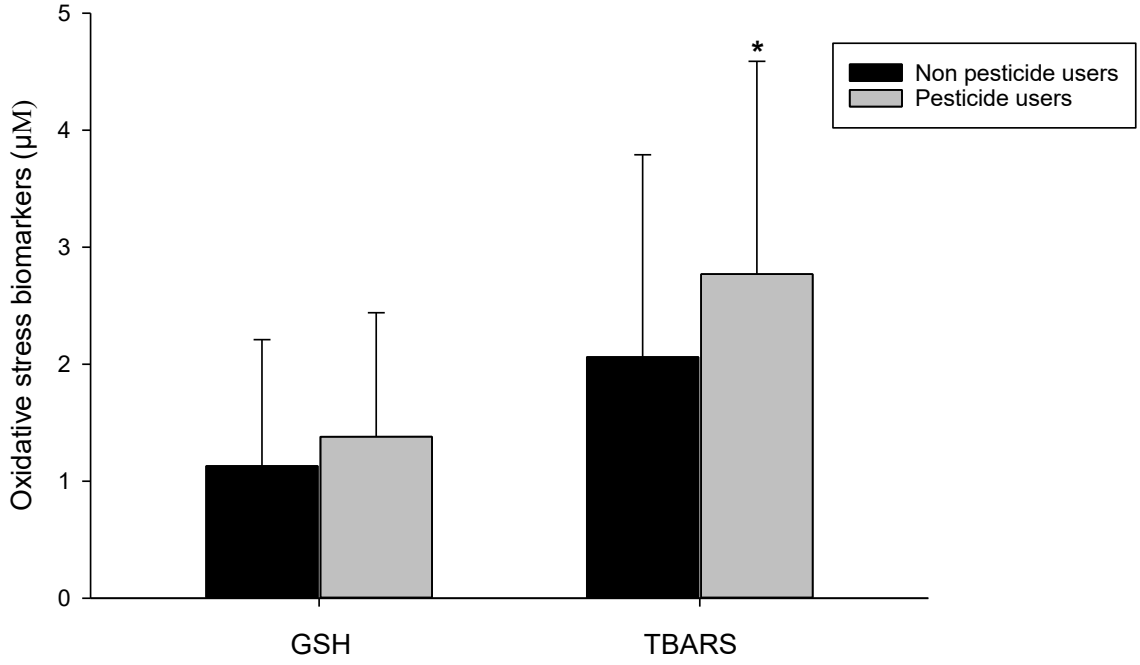

Fig. 1: Oxidative stress among pesticide users and nonusers.

TBARS = Thiobarbituric reactive substances, GSH = Reduced Glutathione. Data expresses mean ± SD of a given parameter. * p< 0.05 (Fisher's Exact Test).

Adjusted Odds Ratio (AOR)

The pesticide biomarker of exposure BuChE displayed a significant association with Glutathione (AOR = 0.782, p = 0.039) and TBARS (AOR = 1.274, p = 0.004) levels. AChE activity was significantly associated (AOR = 0.746, p = 0.014) with GSH. In Salmonella-infected patients BuChE activity showed no significant associations with resistance to Ciprofloxacin (AOR = 1.044, p = 0.895), Ceftriaxone (AOR = 1.714, p = 0.118) or Cefixime (AOR = 1.913, p = 0.404). Similarly, there was no significant association between activity and susceptibility to Ciprofloxacin (AOR = 1.066, p = 0.848), Ceftriaxone (AOR = 1.115, p = 0.747) or Cefixime (AOR = 0.981, p = 0.981).

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www.abjournals.org

Table 5: Adjusted odd ratio of pesticide exposure biomarkers, oxidative stress parameters and antibiotic resistance.

Variable	Co-variate	Crude odds Ratio	*p* value	95% Conf. Interval
BuChE	GSH	0.782	0.039	0.620 - 0.987
BuChE	TBARS	1.274	0.004	1.082 - 1.499
AChE	GSH	0.746	0.014	0.591 - 0.942
AChE	TBARS	1.117	0.177	0.950 - 1.314
BuChE	Ciprofloxacin resistance	1.025	0.937	0.552 - 1.901
BuChE	Ceftriaxone resistance	1.707	0.108	0.888 - 3.280
BuChE	Cefixime resistance	1.474	0.176	0.839 - 2.590
AChE	Ciprofloxacin resistance	1.103	0.760	0.586 - 2.076
AChE	Ceftriaxone resistance	0.987	0.970	0.518 - 1.881
AChE	Cefixime resistance	1.037	0.895	0.596 - 1.804
TBARS	Ciprofloxacin resistance	1.271	0.456	0.675 - 2.391
TBARS	Ceftriaxone resistance	1.809	0.093	0.906 - 3.611
TBARS	Cefixime resistance	1.122	0.698	0.626 - 2.010

Abbreviations: AChE: Acetylcholinesterase, BuchE: Butylcholinesterase, GSH: Glutathione, TBARS: Thiobarbituric reactive substances.

Correlations Analysis Between Pesticide Exposure and Oxidative Stress Biomarkers

The pesticide biomarker of exposure (BuChE) displayed a significant correlation with Glutathione negatively (r = -0.177, p = 0.026) and positively with TBARS (r = 0.181, p = 0.022) levels. AChE activity was significantly correlated negatively (r = -0.215, p = 0.007) with GSH (Table 6).

Table 6: Correlation between biomarkers: pesticide exposure and oxidative stress parameters.

	AChE		BuChE		PON 1	
Parameter	Pearson's "r"	*P* value	Pearson's "r"	*P* value	Pearson's "r"	*P* value
GSH	-0.215**	0.007	-0.177*	0.026	0.052	0.511
TBARS	0.070	0.382	0.181*	0.022	0.074	0.355

Abbreviations: AChE: Acetylcholinesterase, BuchE: Butylcholinesterase, GSH: glutathione, TBARS: Thiobarbituricreactive substances.

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DISCUSSION

Salmonella infection, caused by *Salmonella typhi* and *Salmonella paratyphi*, poses significant public health challenges, particularly in regions with limited access to clean water and poor sanitary conditions. This infection has led to severe health implications such as increased patient mortality and morbidity [22]. Cameroon, like other tropical countries, is facing health challenges of typhoid fever, a challenge exacerbated by increased antibiotic resistance [23]. On the other hand, pesticides, largely used in Cameroon for agricultural and public health hygiene purposes, have demonstrated significant health disrupting effects on unintended targets, such as humans [8,9,11,24]. Exposure to these toxicants in individuals with typhoid fever may further worsen their clinical condition [25]. This study focused on investigating the impact of pesticide exposure on the pathophysiology of Salmonellainfection among patients.

Typhoid fever was predominantly distributed among the younger population (5 to 44 years old), who represented the most affected age group. This may be due to a high activity associated with this group of the population coupled with probable carelessness in using non-potable water or suspicious food items [26]. Consistently, a good proportion of the subjects consumed risky water sources (stream, well, etc.) and relied on street food (88.1%) for their nutrition. Similar observations were made in Dschang and Santa, which are localities of the West and North-West Regions, respectively [18,23]. The high prevalence rate of *Salmonella typhi* (94.3%) compared to *Salmonellaparatyphi* in the study population is consistent with the findings of[3], who conducted a study in another locality of Kumbo in the North-West of Cameroon. This contrasts the observations reported in the West region, where a considerable prevalence of *S. typhi* was noted [23], although lower than that of *S. paratyphi*. This suggests a regional difference in the prevalence of the twoSalmonella serovars which could be related to individual and environmental factors. Previous studies have observed gender difference in the prevalence of typhoid infection, with females being highly affected [3,18,23]. This finding was consistently observed in the present study. The populations attending secondary and higher educations were the most affected by Salmonella infection, suggesting that although the participants may be aware of this health issue, socio-economic factors, such as lack of availability of safe water sources and food items that could still significantly contribute to the disease, impact on these populations.

The majority of the studied population experienced the key disease symptoms including headache, nausea, diarrhea and abdominal pains. The high prevalence of these symptoms (up to 80% of the population) underscores the severe impact of Salmonella infections on health [27]. Notably, pesticide users reported experiencing these symptoms more frequently than nonusers. Pesticide exposure has been shown to induce symptoms including headache, nausea, diarrhea, vomiting, and abdominal cramp [19,28]. Consequently, their presence in a patient's system could exacerbate the health condition, starting from increased clinical symptoms. Globally, all tested antibiotics showed resistance against typhoid infection with the highest being Cefixime. Cefixime, Ceftriaxone and Ciprofloxacin are 3rd-generation antibiotic drugs, with Cefixime and Ceftraxone being cephalosporins while Ciprofloxacin belongs to the fluoroquinolones group. Thanks to their β-lactam rings, cephalosporins bind to the penicillin-binding protein, inhibiting its normal activity and consequently preventing the synthesis of the bacterial cell wall, while quinolones inhibit DNA gyrase and topoisomerase IV, two vital enzymes for bacteria viability [29,30]. The non-variability in the drug resistance as a function of their class could be due to some patient-intrinsic factors, such as individual specific resistance to given antibiotics [31]. Interestingly, an increase in the clinical cases of

Article DOI: 10.52589/AJENSR-BNDRFCVN
DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN

drug resistance was observed in patients using pesticides compared to nonusers. Though not statically significant, this observation stresses the potential contribution of pesticides to cellular pathophysiological mechanisms, leading to a severe impact of the bacteria on the patient's system or to a lower efficiency of the therapeutic agent. One key mechanism of common impact of pesticides and bacterial infection is the induction of oxidative stress. Grippingly, this study demonstrated an increase in thiobarbituric acid reactive substances or peroxidation of lipid molecules in the system of patients exposed to pesticide, as compared to the unexposed individuals. Consistently, pesticide exposure biomarker (BuChE) displayed a significant negative correlation with GSH and a significant positive correlation with TBARS, and AChE displayed a significant negative correlation with GSH. This was in agreement with the substantial decrease in pesticide biomarkers (BuChE and AChE) among users of pesticides compared to nonusers. The enzymes, BuChE and AChE, are both hydrolytic enzymes catalysing the metabolism of ester, amide or thioester bonds of chemicals or biomolecules. They are irreversibly inhibited by pesticides, notably organophosphorus and carbamate insecticides [32]. In the same line, a study has demonstrated the inhibitory potential of antibiotics (especially β-lactam antibiotics) on the two cholinesterases [33]. Therefore, the decrease in cholinesterase activities observed in this study could indirectly contribute to drug resistance in Salmonella infection.

Finally, the findings from this study suggest that Salmonella infection is more highly due to *Salmonella typi* than *Salmonellaparatyphi* and is prevalent in individuals of virtually all ages in Nkwen Health District, Bamenda, Cameroon, irrespective of their education levels. This infection is exacerbated by risk factors such as unsafe water and food sources. Exposure to pesticides not only exacerbates the clinical symptoms of the disease but noticeably contributes to its pathophysiology, mainly through enhancing cellular oxidative stress. These findings underscore the dual threat posed by typhoid infection and pesticide exposure, stressing on the need for integrated approaches to microbial infections such as typhoid fever.

LIMITATIONS

The study and findings above are substantial and represent significant contributions towards the elucidation of pesticide effects among Salmonella patients. However, some related shortcomings worth mentioning include the biomarkers of pesticide exposure (AChE, BuChE and PON1) which are markers limited to some classes of pesticides (notably organophosphorus and carbamates), and may not provide exhaustive information to diverse pesticide categories that might affect patients in the area. Also, the use of AChE, BuChE and PON1 enzyme activities as biomarkers of exposure is limited as these markers do not differentiate between effects of drugs and other confounders. Detection of fingerprints of pesticides and their related metabolites can be better established using methods such High Performance Liquid Chromatography (HPLC) or Gas Chromatography (GC) together with Mass Spectrometry (MS). Also, only two classes of antibiotics commonly used in the local clinical setting were considered in this study: fluoroquinolone (Cefixime) and cephalosporins (Cefixime and Ceftriaxone). Future studies should include other classes in order to have more knowledge on multi-drug resistance in the population. Furthermore, the study was carried out only in one hospital, which makes the sample not representative of the entire population of the North-West region of Cameroon.

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Acknowledgements

The authors gratefully acknowledge the patients who volunteered to participate in the study and the staff of the Microbiology Unit at Nkwen District Hospital of Bamenda, Cameroon.

Authors' Contribution

MPP participated in designing and carrying out the experiments, data analysis and drafting of the manuscript; LE and WA took part in designing and following up the experiments as well as revising the manuscript; AL, CFS and JEY contributed to carrying out the study, data analysis and preparation of the manuscript; MTFP and NAE contributed to designing and followingup the study, preparation, and revision of the manuscript. All authors read the manuscript and agreed to its submission to this journal.

Funding

This study did not benefit from any funding.

Conflict of Interest

The authors declare no conflict of interest regarding the publication of this manuscript.

Data Availability Statement

All data presented in this study are originaland no part of this manuscript has been published or submitted elsewhere. The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Khadka P, Thapaliya J, Thapa S (2021). Susceptibility pattern of Salmonella enteric against commonly prescribed antibiotics, to febrile-pediatric cases, in low-income countries. *BMC pediatrics*, 21: 1-8.
2. Teh AE, Nguimbous S (2020). Prevalence and Associated Risk Factors of Typhoid Fever in Children Attending 'DeoGratias' Hospital in Douala, Littoral Region of Cameroon. Available at SSRN: https://ssrn.com/abstract=3631388 or http://dx.doi.org/10.2139/ssrn.3631388
3. Njoya HF, Awolu MM, Christopher TB, Duclerc JF, Ateudjieu J, Wirsiy FS, et al. (2021). Prevalence and awareness of mode of transmission of typhoid fever in patients diagnosed with Salmonella typhi and paratyphi infections at the Saint Elisabeth General Hospital Shisong, Bui Division, Cameroon. *Pan Afr Med J.*, 40:83. doi: 10.11604/pamj.2021.40.83.16893.
4. Kuehn R, Stoesser N, Eyre D, Darton TC, Basnyat B, Parry CM (2022). Treatment of enteric fever (typhoid and paratyphoid fever) with cephalosporins. *Cochrane Database Syst.*, 11(11):CD010452. doi: 10.1002/14651858.CD010452.
5. Masuet-Aumatell C, Atouguia J (2021). Typhoid fever infection – Antibiotic resistance and vaccination strategies: A narrative review. *Travel Med Infect Dis.*, 40 (2021) 101946. https://doi.org/10.1016/j.tmaid.2020.101946.
6. Punchihewage-Don AJ, Ranaweera PN, Parveen S (2024). Defense mechanisms of Salmonella against antibiotics: a review. *Front Antibiot.*, 3: 1448796. doi: 10.3389/frabi.2024.1448796.
7. Aderemi P, Adeoye A, Sani K, Adesiji RA (2013). Effects of agrochemical on ground water quality. *J Environ Stud.*, 1-7.
8. Nantia **AE**, Kada SA, Manfo TFP, Tangu N, Kaghou MM, Mbouobda HD, et al. (2018). Parastar insecticide induced changes in reproductive parameters and testicular oxidative stress biomarkers in Wistar male rats. *ToxicolInd Health,* 34(7): 499–506.
9. Manfo FPT, Mboe SA, Nantia EA, Ngoula F, Telefo PB, Moundipa PF, et al. (2020). Evaluation of the Effects of Agro Pesticides Use on Liver and Kidney Function in Farmers from Buea, Cameroon. *J Toxicol.*, 2305764. doi: 10.1155/2020/2305764.
10. Ahmad MF, Ahmad FA, Alsayegh AA, Zeyaullah M, AlShahrani AM, Muzammil K, et al. (2024). Pesticides impacts on human health and the environment with their mechanisms of action and possible countermeasures. *Heliyon*, 10(7), e29128. https://doi.org/10.1016/j.heliyon.2024.e29128.
11. Suh FC, Manfo TFP, Nantia AE, Dionysius NN, Fombele NJ, Suh LD, et al. (2024). Use of agrochemicals resulted in anemia and inflammation among farmers in Fako Division, Cameroon. *Drug Chem Toxicol.*, DOI: 10.1080/01480545.2024.2429629.
12. Lee G-H, Choi K-C (2020). Adverse effects of pesticides on the functions of immune system. Comp Biochem Physiol C: *Toxicol Pharmacol.*, 108789. doi:10.1016/j.cbpc.2020.108789.
13. Sule RO, Condon L, Gomes AV (2022). A common feature of pesticides: oxidative stress—the role of oxidative stress in pesticide-induced toxicity. *Oxid Med Cell Longev*., (1); 5563759.
14. Lopes-Ferreira M, Farinha LRL, Costa YSO, Pinto FJ, Disner GR, da Rosa JGDS, et al. (2023). Pesticide-Induced Inflammation at a Glance. *Toxics*, 11(11): 896. doi: 10.3390/toxics11110896.

Article DOI: 10.52589/AJENSR-BNDRFCVN
DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN

15. Bayim BP-R, Ada BF, Nzoegwu NP (2012). Status of Oxidative Stress in Typhoid Fever Patients among Fishers of Calabar, Cross River State, Nigeria. *World J Life Sci and Medical Research*, 1:33.
16. Wangdi T, Winter SE, Bäumler AJ (2012). Typhoid fever. *Gut Microbes*, 3(2): 88–92. doi:10.4161/gmic.18602.
17. Alderton I, Palmer BR, Heinemann JA, Pattis I, Weaver L, Gutiérrez-Ginés JM, et al. (2021). The role of emerging organic contaminants in the development of antimicrobial resistance. *Emerg Contam*., 7: 160-171.
18. Wam EC, Arrey CN, Sama LF, Agyingi, LA, Wam, AN (2019). Comparative study on the use of Widal test to stool culture in the laboratory diagnosis of typhoid fever in Holy Family Hospital Akum, North West Region of Cameroon. *Open Microbiol Journal*,13(1).
19. Manfo TFP, Suh FC, Nantia AE, Moundipa FP, Cho-Ngwa F (2021). Occupational use of agrochemicals results in inhibited cholinesterase activity and altered reproductive hormone levels in male farmers from Buea, Cameroon. *Toxicol Res.*, 10: 192–202.
20. Haagen L, Brock A (1992). A new automated method forphenotypingarylesterase (E.C.3.1.1.2.) based uponinhibition of enzymatic hydrolisis of 4-nitrophenyl acetate. *Eur J ClinChemClinBiochem*., 30: 391-5.
21. Ellman GL (1952). Tissue sulfhydryl groups. *Arch BiochemBiophys.*, 82: 70–7. https://doi.org/10.1016/0003-9861(59)90090-6.
22. World Health Organization (2018). Typhoid Fever. Geneva: World Health Organization.
23. Etouke NTA, Kuh FG, Gomseu DBE, Nzesseu VL, Tamokou JD, Dzoyem JP (2024). Epidemiology of Multidrug-Resistant *Salmonella Typhi* and *Paratyphi* Isolated From Stool Culture. *J Trop Med.*, 3480080. doi: 10.1155/jotm/3480080.
24. Corsini E, Liesivuori J, Vergieva T (2008). Effects of pesticide exposure on the human immune system. *Hum ExpToxicol.*, 27 (9): 671-680.
25. Kurenbach B, Gibson PS, Hill AM, Bitzer AS, Silby MW, Godsoe W, et al. (2017). Herbicide ingredients change *Salmonella enterica*sv. Typhimurium and *Escherichia coli* antibiotic responses. *Microbiology*, 163 (12): 1791-1801.
26. Bhandari J, Thada PK, Hashmi MF, DeVos E (2024). Typhoid Fever. In: StatPearls. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557513/
27. Crump JA, Sjölund-KarlssonM, Gordon M A, Parry CM (2015). Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive Salmonella infections. *ClinMicrobiol*., *28*(4): 901-937.
28. Manfo FP, Moundipa PF, Déchaud H, Tchana AN, Nantia EA, Zabot MT (2012). Effect of agropesticides use on male reproductive function: a study on farmers in Djutitsa (Cameroon). *Environ Toxicol*., 27(7): 423-32. doi: 10.1002/tox.20656.
29. Fàbrega A, Madurga S, Giralt E, Vila J (2009). Mechanism of action of and resistance to quinolones. *MicrobBiotechnol*., 2(1): 40-61. doi: 10.1111/j.1751-7915.2008.00063.x.
30. Bui T, Patel P, Preuss CV (2024). Cephalosporins. . In: StatPearls [Internet]. Treasure Island (FL): StatPearls. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551517/
31. Reygaert WC (2018). An overview of the antimicrobial resistance mechanisms of bacteria. *AIMS Microbiol*., 4(3): 482-501. doi: 10.3934/microbiol.2018.3.482.

Article DOI: 10.52589/AJENSR-BNDRFCVN
DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN

32. Čadež T, Kolić D, Šinko G, Kovarik Z (2021). Assessment of four organophosphorus pesticides as inhibitors of human acetylcholinesterase and butyrylcholinesterase. *Sci Rep*., 11(1):21486. doi: 10.1038/s41598-021-00953-9.
33. Özer E, Mirza H, Tan O, Türkoğlu S (2022). Investigation of anti-cholinesterase and anti-amyloidogenic activities of β-lactam antibiotics. *Turkish Journal of Biochemistry*, 47(3): 359-369. https://doi.org/10.1515/tjb-2021-0277.

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DOI URL: https://doi.org/10.52589/AJENSR-BNDRFCVN