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Original Article

Investigation of Typhoid Fever and their Associated Risk Factors in Children Attending "Deo Gratias" Hospital in Douala, Littoral, Cameroon

Teh Exodus Akwa [1*], Simone Pierrette Nguimbous [2]

[1] Department of Biochemistry, Microbiology and Biotechnology, Kenyatta University, Nairobi, Kenya
[2] Department of Biological Sciences, University of Bamenda, Cameroon
* Corresponding author: Teh Exodus Akwa E-mail: exodusakwateh@gmail.com ORCID: 0000-0003-2611-9774
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ABSTRACT

Typhoid fever is a communicable disease transmitted by the bacteria *Salmonella typhi*, related to serotype *paratyphi* A, B and C. The disease is a significant health concern in most developing countries especially Cameroon.

Objectives: The study aimed at assessing the risk factors associated to typhoid fever in children (0-18 years) attending the "Deo Gratias" hospital in Douala.

Method: A hospital based cross sectional study from August to September 2018 was carried out in children aged 0-18 years suffering from typhoid fever at the Deo gratias Catholic hospital. Widal slide agglutination and stool culture were the diagnostic test used. Positive confirmed cases were administered questionnaires to evaluate the level of knowledge, attitude and practice toward the disease. Data obtained from respondents was analyzed by descriptive statistics. One-way ANOVA and means comparison using Tukey's test ($\alpha = 0.05$) was performed to check whether the population of respondents differed significantly across risk factor practices. Results were finally presented on bar charts, tables and pie chart.

Results: Out of 64 patients tested for typhoid, 44 (68.75 %) were confirmed positive. Typhoid fever was more prevalent in females (52.3 %) than in males (47.7 %), with a high proportion in the ages 5-9 years (38.6 %). A significant difference was observed in population of respondents across risk factor practices.

Conclusion: Water quality have a great impact on the burden of typhoid fever among children. The identification of risk factors associated to the disease is of great importance in the development of rational control strategies of the disease.

Keywords: *Salmonella typhi*, Widal test, typhoid fever, water quality

INTRODUCTION

Typhoid fever is an infection having as causative agent *Salmonella typhi* related to the serotype *paratyphi* A, B and C [1]. This bacterium is a significant cause of morbiditity and mortality especially in developing countries and exhibits multiple antibiotic resistance [2]. Studies by Mweu and English [3] shows that this disease is associated to low socio-economic status and poor hygiene, having humans as the only natural host of the infection since the bacteria grows best at 37 °C which corresponds to the human body

temperature. Transmission of the disease is through faecal oral route from contaminated food or water [4]. Major symptoms of the disease includes; malaise, fever, vomiting, constipation, splenomegaly and hepatomegaly [5]. The disease can result to major complications such as internal haemorrhage and perforation [5]. In the absence of effective treatment, this disease has a fatality rate of about 10 to 30 % [6]. Typhoid fever is a threat to many tropical countries showing a worldwide estimate of about 212 million cases with 129,000 deaths yearly with children and young adults being the vulnerable groups [7].

Widal test, which was first introduced by F. Widal in 1896, is widely used in the diagnosis of typhoid fever. This is because it is relatively cheaper, easy to perform and requires minimal training and low sophisticated equipment [8]. This test depends on agglutination reaction between *S. typhi* somatic Lipopolysaccharides O antigen (TO) and flagellar H antigen (TH). In most health facilities in Cameroon, the Widal test is always confirmed with a second test which is the stool culture test. Antibiotic therapy is the only effective treatment for typhoid fever. Commonly prescribed antibiotics include: Ciprofloxacin (Cipro), Azithromycin (Zithromax) and Ceftriaxone [9].

Studies carried out by Khan [10] in Karachi, Pakistan indicates that children of age between 2 to 16 years are at a higher risk of contracting typhoid disease. Reports from the Cameroons' Public Health ministry shows a frequent diagnosis of typhoid fever in children in health facilities in Cameroon and has resulted in a public scare [5]. It is thus considered an endemic disease in Cameroon. One major challenge in the treatment of this disease in Cameroon is the high costs of its drugs. Control strategies to the disease is a possible way out to reduce the disease spread. However, absence of information associated to the risk factors of typhoid fever especially in children in Cameroon has made it not really possible to bring about effective control strategies to manage the disease. To better direct public health interventions, we conducted a study to identify the risk factors for developing typhoid fever in children in Douala, Cameroon. From the findings of this study, the knowledge will help to bring about rationale control strategies of the disease thus mitigating its spread.

MATERIALS AND METHODS

Study Design

A hospital based cross sectional study was conducted from August to September 2018 with the goal of investigating the associated risk factors of typhoid fever in children (0 – 18years) attending "Deo Gratias" hospital in Douala, Littoral region of Cameroon. The study involved obtaining blood and stool samples from patients suspected of having typhoid fever. Patients who were confirmed positive for typhoid fever were administered structured questionnaires. For patients less than 12 years of age their parents or guardian were required to fill the questionnaire. Questions were based on demographics of patients and typhoid fever associated risk factors. Questions on risk factors were related to hygiene habits, sanitation conditions and nature of households.

Study Area

The study site was the "Deo Gratias" hospital in Douala, Littoral region of Cameroon. Cameroon is a country located in the central part of Africa. The country is comprised of ten regions. The Littoral region of Cameroon is the largest in size and the most populated of the all the ten regions that make up Cameroon with a population of about 2, 768 436 inhabitants [11]. Douala is the capital of the littoral region and also the economic capital of Cameroon. It is the most populated town in Cameroon [12]. Water sanitation in Douala is poor which greatly contributes to water borne diseases such as typhoid and cholera [13].

Study Participants and Collection of Samples

Participants of the study were patients of age between 0 to 18 years who tested positive for typhoid fever. A total of 64 patients showing symptoms of typhoid fever and seeking medical attention at the Deo Gracias Catholic hospital during the period of August to September were tested. Testing of typhoid disease was done with the use of blood and stool samples. Blood specimens were collected into vacutainer tubes containing no preservative/additive (red cap tubes) and tests were performed using the Widal slide agglutination method. Stool samples were collected in sterile containers and inoculated into Salmonella Shigella Agar (SSA) suitable for cultivation of *Salmonella typhi*. Structured questionnaires were further administered to positive confirmed patients to evaluate the level of knowledge, attitude and practice towards the prevention and control of the disease, as well as their self-management abilities.

Laboratory Analysis

The Widal test was used as the presumptive serological diagnostic test for typhoid fever. The test determined the presence of agglutinins (antibodies) in the blood of an infected person against the H (flagellar) and O (somatic) antigens of *S. typhi* and *paratyphi*. The slide agglutination

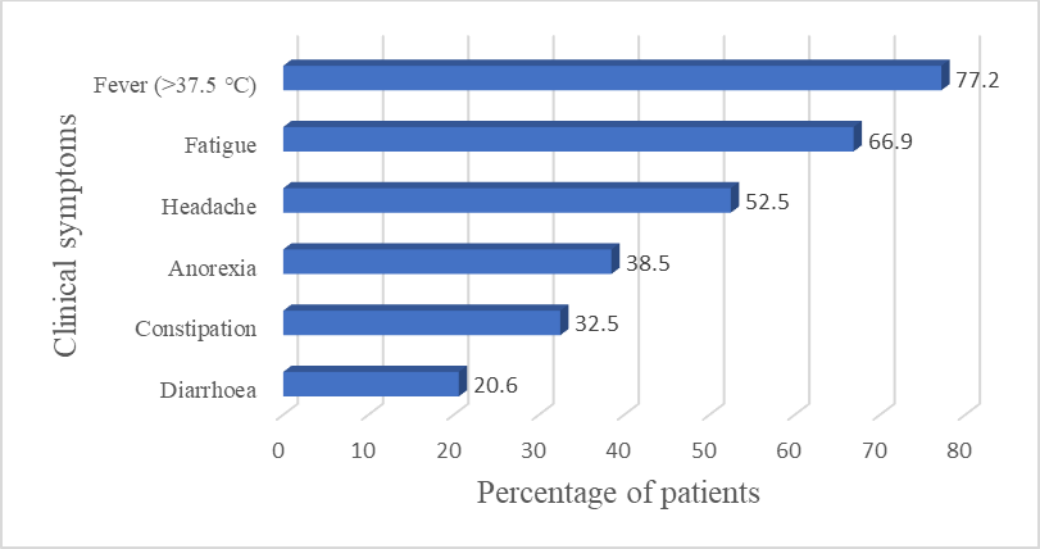

Figure 1. Distribution of clinical signs and symptoms among study participants

test was used. Blood was collected in a vacutainer tube and centrifuged. With the use of a calibrated pipette, 50µl of serum was transferred on each circle of a Widal plate (which consisted of 8 rows of circles). A drop of reagent (TO, AO, BO, CO, TH, AH, BH, CH) respectively was added beside each drop of serum. Each drop of serum was mixed with the drop of reagent in a circular manner, using a separate mixing stick for each. The Widal plate was then gently swirled in a circular manner and macroscopically visualised for agglutination within 2 minutes.

Positive results were indicated by the appearance of a visible agglutination within a minute, formed due to the reaction occurring between antibodies present in the infected person's blood (serum) and the antigens specific for *S. typhi* and *S. paratyphi*.

Results were recorded as 1/20, 1/40, 1/80, 1/160 etc. depending on the concentration of the agglutination observed. Negative results were indicated by the absence of agglutination between the patient's antibodies in serum and specific *Salmonella* antigens. Negative results were noted as "non-reactive" (NR), indicating the absence of a reaction (agglutination).

Stool samples collected were inoculated into Salmonella Shigella Agar (SSA) suitable for cultivation of *Salmonella typhi* and incubated at 37 °C for 48 h. it was then subjected to Gram stain and biochemical test for identification of Salmonella colonies.

A confirmed typhoid fever case was defined as a patient with positive Widal test and stool culture for *S. typhi* associated with typical clinical symptoms.

Result Analysis

The data obtained from questionnaires by respondents was analysed by descriptive statistics. The data was entered in a spread sheet, Microsoft Excel and normality determined. One-way ANOVA and means comparison using Tukey's test ($\alpha = 0.05$) was performed to check whether the population of respondents differed significantly with respect to risk factors tested. Results were finally presented on bar charts, tables and pie chart.

Research Ethics

Prior to the sample collection, verbal and written details of the study was provided in both English and French. Written informed consent was obtained from all the participants or their guardians which was approved by the hospital management.

RESULTS

Clinical and Demographic Presentation of Participants

Clinical presentation of participants

Common symptoms shown by patients who participated in the study included fever, fatigue, headache and anorexia. Amongst the symptoms, most of the patients presented with fever (77.2 %) having temperatures ≥ 37.5ºC (**Figure 1**). Fatigue was also common in the patients. Some of the patients acknowledged that before being brought to the hospital for check-up they had already taken medications to reduce fever.

Table 1. Presentation of typhoid cases using Widal and Stool culture test

***Salmonella typhi* diagnostic test**			**Stool culture test (Salmonella colony count)**		
			Present	Absent	Total Widal count
Widal test	Widal Positive	Salmonella count in widal	44	11	55
		Percentage count	88.0	78.58	85.93
	Widal Negative	Salmonella count in widal	6	3	9
		Percentage count	12.0	21.41	14.06
Stool culture test	Total salmonella colony count		50	14	
	Total percentage count		78.13	21.87	

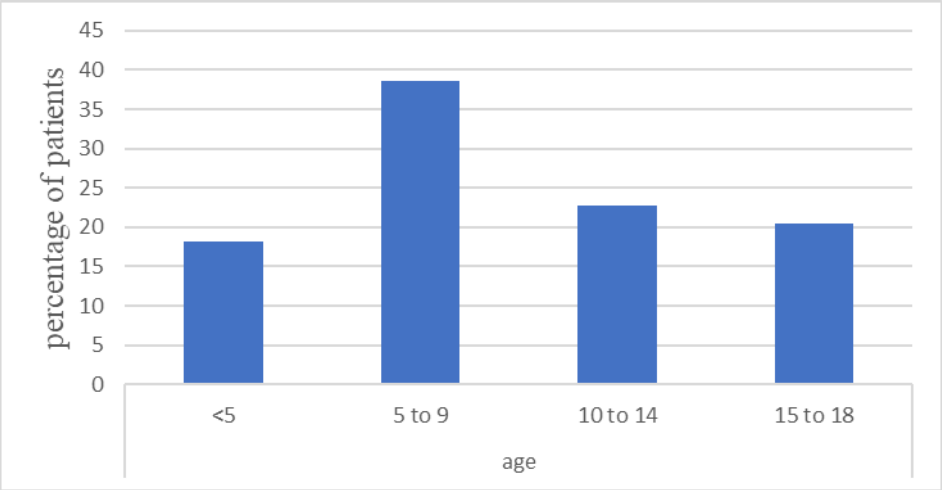

Figure 2. Demographic presentation of confirmed cases according to age

Presentation of typhoid cases using Widal and Stool culture test

Out of the 64 patients tested showing typhoid symptoms in this study, 85.93 % (n= 55) tested positive for typhoid with the use of Widal as diagnostic tool only, 78.13 % (n= 50) tested positive for typhoid based on stool culture while 68.75 % (n= 44) tested both positive for Widal and stool culture (**Table 1**). Thus 68.75 % was considered as confirmed cases for typhoid and were administered questionnaires on typhoid risk factors.

Sensitivity and specificity values of the Widal test obtained were 88.0 % and 21.41% respectively. These values were computed based on comparison to the stool culture technique.

Presentation of clinically confirmed cases according to Age and Gender

All patients who were confirmed positive for typhoid responded to the structured questionnaires involving its associated risk factors. A total of 44 patients were confirmed positive of which 23 (52.3 %) were females while 21 (47.7 %) were males. Of this, 18.2 % were in the group of below 5 years of age, 38.6 % were in the range of 5 to 9 years, 22.7 % were in the range of 10 to 14 years and finally 20.5 % were in the group of 15 to 18 years old (**Figure 2**). Mean age of patients was 10.1 ± 7.8 years.

Assessing Risk Factors Associated with Typhoid Fever

Source of drinking water

Sources of drinking water identified by patients included pipe borne, river, stream and wells. A percentage of 53.5% was obtained from respondents on consumption of pipe borne water while rivers, wells and other sources had 13.3 %, 22.5 % and 10.7 % response as sources of water consumption (**Figure 3**).

A one-way ANOVA (**Table 2**) carried out on the data obtained from drinking water sources showed a significant difference ($P < 0.05$) between the mean population of respondents' on the sources. A majority of the respondents used pipe borne as the major source of drinking water (23.98 ±3.20). There was no significant difference in the population of respondents whose source of drinking water was wells, river, streams and other sources.

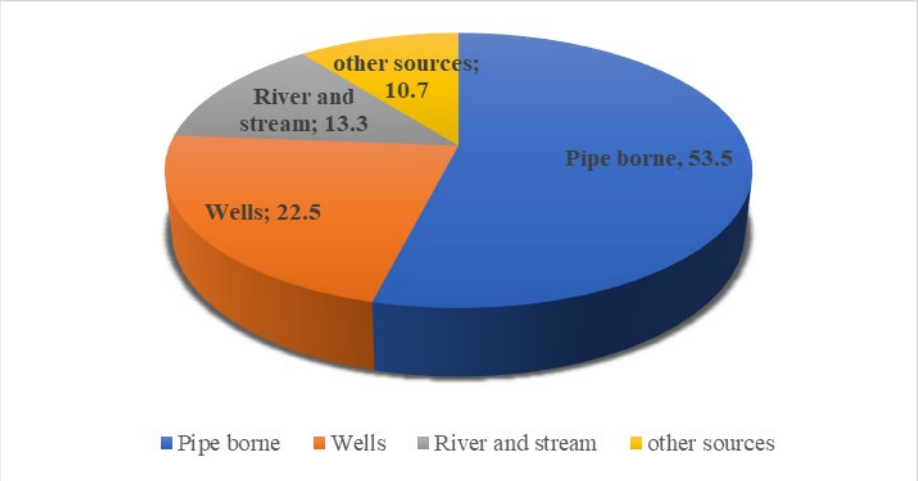

Figure 3. Distribution of patients according to drinking water sources

Table 2. Mean population distribution of respondents on sources of drinking water

Sources of drinking water	Mean population of respondents
Pipe borne	23.98±3.20[a]
Wells	9.90±1.90[b]
River and stream	5.80±1.50[b]
Other sources (alternate source)	4.70±1.80[b]
Mean respondents P= 0.001 (P<0.05)	11.09±2.10

Values are expressed as means ± SE

[a,b]Means accompanied by different superscripts differ significantly at P<0.05

Table 3. Mean distribution of respondents according to methods of household water treatment

Method of water purification	Mean population of respondents
None	18.99±2.90[b]
Boiling	7.00±1.40[c]
Use of water filters	18.00±1.40[b]
Use of cotton wool	0[a]

[a,b]Means accompanied by different superscripts differ significantly at P<0.05

Household water treatments method used

Household water treatment methods outlined in the questionnaire included; boiling of water, filtering of water using purchased water filters and use of cotton wool as local household filters. A significant difference was recorded among participants on use of treatment methods. Majority of the respondents did not use any treatment method on water before drinking. Others used either boiling or filtering of the water as their water treatment technique (**Table 3**).

Table 4. Distribution of respondents according to number of members in household

Number of children	Percentage (number)
Less than 3	15.9 (7)
3-5	68.18 (30)
6-8	15.9 (7)
More than 8	0

Number of members in households

Patients who participated in the study lived in household with size ranging from one to eight members. A higher proportion of patients was obtained in households of size between of 3 to 5 members (66.7 %) (**Table 4**).

Socioeconomic status index

Socioeconomic status index was considered based on monthly income of parents or guardians in households. The status was categorized as follows; high socio-economic status index (>150,000 CFA), medium socioeconomic status index (between 100,000 CFA to 150,000 CFA) and low socioeconomic status index (< 100,000 CFA). A greater proportion of the patients (50 %) came from families with medium socioeconomic status index.

DISCUSSION

Based on our knowledge, this is the first study done on the association of risk factors to typhoid fever in this part of Cameroon. The gender distribution of typhoid disease in this study was 47.7 % for males and 52.3 % for females, suggesting that typhoid fever was more prevalent in females than in males among the age group in that locality. Similar research done by [14,15] in Bangladesh and South Africa showed that typhoid fever correlated with gender and case fatality is higher in females compared to males. In Douala a high proportion of food handlers are females with

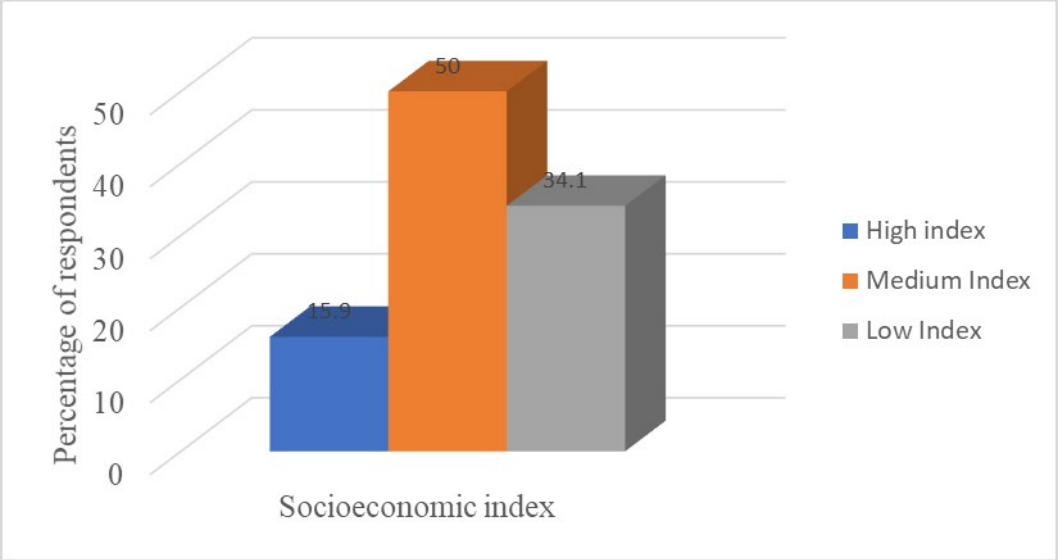

Figure 4. Distribution of patients according to household socioeconomic index

many working in different restaurants/hotels. Many of these restaurants are small and located in insanitary areas. Besides that, a large number of street food vendors are also working in approximately all localities of Douala where there is almost no provision of sink and toilet. Hand washing is an established way to prevent disease transmission, but this basic step which breaks the infection chain is not routinely performed by most of the food handlers of Douala. This could be a possible reason accounting for the higher prevalence of typhoid in females than males.

A greater proportion of positive cases was detected among children with age range 5 to 9 (38.8 %) while a lesser proportion of patients was found in the age group below 5years (18.2 %). One reason for the high prevalence observed in the age group 5 to 9 is the underdeveloped immune system in growing children, this makes them more vulnerable to this enteric pathogen. A low prevalence noted in children less than 5 years of age may probably be due to their controlled diet and drinking water at these tender ages by their parents.

As regards socioeconomic status index, high income category had a lesser prevalence of typhoid (15.9 %) relative to lower income category (34.1 %) and middle-income category (50 %). Similar studies done by Vollaard [16] show that the prevalence of typhoid infection was higher among lower income category households. Low-income category household have high tendency of purchasing and eating cooked food from street vendors which predisposes them to typhoid infection. Street vendors have limited facilities for storing food and cleaning of dishes. This poor hygiene practice is a vehicle for disease transmission. Furthermore, low-income category practice poor household hygiene due to lack of means of available portable water connected to their houses. Ram *et al*. [17] also identified socioeconomic status as a significant risk factor associated in the occurrence of typhoid fever.

Patients who took part in the study lived in household of varied sizes. Research indicates that household contact is a major risk factor associated to the spread of typhoid infection. Vollaard [16] found that the prevalence of typhoid was higher in households containing more than 6 members. Crowding was seen to be a risk factor associated with typhoid fever among households.

Most epidemiological studies have related the risk factors to typhoid fever of being waterborne or foodborne [18]. Findings obtained from the data showed a significant difference ($P < 0.05$) between the mean population of respondents' on the sources of drinking water. A majority of the respondents used pipe borne water as a source of drinking water though others still used wells, rivers and streams as their main source. Concerning sources of drinking water, UNICEF categorized water sources as improved drinking water source or unimproved drinking water source [19]. Piped water in dwelling, yard or public taps was classified under improved drinking water source while unprotected springs and dug wells were classified as unimproved source of water. This classification was used to distinguish safe water sources from unsafe sources [19]. People who drink water from safe sources stand a lower risk of typhoid infection than those who drink from unsafe sources [20]. Similar research carried out on microbial analysis of household wells revealed a high bacterial load and resistant strains of *Salmonella enterica* serover Typhi [21].

With respect to household water treatment methods, a significant difference (P <0.05) was observed among the population of respondents. Some respondents did not use any household treatment method for water. Water sanitation in the city of Douala is very poor. Absence of household water treatment could greatly contribute greatly to the prevalence of typhoid fever. Studies carried out by Ram, [17] in Bangladesh demonstrated that drinking of unboiled water at home was a major risk factor in the occurrence of typhoid fever. Boiling of water in clean containers before drinking could reduce the risk of typhoid fever. This is due to the fact that the *Salmonella typhi* bacteria grows best at a temperature of 37°C thus very high temperatures kills the bacteria. Boiling, the use of ceramic filters, bleach addition and solar disinfection has been household water treatment interventions introduced by the WHO [21].

LIMITATIONS

One possible limitation of this study was the limited number of participants. This which could greatly affect the statistical power of the study. Responses provided in the questionnaire for age group below 12 years was provided by parents and guardians which could introduce recall bias as regards the study.

CONCLUSION

Our findings show an increase risk of contracting typhoid fever in low-income homes, crowded households and poor and untreated water sources. The results from the study have a lot of significance to health experts. Firstly, it highlights improvement of sanitation and hygiene as the most effective way to prevent the spread of the disease especially in children. Nonetheless, our findings also highlight the need for more sensitization of the public concerning the mechanism of transmission and effective control or preventive methods of the disease.

ABBREVIATIONS

WHO : World Health Organisation,

UNICEF : United Nations International Children Emergency Fund

ANOVA : Analysis of variance

Author contributions: All authors were involved in concept, design, collection of data, interpretation, writing, and critically revising the article. All authors approve final version of the article.

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Declaration of interest: The authors declare that there is no conflict of interest regarding the publication of this article.

Data availability: Data generated or analysed during this study are available from the authors on request.

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