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Study of the Resurgence of Typhoid Fever in the Commune of Doba in Chad

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Authors' contributions

This work was carried out in collaboration among all authors. Author BA supervised and contributed to writing the original draft. Author MAD introduced the concept. Author WM carried out the survey. Author AD managed the software work and monitoring. Author AO was involved in the developing the methodology. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of this study was to determine the factors behind the increase in the number of cases of typhoid fever in the commune of Doba.
Place and Duration of Study: Our study was carried out in the District and Provincial hospital and the Christian Assemblies in Chad (ACT) health center of Doba, from July to August 2022.
Methodology: A total of 756 Widal and Félix tests according to the slide agglutination technique described by Raobijaona and Ranaivo-Harisoa were carried out in three health facilities in order to

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confirm the reliability of the test within these facilities. Surveys, using survey forms, were carried out in 120 households, with 95 households participating in our study.
Results: The results showed a fairly high typhoid fever prevalence rate (72.52%), with all households surveyed (100%) using self-medication antibiotics. We also noted a high frequency of antibiotic use without a doctor's prescription. Non-compliance with hygiene and sanitation rules was noted in the majority of households (80%), which ate food without carefully washing their hands with soap and water. Most of the households surveyed (52%) had no toilet, which encourages open defecation.
Conclusion: Despite its unreliability, the Widal and Félix serodiagnosis is the test frequently requested and carried out. Failure to comply with hygiene measures and excessive self-medication, at the root of the selection of resistant bacteria, have been partly identified as factors that have contributed to the increase in the number of cases of typhoid fever in Doba.

Keywords: Typhoid fever; widal et félix; antibiotic resistance; salmonella; hygiene and sanitation.

1. INTRODUCTION

Typhoid fever is an acute infectious disease caused by ingestion of Eberth's bacillus, *Salmonella typhi* or, more rarely, *S. paratyphi* A, B or even C. Transmission is essentially fecal-oral, and can be direct from human to human via dirty hands or indirect via drinking water and various foods contaminated with faeces (World Health Organization, 2018).

It is fatal and febrile, with young people at greater risk of contracting the disease. Without treatment, its case-fatality rate is 10-30%, falling to 1-4% with appropriate therapy (Parry *et al*., 2011). Common symptoms include long-lasting fever, chills and abdominal pain (Raobijaona & Ranaivo-Harisoa, 2000; Mariko, 2021). On the other hand, a non-specific symptom profile complicates the clinical diagnosis, with symptoms common to other diseases occurring in typhoid fever endemic areas (Grace *et al*., 2022; Xiang *et al*., 2023). The mainstay of laboratory confirmation of cases remains blood culture, with a limited sensitivity of around 40-60% (GBD, 2020)**,** partly due to widespread self-medication prior to visiting a health center.

It is estimated that there are between 11 and 21 million cases of typhoid fever, with between 128,000 and 161,000 deaths, and 6 million cases of paratyphoid fever, with 54,000 deaths annually (Kernbaum, 1988). The majority of cases occur in South-East and South Asia and sub-Saharan Africa.

While the incidence of typhoid fever has fallen sharply in countries with a high standard of living, to less than 1 case per 100,000 inhabitants, it remains high in developing countries, at 130 cases. Typhoid fever is endemic in the tropics and the Third World, with epidemics of varying severity (ANSES, 2014). The emergence of antimicrobial resistance is a significant challenge, with several recent major epidemics caused by multi-antibiotic-resistant *S. Typhi* in Africa and Asia (Ministry of Public Health, 2017; Ministry of Public Health, 2016).

In Chad, typhoid fever is a public health problem that needs to be addressed in view of the high demand for research into this pathology in the relevant departments within hospitals. In 2017, reference consultation services notified 25,946 probable NC (Ministry of Planning and Development, 2009). Adults aged 15 and over (302 NC/100,000 adults) are 7 times more affected than children aged 5-14 (42 NC/100,000). Infants are less affected than other age groups (Ministry of Planning and Development, 2009).

In Logone Oriental province, the typhoid fever detection rate was 39% in 2017 (Ministry of Planning and Development, 2009). Today, there is a considerable increase in cases of typhoid fever in the province of Logone Oriental, particularly in the commune of Doba. This worrying situation should be of concern to all those involved in health, as well as to the population itself. To this end, a better understanding of the epidemiological situation of *Salmonella Typhi* and Paratyphi in the province of Logone Orientale and in the commune of Doba in particular, as well as the causes that contribute to it, remains essential for appropriate control of this disease.

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out in the commune of Doba, capital of the Province of Logone Oriental. It is situated between 8.666° North Latitude and 16.850° East Longitude. The commune of Doba

is divided into 4 arrondissements with 24 districts. It also has two (02) hospitals and three (03) health centers for a population of 106,403 inhabitants, spread over 15,200 concessions (Essayagh *et al*., 2020)**.**

2.2 Sampling

Our work has involved clinical tests conducted on patients who have come for fever complaints and surveys using survey forms between July and August 2022, a period of high demand for Widal and Félix examinations (Chardon and Brugere, 2014). It involved both hospitals and households.

2.2.1 In households

A total of 120 households were selected on a voluntary basis to take part in the survey. All arrondissements were covered, with the majority of households concentrated in the 4th arrondissement.

Within the concessions, the survey targeted mothers or guardians of children, i.e. the heads of household. And if there were several households in the concession, in each household the woman or the child's guardian, i.e., the head of the household, was asked to answer the questionnaire. On the other hand, if there were several women in the same household, only one should be interviewed.

2.2.2 In health facilities

Patients diagnosed with typhoid fever and referred for the Widal and Félix tests were systematically collated. Subjects were identified in two (02) hospitals (the district hospital and the Provincial hospital) and one (01) health center (the Christian Assemblies in Chad (ACT) health center) in the commune.

It should be noted that our survey covered adults and children, regardless of sex, with an age range of between 1 and 85 years.

Table 1 shows the variables defined for the study.

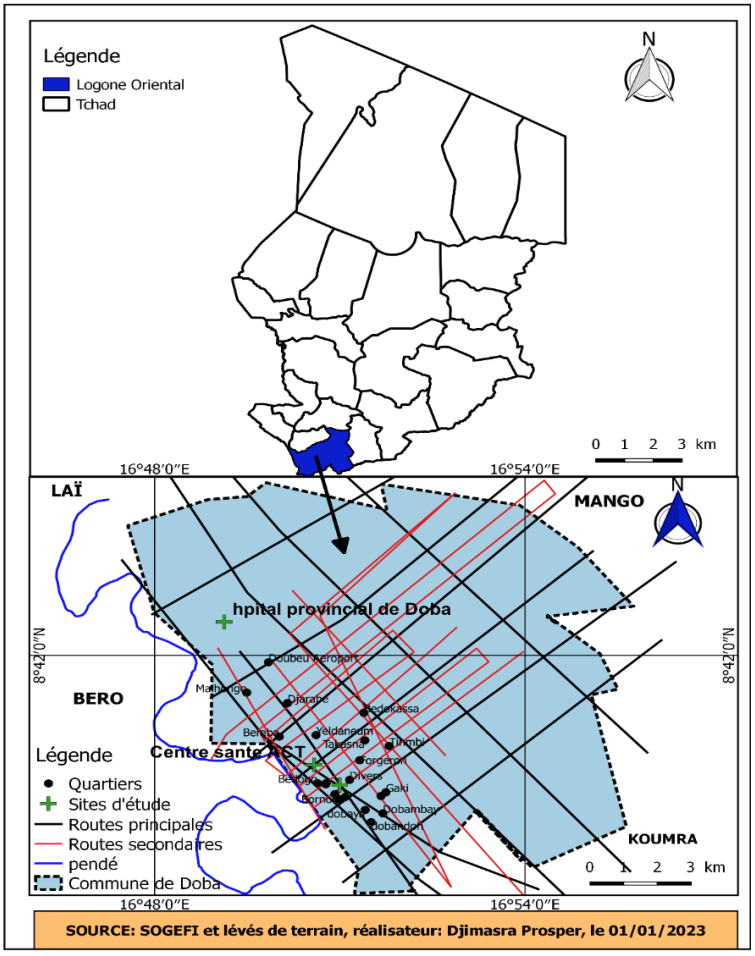

Fig. 1. Location map of the study area

Table 1. Variables studied

Variable	Type	Collection technique
Age	Quantitative	Interview
Sex	Qualitative	Direct observation
Ethnicity	Qualitative	Interview
Profession	Qualitative	Interview
Duration of symptoms	Quantitative	Interview
Result of Widal and Félix serodiagnosis	Qualitative	Direct observation
Result of control test	Qualitative	Direct observation

2.2.3 Sample size

The minimum sample size was calculated using the following formula use by Guienne *et al*., (2017):
N = [Z^2×p× (1-P)] /M2, where: N = required sample size; Z = 95% confidence level (standard value of 1.96); P = estimated prevalence of typhoid fever cases between July and August 2022 in the commune of Doba; M = 5% margin of error (standard value of 0.05).
The prevalence (P) of typhoid fever between July and August 2022 was:
P = (Number of positive cases / Number of suspected cases) x 100

2.3 Widal and Félix Serodiagnosis

2.3.1 Test rationale

The choice of this test is based on its multiplicity of tests and its use as a mass screening and peripheral diagnostic test. Its performance compared with the reference serological test should also be noted.

2.3.1.1 Performance of the test

A control test was used to check the reliability of the examinations carried out in the health facilities concerned. It consisted of collecting sera that had already been tested at the health centres in order to confirm its reliability.

For our study, 37 sera stored in dry tubes and closed at -20°C or at lower temperatures were thawed and homogenised before being tested on 746 samples.

At the Christian Assemblies health center in Chad, the slide agglutination technique described by Guienne *et al*., (2017) was used. To a drop of serum corresponding to 50µl on a clean slide, a drop of antigenic suspension O or H (2.5µl) of *Salmonella* T, A, B or C respectively is added. The mixture obtained is then homogenized on the plate and placed on a rotary shaker at 100 rpm for 3 minutes. Positive reactions result in lumpy agglutination of the mixture containing the antigen.

At the district hospital, on the other hand, we used the agglutination technique in tubes after dilution 1:10. To 900µl of distilled water, 100µl of serum was added and then 1/100 of the mixture was taken for each O and H tube. Next, 900µl of the antigenic suspensions O or H of Salmonella T, A, B or C respectively was added to the corresponding tubes and centrifuged for 5 minutes at 3000rpm. The positive tubes showed clumpy agglutination for the O antigen and dusty smoke for the H antigen, observable under light after gentle shaking of the tube.

2.3.1.2 Test evaluation criteria

Internal validity criteria: Sensitivity and specificity attest to the intrinsic validity of diagnostic tests. In the case of typhoid and paratyphoid fevers, our analysis focused on the validity of the Widal et Félix test or plate agglutination test.

The reference diagnostic test used for our study is the dilution agglutination test, described as a control test (World Health Organization, 2018).

Sensitivity: the sensitivity of the test defines its ability to correctly identify individuals carrying the disease. It corresponds to the ratio of the number of subjects recognized as ill by the plate agglutination test to the total number of ill subjects (identified by the reference test).

It was determined using the formula: Sensitivity = VP / (VP + FN) (Guienne *et al*., 2017)

where: VP = True Positives (positive with the reference test and the plate agglutination test) and FN = False Negatives (positive with the reference test but negative with the plate agglutination test).

Specificity: specificity is the ability of the test to correctly identify individuals who are not carriers of the disease (Baratloo, 2015).

The formula used: Specificity = VN / (FP + VP)

with: VN = True Negatives (negative with the reference test and the plate agglutination test); FP = False Positives (positive with the agglutination test but negative with the reference test), corresponds to the ratio of the number of subjects recognized as not sick by the plate agglutination test to the total number of subjects recognized as not carrying the disease (identified by the reference test).

External validity criteria: The Positive Predictive Value (PPV) indicates the probability of a subject actually being ill when the test is positive. It is a function of the sensitivity, specificity and prevalence of the disease (Safari *et al*., 2015). It is calculated using the formula described:

PPV = (Preval. x Sensitivity) / [(Preval. x Specificity)] + [(1 - Preval.) x (1 - Specificity)]

The Negative Predictive Value (NPV) is the probability that a subject is actually not ill when the test gives a negative result. It depends on the sensitivity, specificity and prevalence of the disease and is calculated by the formula:

NPV = ((1 - Preval) x (Specificity)) / [(1-Preval) x (Specificity)] + [(Preval) x (1-Sensitivity)]

The positivity threshold, an arbitrary variable that separates positive results from negative results, is characterised in our study by the observation of the presence of agglutination on the slide.

2.4 Characterisation of Behaviors Favoring the Transmission of Germs Responsible for Typhoid fever in the Population

Direct observation of the level of hygiene and sanitation in the various households surveyed was used to support or reject the information collected from patients diagnosed in hospital facilities.

The various points covered in the interview focused mainly on the state of health of the children, in particular the presence of diarrheal diseases, the supply of drinking water and the overall level of individual and collective hygiene within the household.

To this end, a direct observation guide was used in the various neighborhoods.

2.5 Identification of Practices Favoring the Selection of Resistant Bacteria Within the Population

The literature on the use of antibiotics in human populations was used to identify the risk factors that could be involved in the emergence of resistant bacteria responsible for typhoid fever. For practical reasons, the study was limited to two (02) main risk factors for which further details are required for their analysis. These were the presence of self-medication and non-compliance.

The survey was conducted among randomly selected residents of the commune of Doba, whether or not they attended the consultation.

2.6 Statistical Analysis

The database was created and managed using Access software (Microsoft office corporation 2019). Quantitative data were entered using Excel (Microsoft office corporation 2019) and analyzed using Statistical Package for the Social Sciences 17.0 (SPSS). The mean, standard deviation, minimum, maximum and median of the sensitivity, specificity, positive predictive value and negative predictive of publications were calculated.

3. RESULTS AND DISCUSSION

3.1 Survey Results

Of the 120 households identified, only 95 gave their consent to participate in our study and to answer the proposed questionnaire. This represents a participation rate of 79.16%. The remaining 25 households (20.84%) categorically refused to participate.

3.2 Typhoid Fever Prevalence Rate

From July to August 2022, 746 patients suspected of having typhoid fever were diagnosed. Of these, 541 tested positive for the Widal et Félix serology, giving a prevalence rate of 72.52%. These results are shown in Table 2.

Table 2. Typhoid fever prevalence rate

Periods	Suspected cases	Number of positive cases	Percentage (%)	Negative cases	Percentage (%)
July	377	293	77.72%	84	22.28%
August	369	248	67.21%	121	32.79%
Total	746	541	72.52%	205	27.48%
P-Value			0,349		

Our results show a high incidence of typhoid fever, which is similar to those of Sauch *et al*. (2010), who found an annual distribution revealing a summer peak from July to October, in relation to rainfall. Two phenomena could explain this high incidence of typhoid fever in the hot, rainy season. Firstly, the rainy season is marked by major problems with drinking water supplies and sanitation. On the other hand, so-called 'water-borne' diseases, including typhoid fever, are rife at this time of year (World Health Organization, 2018; Chardon and Brugere, 2014). Our results are in line with those obtained in 2002 by Sako in Yopougou, Abidjan, and Lefebvre in Senegal.

3.3 Patient Characteristics

Age (Table 3) and sex (Table 4) were used to characterize the patients diagnosed.

The presence of salmonella was observed in all the age groups identified (Table 5), with the majority of cases observed after the incubation period (Table 6).

The age group between 11 and 40 was the most represented, with a frequency of 55.08%, and an average age of 25. The minimum age was 1 and the maximum 85. The incidence of typhoid fever is much higher in young adults. This could be explained by the fact that older children and adults can become infected outside the family environment.

Table 4 shows that women are more affected than men, with a frequency of 58.96%. The work of Sheded *et al*. (2018) in Egypt and Mariko (2021) in Bamako in Mali showed a male predominance, which is contrary to our results. This is contrary to our results. There seems to be no explanation for these differences.

As shown in Table 5, all the salmonella serotypes responsible for typhoid fever were found. However, there was a predominance of *S. Typhi* strains (44.17%), confirmed by the Widal et Félix serodiagnosis. This is the only confirmatory test for typhoid fever carried out in hospitals and health centers in the commune of Doba.

The data in Table 6 show the reliability of the Widal et Félix test with advanced cases (73.19%) of typhoid fever.

3.4 Practices Favoring the Selection of Resistant Bacteria in the Population

The results in Table 7 show the practices that encourage the selection of resistant bacteria. They reveal the use of self-medication antibiotics in all households surveyed (100%). In 11 (11.58%) households, antibiotics are used without a doctor's prescription, due to a lack of means, and in 84 (88.42%), due to experience or habit.

We can thus note a high frequency in the use of antibiotics without a doctor's prescription in view of the percentage of households systematically resorting to it (56%) in the presence of a case of illness, compared with 44% referring to a doctor. For 88.42% of households, the main reasons for self-medication are related to experience, to which can be added the economic factor for the remaining households (11.58%).

Table 3. Typhoid fever prevalence rate according to age

Age groups	Effectif			
	Positive	Percentage	Négative	Percentage
1 to 10 years	146	73,73%	52	26,27%
11 to 40 years	298	72,68%	112	27,32%
41 years and over	97	70,28%	41	29,72%
P - Value			0,039	

Table 4. Prevalence rate of typhoid fever according to sex

Widal and Félix serodiagnosis	Gender	
	Male	Female
Positive	222 (41,03%)	319 (58,96%)
Negative	94 (45,85%)	111 (54,14%)
P value		0,067

Table 5. Distribution of Salmonella serotypes identified

Sérotypes	Number positive	Percentage
S. Typhi	239	44,17%
S. Paratyphi C	49	9,05%
S. Paratyphi B	116	21,44%
S. Paratyphi A	137	25,32%

Table 6. Typhoid fever prevalence rate by incubation period

Widal and Félix serodiagnosis	Less than 8 days	More than 8 days	Total
Positive	145 (26,80%)	396 (73,19%)	541 (100%)

Table 7. Risky practices in the selection of resistant bacteria

Practices	Households	
	Yes	No
Practice of self-medication	95 (100%)	0 (0%)
Systematic self-medication in the event of illness	56 (59%)	39 (41%)
Antibiotic use by habit / experience	84 (88,42%)	11 (11,58%)
Choice of antibiotic by habit / experience	58 (61%)	37 (39%)
Referral to a doctor after failure to self-medicate	38 (40%)	57 (60%)
Compliance with doctor's prescription	27 (28,42%)	68 (71,58%)
Discontinuation of treatment after improvement in state of health	85 (89,47%)	10 (10,53%)

Our surveys also revealed a reliance on habit and experience in the choice of antibiotic molecules. This practice can be a significant risk factor, resulting in antibiotic treatments that are inappropriate, ineffective or even useless in the face of the pathogens present. Such as unsuitable spectra, non-bacterial microbial agents and/or ill-defined dosages (Ministry of Public Health, 2017; Guienne *et al*., 2017; Sanders *et al*., 2011).

It is highly regrettable to note that in our study, 60% (n=57) of households implement a second treatment before seeking medical attention. Indeed, any use of antibiotics again exposes bacteria to selection pressure (Sanders *et al*., 2017; Kathleen, 2019) and the multiplicity of treatments is a risk for the selection of multi-resistant bacteria (Haenni *et al*., 2012).

Our study also shows that 28.42% of patients adhere to their doctor's prescriptions, as opposed to 71.58% who, due to lack of resources, fall back on lower-cost generic antibiotic molecules and, once their health has improved, stop treatment or modify the dosage and frequency of antibiotic administration. It should not be forgotten that changes in antibiotic dosage, duration or frequency of administration are risk factors for the emergence of resistant bacteria. It can also lead to a lack of bacteriological cure for the patient, and be responsible for chronic carriage of virulent bacteria (Sanders *et al*., 2017; Degbey, 2011).

Our surveys revealed, among other things, abundant use of ciprofloxacin with a proportion of 56.4%, followed by Ceftriaxone (31.4%). This is very similar to the results obtained by Sheded *et al.* (2018) in Egypt where 47.5% treatment was based on the use of 3rd generation cephalosporin and 35.4% quinolone. With a relapse rate observed for 21.1% of patients on cephalosporins (Sheded *et al.,* 2018). The information gathered suggests that these antibiotics are used because of their extended spectrum of action, availability and ease of administration.

Table 8. Tools and frequency of hand disinfection before eating

Hand disinfection tools and frequency	Workforce	Percentages
Plain water	76	80%
Water with soap always	11	11.58%
Water +Soap occasionally	08	8.42%
P-value		0,057

Table 9. Hygiene and sanitation factors in households

Hygiene and sanitation	Existing	Percentage	Non existing	Percentage
Wells	76	80%	19	20%
Latrines	43	45.03%	52	54.73%
Garbage cans	13	13.68%	82	86.32%
Sumps	0	0%	0	0%
Boreholes	32	33.68%	63	66.32%
Taps	43	45.26%	52	54.74%

3.5 Behaviours Favouring the Transmission of the Typhoid Fever Germ Within the Population

We noted that very few households (11.58%) regularly used soap to wash their hands before eating, which is well below the rate of households (80%) simply using water without soap, but higher than that of households (8.42%) using it occasionally (Table 8).

This situation calls for a wide-ranging information and awareness campaign to link the level of hand hygiene in particular with the onset of diarrheal diseases such as salmonellosis among the population.

The main sources of household water supply in the commune of Doba during the rainy season are wells (80%), pumps or boreholes (33.68%) and taps (45.26%) (Table 9). In the dry season, water comes from traditional wells and pumps.

Traditional wells are the primary source of drinking water in both wet and dry seasons. This water is very often consumed directly in households, without prior treatment. It is only treated in 29 households (38.15) and bleached in 30 (39.47%).

The conditions under which drinking water is collected, transported, stored and handled can contribute to contamination at several levels: drawing water, buckets and ropes lying on the ground, the container or transport vessel, the cup used to draw water from the canary, and poor maintenance of the cup (Grondin, 2005).

To circumvent these sources of contamination, containers should be covered for transport and home storage. These containers must also be kept out of the reach of children, pets and insects. Water should be removed from storage containers by siphoning, rather than using cups, which are often exposed to insects and dust (Ngnikam *et al*., 2007).

The length of time water is stored in the home seems to be a major factor in its quality deterioration.

quality deterioration. It can be seen that the longer the water is stored, the greater the deterioration in water quality. After three days, over 80% of water samples analyzed were of poor quality (Sheded *et al*., 2018). Similarly, there is a low presence of latrines (48%) in households, which would favor the dissemination of germs in the wild, a major factor in the spread of typhoid fever (World Health Organization, 2018; Chardon and Brugere, 2014) in the commune.

4. CONCLUSION

In sum, our study shows that typhoid fever has a high incidence, with a prevalence rate of 72.52%. Although known to the population (especially in urban areas), this disease continues to cause public health problems in Chad, and particularly in the commune of Doba, the resolution of which requires multi-sectoral collaboration for epidemic control, prevention and vaccination. Despite its unreliability, the Widal et Félix serodiagnosis is the most frequently requested test performed by our practitioners. Failure to comply with hygiene measures and excessive self-medication, which are at the root of the selection of resistant bacteria, are partly identified in this study as

factors that have contributed to the increase in the number of typhoid fever cases in the commune of Doba.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

ETHICAL APPROVAL

This study was approved by the National health policy 2016-2030

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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