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Determinants of Typhoid Fever Occurrence in Regions with High Risk of Contracting Communicable Diseases: Systematic Review and Meta-analysis

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Abstract: Typhoid fever (TF) typically manifests itself as prolonged high fever, relative bradycardia, splenomegaly, and abdominal symptoms. Socioeconomic factors, including educational level, poor sanitation and hygiene conditions,, social assistance, access to safe food, and misuse of antibiotics contribute to the dissemination and persistence of *Salmonella* infections in urban, suburban, and rural areas. The combination of these factors creates conditions for the permanent occurrence of TF, which is the most common cause of hospitalization and death in low incoming countries. This study aimed to assess the relationships between the risk factor and TF occurrence. The systematic review was conducted following the PRISMA guidelines and submitted for registration at the International Prospective Register of Ongoing Systematic Reviews (PROSPERO). A literature search was conducted using MEDLINE/PUBMED (National Library of Medicine), MEDLINE (Bireme), Science Direct and B-on databases, between June and August of 2022. Of 2,246 articles, 42 were included. Of these studies, 24 were included in the systematic review, and 9 were included in the meta-analysis. The prevalence of Typhoid fever ranged between 1.1% and 93%. The factors associated with TF were as follows: contaminated food, untreated drinking water, incorrect hygiene practices, contact with someone who had TF, a lack of knowledge about TF, living in a refugee camp or nearby. There was a clear association between TF and contaminated food, untreated drinking water, incorrect hygiene practices, contact with someone who had TF, a lack of knowledge of TF, and living under inadequate conditions.

Keywords: *Salmonella typhi*, Intake Food, Drinking Water, Hygiene Practices, Typhoid Fever

1. Introduction

Salmonella enterica serovar Typhi (*S. Typhi*) and the related serovar *S. Paratyphi* are the etiological agents of typhoid fever (TF) and paratyphoid fever, a severe gastrointestinal infection transmitted through the ingestion of food and water contaminated with feces and/or urine of patients or by symptomatic carriers of the bacteria [1-3]. TF typically manifests itself as prolonged high fever, relative bradycardia, splenomegaly, and abdominal symptoms [4–6]. Globally, there are an estimated 22 million cases and 260,000 deaths annually [7–9]. Children under 5 years, adolescents, and adults up to 45 years in the endemic areas of southeast and central Asia, Latin America, and Africa are commonly most affected [10–13].

In the endemic areas, water supply is generally poor, and people with acute illness or asymptomatic carriers can contaminate the surrounding water through feces, which contain high concentrations of these bacteria, thus triggering community contamination [5, 14]. In addition, socioeconomic factors, including educational level, poor sanitation and hygienic conditions, social care, access to safe food, and misuse of antibiotics contribute to the dissemination and persistence of *Salmonella* infections in urban, suburban, and rural areas [13, 15].

The combination of these factors creates conditions for the permanent occurrence of TF caused by the consumption of water and/or food contaminated by *Salmonella* [4, 16, 17]. The Bill & Melinda Gates Foundation (BMGF) strives to reduce or even eradicate TF, but the lessons of eradication efforts remain instructive [18]. In this context, this paper provides an overview of the relationship between the risk factors of TF occurrence in the world.

2. Methods

2.1. Search Strategy

This systematic review was based on the Preferred Reporting Items for Systematic Reviews (PRISMA) [19] and registered in the International Prospective Register of Ongoing Systematic Reviews (PROSPERO). The search was conducted in June and August 2022, using the MEDLINE (PubMed), MEDLINE (Bireme), and Science Direct and B-on databases. We used the following descriptors: *Salmonella typhi* AND *Salmonella* infections AND Food contamination AND water contamination effects AND cross-contamination AND child AND pregnant women AND frail elderly AND immunosuppressed patients AND tropical zone AND climate effects AND gastrointestinal diseases AND typhoid OR Typhoid Fever, provided by Health Science Descriptors (DeCS) [20], in English, Portuguese, French, and Spanish, without filters.

This review aimed to answer the following research question: "*What are the determinants of the exposition, occupational and knowledges are associated with TF occurrence in countries where communicable diseases also occur*?". To answer this question, were delineated the PECOS as follows: Population – any age group; Exposition: living in region with the presence of *Salmonella typhi* in food and/or drinking water with inadequate hygiene practices and sanitation and recent contact with someone who had TF low social economic status, low education level and disbalances biological parameter; Comparator – living in an urban city or region where *Salmonella typhi* is not present in food and drinking water, adequate hygiene practices and sanitation, or without having had contact with someone who had TF higher social economic status and education level, balanced biological parameter and the outcomes; Studies – observational studies [21].

2.2. Inclusion Criteria

To be included in this study, the articles needed to contain information about the association or relation with food, water, hygiene practices, and TF cases. The studies also had to address the effects of poor sanitation, detailing the prevalence or incidence of the people with percentage (%) those consumption of contaminated water and or food and TF occurrence. And other hand we included also all studies that showed other results that were associated with TF and which were not expected Systematic reviews, manuscripts, and articles that assessed diagnoses, laboratory tests, laboratory specimens, sample sizes of the cases and controls, samples of foods and water analyzed; studies that described the treatment or use of vaccines were excluded.

2.3. Result Screening and Data Extraction

All articles were recorded in a spreadsheet in Microsoft Excel® after completing searches and eliminating duplicates for each database and among databases. Three researchers selected the articles independently. In the case of divergence, the researchers discussed the article and reached an agreement. This review used cohort, longitudinal case-control, and repeated cross-sectional studies.

2.4. Assessment of the Quality of the Studies

The quality of the studies was assessed according to the checklist of the Joanna Briggs Institute (JBI), Critical Appraisal Tools of the Faculty of Health and Medical Sciences at the University of Adelaide, South Australia [22]. Based on the checklist, each question should be answered through four options: Yes (Y), No (N), Unclear (U), and Not Applicable (NA). The bias risk percentage calculation was performed based on the amount of "Ys" in the checklist. When "NA" was selected, this question was not considered in the calculation, according to the guidelines of the JBI. This tool classified the studies as follows: up to 49% was considered a high risk of bias, from 50% to 70%, the risk of bias was moderate, and above 70%, there was a low risk of bias. The risk of bias was not used as an inclusion criterion.

2.5. Meta-Analysis

All articles that presented odd ratios regarding *Salmonella typhi* in drinking water and food, hygiene practices, knowledge of the TF disease, contact with persons with TF, and living in a camp of refuge or in the neighborhood and confirmation of TF diagnosis were included in the meta-analysis. The generic inverse-variance pooling method was used to combine associations from different studies into one pooled odds ratio estimate (Mathias Harrer, Pim Cuijpers, Toshi A. Furukawa & Ebert., 2021). The associations were systematized, and the meta-analysis was conducted in the software RStudio (IDE) version 4.0.4 with the metafor package. In addition, the information was plotted on a graph, using the forest function of the metafor package to generate forest plot graphs [23]. To detect studies that contributed to heterogeneity and the overall result, the Funnel plot was evaluated using the metafor package to perform Funnel plot graphs [24]. The plot's horizontal axis illustrates heterogeneity, whereas the vertical axis illustrates the influence of a study on the overall result. Studies located in the inside of the quadrant significantly to both factors [25].

3. Results

A total of 2,246 articles were found in all databases. After elimination of duplicates and reading titles, abstracts, and complete articles, we included 31 studies. After reading the eligible articles, we excluded 7 articles, resulting in a total of

24 articles (Figure 1). The studies provided data from 1990 to 2020 and these were conducted in Latin America, the Eastern Mediterranean region, Southeast, Central, and Eastern Africa, Central, Southwest, East, Western, and Meridional Asia, the United Kingdom, Southeast Europe, and the Western Pacific. The sample size varied between 33 to 8,918 people of all ages and gender. Of these studies, 10 showed results only for children (3 in under five-year-old childes and 7 in children between 5 and 15 years), 8 showed results for all ages, and 6 showed results only for adults.

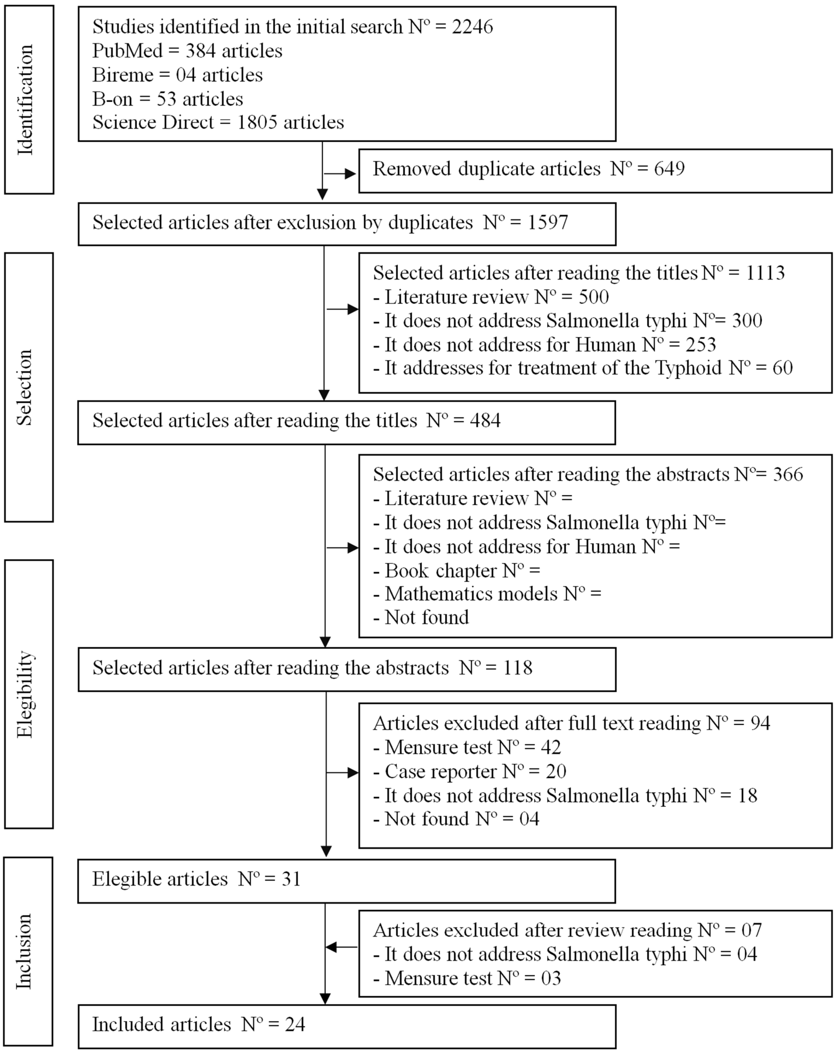

Figure 1. *Identification and selection of articles.*

Of the 24 studies assessed, 100% reported the occurrence of TF and the global range variety between 1,1% in Indian children to 93% in Vietnamese and Turkey. In Indian children, the prevalence was higher (2,6%) in children that consumed contaminated drinking water compared 0.2% observed in children did not consume contaminated drinking water [26]. In Vietnam TF was reported in people of all ages and occurrence of TF were associated with food intake, contact with positive TF cases, people of the low social economic status and people drinking untreated water [27]. In Turkey occurrence of TF was shown in people under 30 years and these were associated with abdominal distention symptoms [28].

In all studies, the prevalence of TF was associated with principal variables related to TF occurrence. In 10 (41.7%) studies, there was an association between TF and contact with someone who had TF and lived in the same household, community, or hospital [27–36]. In 9 (37.5%) studies, the occurrence of TF was associated with inadequate hygiene practices [27, 29, 32–34, 36–38] whereas in 6 (25.0%) studies, there was an association with the consumption of contaminated food [27, 30, 31, 33, 37, 39]. In 5 (20.8%) studies, untreated water was associated with TF [26, 27, 31, 34, 39] and the patients were younger than 30 years [28, 36, 38, 40, 41]. In 4 (16.7%) studies, there was no schooling [27, 37, 42], and the subjects lived in refugee camps or in a community [27, 31, 37, 43]. In 3 (12,5%) studies, the subjects had no knowledge of TF (Table 1) [33, 36, 37].

Only few studies, TF occurrence was higher in people with a low socio-economic status [29–31], with an imbalance of biochemical parameters [43, 44], in males [27, 31, 33, 39, 45], in people with clinic symptoms such as diarrhea or abdominal distention [28, 38, 46], in people that travelled [27], in summer

[41], and in people younger than 30 years (Table 1) [28, 38, 41].

The typhus fever-associated factors were as follows of the odds ratios and 95% of the confidence interval were: for people who had consumed untreated drinking water and contaminated food, 4.33 [27, 31, 39]; incorrect hand washing, 6.50 [27, 31, 37, 39]; contact with someone who had TF, 2.01 [33, 36, 37]; no knowledge about TF, 2.90 [27, 28, 31, 33, 35, 37]; living in a refugee camp or in a community, 2.15 [33, 36, 37]; confirmed diagnosis, 3.60 (Figures 2, 4, 6, 8, 10, and 12) [27, 31, 37].

Despite the high heterogeneity, all studies included in the meta-analysis showed a direct and strong association, corroborating the systematized result. Based on the Funnel plot, all studies contributed to heterogeneity (Figures 3, 5, 7, 9, and 11). However, four studies could be highlighted [28, 31, 33, 39], and one study [35], influenced more the meta-analysis related to TF occurrence because of the contact with someone who had TF (Figure 9), but it did not reduce heterogeneity.

The studies included in this review had a low risk of bias, with positive responses greater than 70%, indicating optimal methodological quality [22]. According to the quality analysis of the studies, 75% of the studies did not report a completed follow-up. However, the other items were attended in all studies. Therefore, the authors consider that all articles had a high methodological quality (Figures 14, 15, and 16).

Table 1. *Characterizations and main outcomes of the studies.*

Author, Year and country	**Sample/ages**	**Prevalence**	**Prevalences distribuition (test)**	**Associations of the exposition variable with TF occurrence**			
Alvarez et al, (1190) [29], Santiago – Chile	40 children ages for 7 to 9 yrs old Group A: 20 (Low SES) Group B: 20 (Higher SES)	Global: n=23 (57,5%)	Group A: n=13 (65%) Group B: n=10 (50%) - - -	Recently contact of the children with their TF mother	Low SES	Higher SES	
				Purchase of sweets and similar products without wrapper	66,6%	11,8%	p<0,001
				Adequate purchase of sweets and similar products	30,0%	75,0%	p<0,01
				Underclothes dirtied with faces in child`s	80,0%	40,0%	p<0,001
				Dirty edges of toilet bowl in children	75,0%	35,0%	p<0,001
Alvarez et al, (1190) [30], Santiago - Chile	527 children ≥ 6 to 9 yrs old	Global: n= 264 (50%)	- - - (Widal test Hemogram)			x^2 (GL)	
				Family with children who had carrier		4,029 (1); p<0.05	
				Presence of the *S. Typhi* in Low SES people		4,043 (1); p<0.05	
						To had carriers *S. Typhi* don't to have any disease	
				Buy unwrapped sweets		7,60 (1); p<0.01),	
				Don't to have toilet		Fisher test =SD, p<0.05	
				Inadequate wash hand		Fisher test =SD, p<0.05	
				Inadequate food preparation		4,902 (1); p<0.05	
				Fecal-oral cycle		Fisher test =SD, p<0.01	
Benkorbi et al, (1992) [45], El-Kettar, Argelia	1310 children ages between 5 and 14 yrs old	Global: n=123 (9,3%)	Complication with TF: more than in male (67.4%) (p=0.0001).			People to have complication of this diseases too x^2 (GL)	
				Male		11,99 (1); p=0.0001	
Trevett et al, (1994) [46], Papua New Guinea	33 patients > 18 yrs old Ataxia group: n=14 No ataxia group: n=19	Global: n=14 (42,4%)	Costal region: 64,3% (Kodak XAR 5® film (Sigma))		Ataxia	No ataxia	
				Unsteadiness/falls	14	5	p< 0.0005
				Tremor	11	1	p< 0.005
				Hypotension	6	1	p< 0.05
				Sodium (rnmol/L)	125.3 (4.6)[a]	132,4 (4.6)	p< 0.005
				Albumin (g/L) a: means (standard deviation	24,2 (4,3)[a]	28,6 (5,7)	p<0.05
Sinha et al, (1999) [40], Kalkaji, New Delhi, India	6454 patients of all ages	Global: n=63 (9,8%)	Ages: Under 5 (27,3%) 6-19yrs (11,7%) 20-40yrs (1,1%) (Blood culture)	Between incidences ages:		Difference of incidence of TF in age under 5 Difference in % (95% IC)	
				5 – 19 yrs		15,6 (4,7; 26,5) p< 0.001	
				19 – 40 yrs		26,2 (16,0; 36,3) p< 0.001	
				Morbidity was associated with TF in children under five.			
Aghanwa and Morakinyo (2001) [38], Lagos -southwest Nigeria	136 patients >15 yrs old	Global: n=136 (100%)	- - - (Widal test)			People with psychiatric comorbidity too x^2 (GL)	
				Ages between 16 and 20 years old		5,83 (1); p=0.01	
				Deaharea		6,71 (1); p=0.009	

Author, Year and country	Sample/ages	Prevalence	Prevalences distribuition (test)	Associations of the exposition variable with TF occurrence			
Luxemburger et al, (2001) [31], Vietnam	437 patients of all ages	Global: n=139 (93%)	Age <15 yrs old (70%) Man (51%) Live in town (63%)	Unadequatted biochimic indicator	7,12 (1); p=0.01		
					OR (IC 95%)		
				Recently contact in hospital	4,3 (1,4; 13,4); p=0.01[1]		
				Recently contact in community	11,9 (2,3; 60,7); p=0.04[1]		
				Low SES in hospitalization patients	2,5 (1,3; 5,1); p=0.02[1]		
				Low SES in community people	2,9 (1,5; 5,3); p=0.01[1]		
				Eating ice-cream every day	8,0 (1,7; 170,6); p=0.04[2]		
				Eating shellfish regular (≥ once per month)	0,5 (0,3; 1,0); p=0.02[1]		
Tran et al, (2005) [27], Son La – Hanoi: Vietnam	617 patients of all ages	Global: n= 90 (14,7%)	Sex: Male (73,4%) Female (26,6%) Age: 20-40 had more cases Under 5 yrs. not detected		OR (95% CI)		
				No schooling	2,0 (1,0; 3,7); p=0.03[1]		
				Contact	3,3 (1,7; 6,2); p=0.001[1]		
				Living in neighborhood	4,2 (2,2; 8,0); p<0.001[2]		
				History travel	4,3 (1,2; 14,7); p<0.01[2]		
				Eating outside	6,4 (1,3; 32,2); p<0.01[2]		
				Eating shellfish	1,8 (1,1; 3,2); p<0.04[2]		
				3-4 times/week	9,7 (2,9; 33,0); (x^2=15,5) p<0.001[2]		
				Untreated water	3,9 (2,0; 7,5); p<0.001[1]		
				Sewage disposal directly to the environment	4,2 (1,0; 5,8); p<0.03[2]		
				1. OR adjusted. 2. Unadjusted OR			
Sur et al, (2006) [32], Kolkata - India	3371 individuals of all ages	Global: n=95 (2,8%)	- - - (Widal test, Blood culture and Ultrasongraphy: USG)		People with Malaria too	Only TF people RR (95% IC)	
				Household member with Malaria	0,2 (0,0; 0,9) p<0.05	- - -	
				Household member with TF	- - -	3,8 (1,5; 9,4 p<0.01	
				Do not regularly wash hand after defecation	- - -	1,9 (1,1; 1,7) p<0.05	
Siddiqui et al, (2006) [41], Karach-Pakistan	1248 children <16 yrs old	Global: n=341 (27,3%) Incidence: 11,7%	Higth incidence of TF was May to June and October (summer months) p<0.05 (Blood culture and Typhidot test)		People measured with Blood culture	measured with Typhidot test	
				RR (95% CI)			
				Ages >5 – 10*	2,5 (1,3; 5,0)	2,1 (1,5; 2,8) p<0.05	
				Ages >10 – 15	2,0 (1,0; 4,7)	2,5 (1,7; 3,6) p<0.05	
				Higth incidence of TF was May to June and October (summer months) p<0.05			
Hosoglu et al, (2006) [28], Turkey	260 patients ≥ 15 to 30yrs old	Global: n=121 (93%)	- - - (Widal: 46%)		OR (95% CI)		
				Age ≤30yrs	5,06 (1,49; 17,24); p=0,01		
				Abdominal distention	81,58 (8,63; 771,39); p<0,001		
				Confusion	23,37 (6,31; 86,63); p<0,001		
				Positivity in widal test	15,24 (4,17; 55,65); p<0,001		
Naheed et al, (2008) [47], Bangladesh	867 children under 5 yrs old	Global: n= 43 (4,95%)	Ages: <5yrs old (63%) (Blood culture: 5%, Tubex™: 22% e Typhidot®: 26%)	With negative results of Blood culture			
				Tubex test	+	-	
				Typhidot tes	+	-	
				Duration of fever when sample collected (median days)	3 (1-21)	3 (1-30)	p<0.05
				Illness requiring hospitalization n (%)	0	8 (2)	p<0.05
				Duration of fever after the initiation therapy (median days)	3 (1-36)	2 (1-36)	
Siddiqui et al, (2008) [33], Karach-Pakistan	253 children for 1 to 15 yrs old	Global: n=88 (34,8%)	Male (59,1) Drinking water tap (81.8%) With flush toilet (61,4%) (Typhidot)	OR (95% CI)			
				Never Food kept in fridge	2,4 (1,3; 4,7)	p<0.05	
				Never Food reheated for child	2,8 (1,1; 7,0)	p<0.05	
				Taking meal outside home (1-6 times a week)	6,3 (1,8; 22,0)	p<0.05	
				Number of persons in household	1,9 (1,2; 3,1)	p<0.05	
				Lack soap for hand washing	2,6 (1,1; 6,3)	p<0.05	
				No use medicated soap	11,2 (1,3; 97,6)	p<0.05	
				Lack awareness about contact with a case of TF	3,7 (1,6; 8,4)	p<0.05	
Yu et al, (2008) [48], Taiwan	33 patients for 1 to 68 yrs old Group I: ≤17 yrs old: n=14 Group II: >17 yrs old: n=19	Global: n=33 (100%)	- - - Widal test		Group I	Group II	
				Travel	1	9	p<0.045
				Chill symptom	1	11	p<0.004
				Total leukocytes	8093 (948)	5458 (476)	p=0.012
				- Segments (%)a a. means (standard deviation)	61 (4)	72 (3)	p=0.038
Dhadwal & Shetty, (2008) [26], Kolkata - India	8918 children ages 5 to 17 yrs old	Global: n=98 (1,098%)	Consummer contaminated water: 2,63% than		RR (95% CI)		
				People who consumed contaminated water	13,7 (10,8; 16,12)	p<0.00	

Author, Year and country	**Sample/ages**	**Prevalence**	**Prevalences distribuition (test)**	**Associations of the exposition variable with TF occurrence**
Ademuyiwa et al, (2012) [44], Abeokuta-Nigeria	139 patients for 12 to 46 yrs old	n= 43 (37,4%)	these did not 0,19% (Widal test) Cont TF PCV + ++ RBC GSH ++ + RBC CAT - ++ Plasma CAT - ++ Plasma GST + ++ P<0.05 (Widal: 37%)	Correlation coefficient (r) Plasma GSH vs RBC CAT 0,305; p=2x10-4 Plasma CAT vs RBC CAT 0,481; p=1x10-9 RBC CAT vs RBC GSH -0,270; p=9x10-4 Plasma GSH vs RBC GSH 0,326; p=7x10-5
Sahu et al, (2016) [49], Odisha -India	52 patients for 4 to 14 yrs old	Global: n=32 (61,5%)	- - - (Widal, Blood culture, Ultrasonography: USG)	People with Splenomegaly too; other with MLNs Follow-up scan in day 5 32 (100%) 30 (100%) Follow-up scan in day 10 29 (90.6) 21 (70) Follow-up scan in day 15 19 (59.3) 12 (40%) p<0.05
Ali et al, (2017) [34], Congo	320 Children >7yrs old and adults	Global: n=320 (100%)	n=59 (Military camp) n=261 (general population)	To share only one latrine in household (P=0.02), Available soap in household (P=0.006), Taps in household as principal source of water (P<0,001), Ease of accessibility of drinking water (P=0.03), Affordable or treated/protected water (P<0.001), Capacity of water containers and principal water container cover (P<0.001)
Darton et al (2017) [35], United Kingdom	41 people for 18 to 60yrs old	Global: n=24 (58,5%)	- - - (PCR 8,3%, Blood culture: 7,9%)	OR (95% CI) Early stool shedding and culture-PCR assay positivity Fisher test; p=0.63 Early positive PCR result was not predictive of subsequent reinfection 0,57 (0,12; 2,71); Development of *S. Typhi* bacteremia 0,50 (0,10; 2,44); p = 0,45 Confirmation of typhoid diagnosis capacity between Culture-PCR and blood culture both positive t-test (−0,75; 2,22); p = 0,31
Kabwama et al, (2017) [39], Uganda	111 patients for all ages	Global: n=56 (15%)	Men: 60%, Age 20-39yrs: 85% (TUBEX® TF test, blood culture)	OR (95% CI) Drank locally packaged water 8,9 (1.60; 49.00); Drank locally-made passion fruit juice 4,6 (1.90; 11.00); Drank locally-packed pineapple juice 2,0 (0.74; 5.20); Drank cold Millet porridge 2,8 (0.76; 10.00); Consumed one 1,9 (0,68; 5,10), two 3,0 (0,80; 11,0) three to four 29,0 (3,2; 26,0) sources of water X^2= 14.65, p < 0.001.
Nahimana et al, (2017) [36], Maham Camp-Rwanda	671 burundian people ages above 15 yrs	Global: n= 170 (25,3%)	The proportion of people who reported to always wash their hands before eating and after using the latrine had increased significantly to 71.3% and 71.7%, respectively (p < 0.001).	>6 months living in refugee camp Adjusted OR (95% CI) Not wash hand before eating 1,86; 95% IC: 1,17-2,29; p=0.008 Not wash hand after using latrine 2,24; 95% IC: 1,40-3,61; p=0.001 Not heard about TF 2,31; 95% IC: 1,59-3,35; p<0.001 Not know how spreads TF 1,80; 95% IC: 1,25-2,58; p=0.002 Not know how is prevented TF 1,76; 95% IC: 1,22-2,52; p=0.002 Fecal disposal other than pit latrine 0,10; 95% IC: 0,02-0,36; p=0.001 Ages ≥ 35 yrs old Not wash hand before eating 1,47; 95% IC: 1,01-2,16; p=0.045 Not wash hand after using latrine 1,47; 95% IC: 1,05-2,32; p=0.047 Not received health education 0,64; 95% IC: 0,44-0,92; p=0.016
Nyamusore et al, (2018) [37], Rwanda	1030 patients of all ages	Global: n=260 (13,7%)	5 – 14 yrs old: 24,4% - - - Water used: Hannah Photometer for chlorine (RFC) and faecalis coliforms (TTP): 100% water up	>6 months living in refugee camp Adjusted OR (95% CI) Not wash hand before eating 1,86; 95% IC: 1,17-2,29; p=0.008 Not wash hand after using latrine 2,24; 95% IC: 1,40-3,61; p=0.001 Not heard about TF 2,31; 95% IC: 1,59-3,35; p<0.001 Not know how spreads TF 1,80; 95% IC: 1,25-2,58; p=0.002 Not know how is prevented TF 1,76; 95% IC: 1,22-2,52; p=0.002 Fecal disposal other than pit latrine 0,10; 95% IC: 0,02-0,36; p=0.001 Ages ≥ 35 yrs old
Ndako et al, (2020) [43], Omuran -	400 patients between 18 and	Global: n=200 (50%)	Masc Femin Cont PCV +++ + ++	OR (95% CI) Time spend in refugee camp > 6 months 2,89 (1,98; 4,20); p=0.000)²

Author, Year and country	Sample/ages	Prevalence	Prevalences distribuition (test)	Associations of the exposition variable with TF occurrence	
Nigeria	60 yrs old	Mile (50%) Female (50%)	WBC ++ +++ -	To have pre-school level	2,07 (1,11; 3,84); p=0.021[2]
			NEUT ++ - +++	To have in family member treated for TF in last 3 months	2,65 (1,84; 3,79); p=0.000[1]
			LYMP - + +++		
			ESR ++ +++ -	No heard about TF before the outbreak	1,63 (1,12; 2,38); p=0.011[1]
			HAEC +++ + +	Rarely washing hands after using the latrine	1,78 (1,21; 2,62); p=0.003[1]
			P<0.05		
				Be most common source for food prepared at home	2,75 (1,53; 4,96); p=0.001[1]
				Be most common to get food in community market	11,39 (2,10; 61,75); p=0.005[1]
				Be frequency of jerry-can washing in sometimes	2,07 (1,32; 3,25); p=0.002[2]
				1. OR adjusted. 2. OR not adjusted	
Masinaei et al, (2020) [42], Tehran- Iran	2474 patinetes the all ages	Global: n=all	Male: n=1112 (44,95%)		RR (95% CI)
				Win speed (km/h)	1,39 (1,15; 1,69) p<0.05
			Female: n=1362 (55,04%)	Public sewerage system:	0,76 (0,63; 0,92) (p<0.05)
				Years of schooling:	0,78 (0,65; 0,95) (p<0.05)
			Rural (38,97%)	Wealth index:	0,59 (0,55; 0,63) p<0.05
			Urban (61,93%) Ages: <15yrs (36,98%) vs 15 – 59 (53,19%) - - -	Urbanization	0,59 (0,48; 0,76) p<0.05

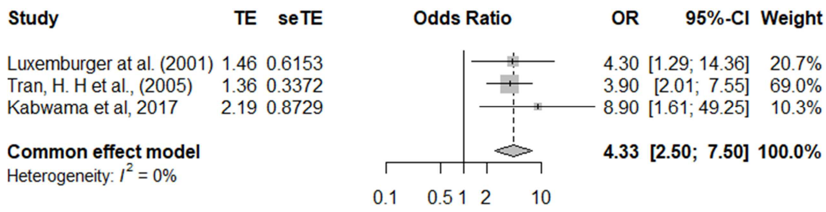

Figure 2. *Forest plot for association using odds ratio between consumption untreated drinking water and TF occurrence.*

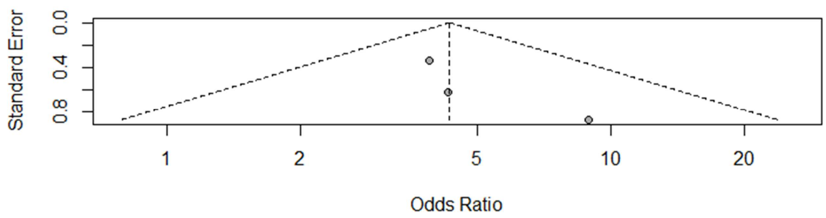

Figure 3. *Funnel plot of the studies identified in figure 2 that contributed to heterogeneity.*

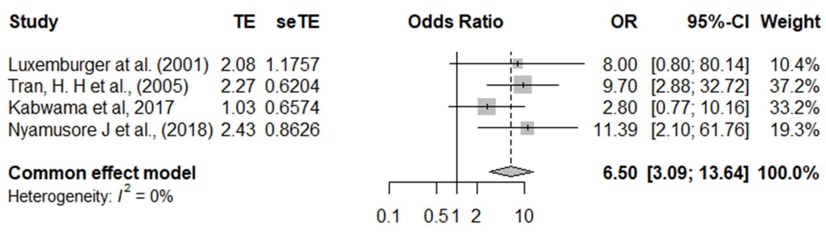

Figure 4. *Forest plot for association using odds ratio between food intake in risk for microbeam contamination and TF occurrence.*

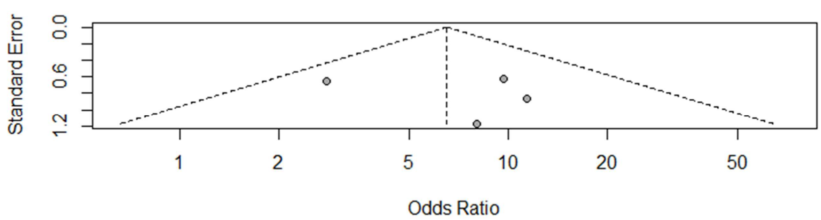

Figure 5. *Funnel plot of the studies identified in figure 4 that contributed to heterogeneity.*

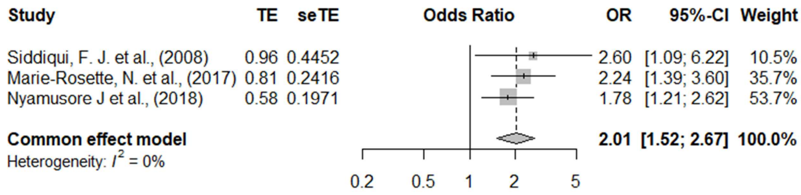

Figure 6. *Forest plot for association using odds ratio between incorrect wash hand and TF occurrence.*

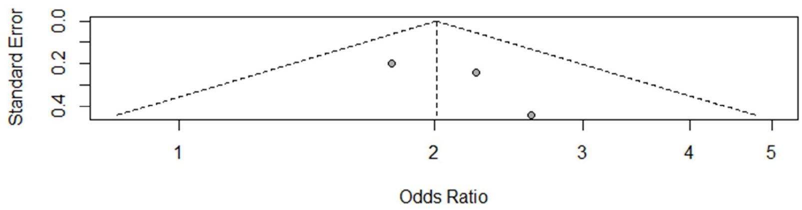

Figure 7. *Funnel plot of the studies identified in figure 6 that contributed to heterogeneity.*

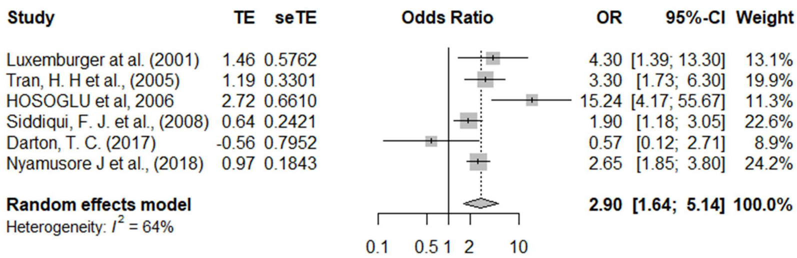

Figure 8. *Forest plot for association using odds ratio between contact with someone who had TF occurrence.*

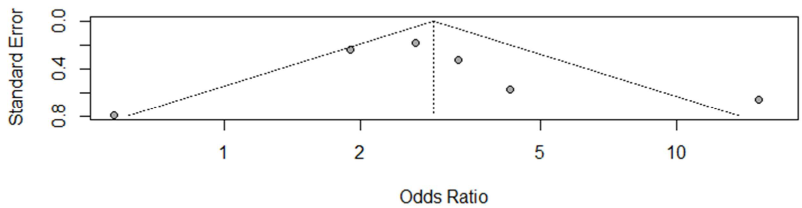

Figure 9. *Funnel plot of the studies identified in figure 8 that contributed to heterogeneity.*

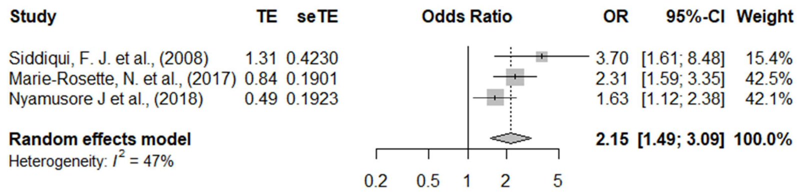

Figure 10. *Forest plot for association using odds ratio between lack knowledge's about TF disease and TF occurrence.*

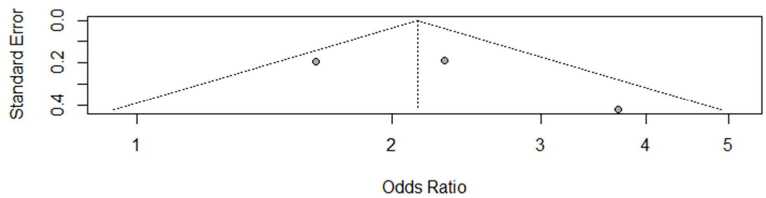

Figure 11. *Funnel plot of the studies identified in figure 10 that contributed to heterogeneity.*

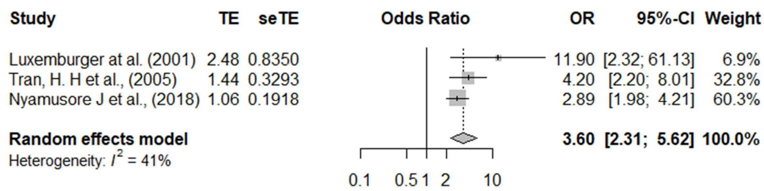

Figure 12. *Forest plot for association using odds ratio between living in refugee camp or neighborhood and TF occurrence.*

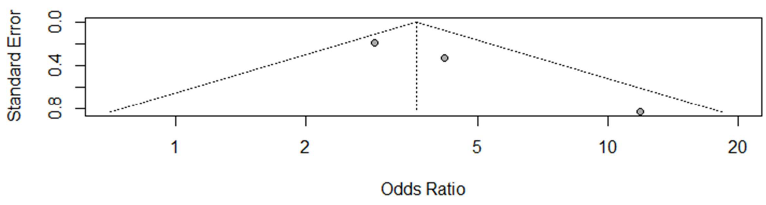

Figure 13. *Funnel plot of the studies identified in figure 12 that contributed to heterogeneity.*

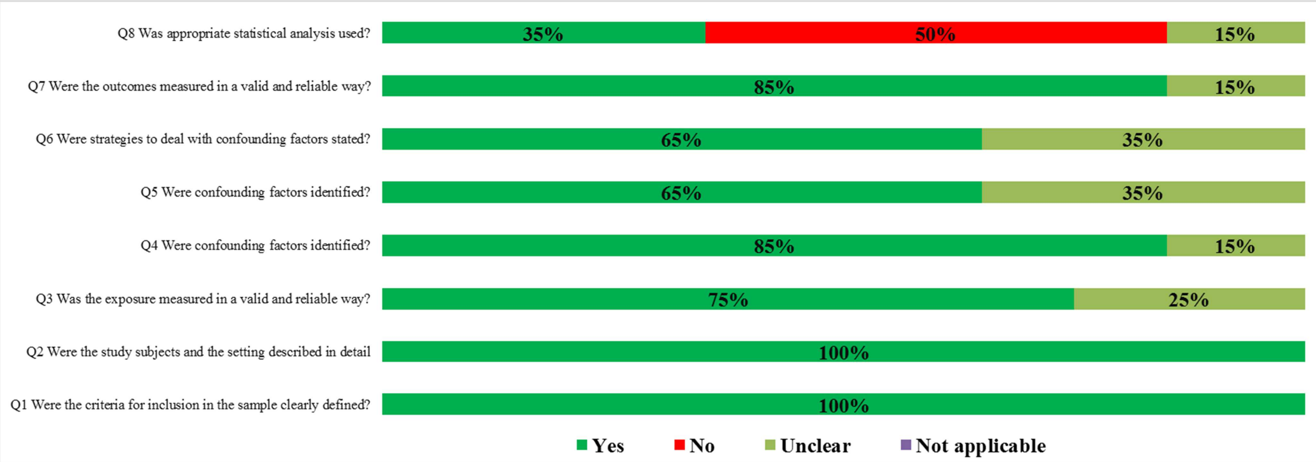

Figure 14. *Quality of cohort studies included.*

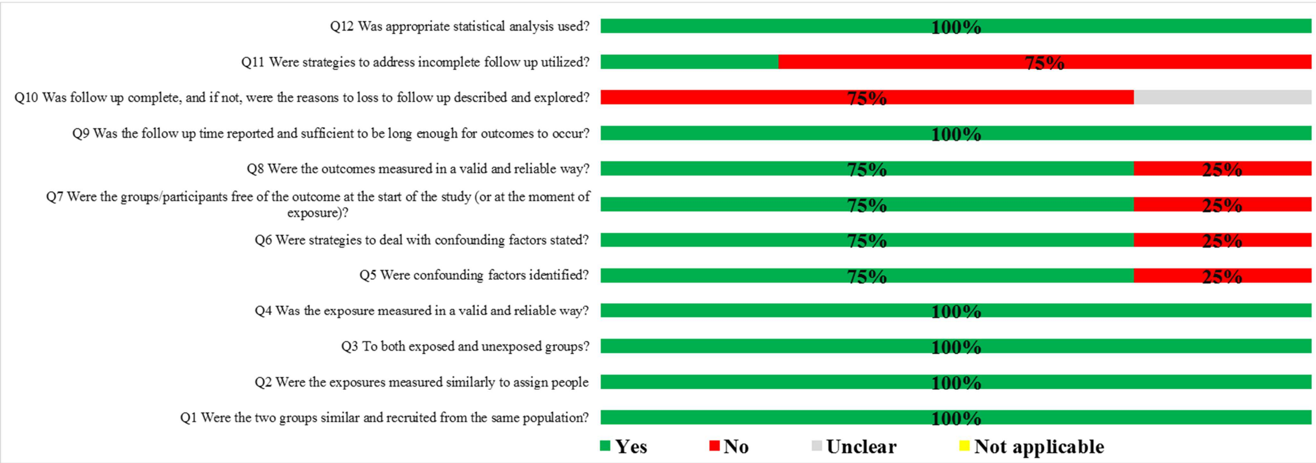

Figure 15. *Quality of case-control studies included.*

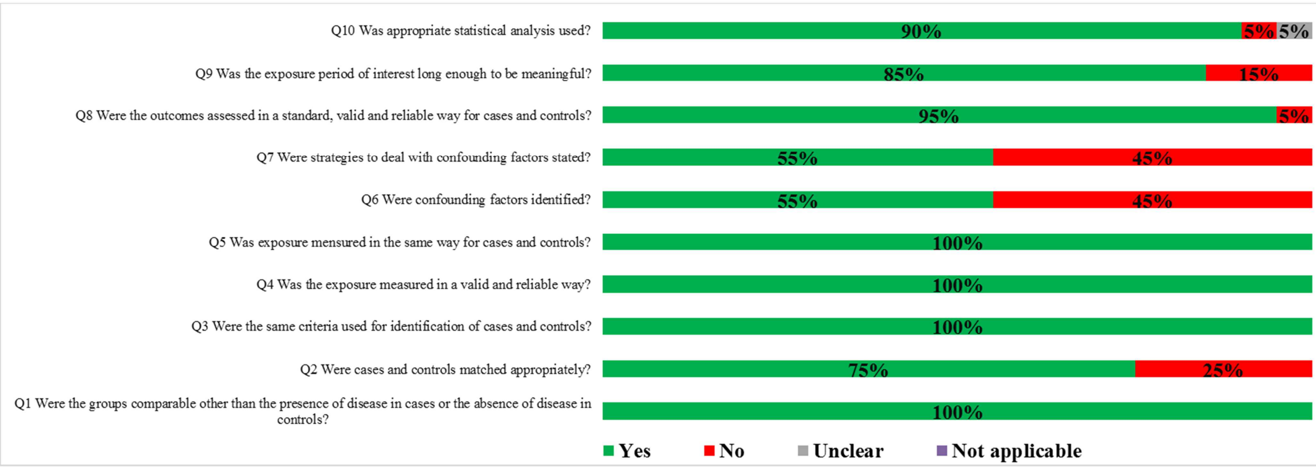

Figure 16. *Quality of cross-sectional studies included.*

4. Discussion

Based on our findings, there was a strong positive association between the occurrence of TF and untreated drinking water, contaminated food, inadequate hygiene practices, contact with someone who had TF, a lack of knowledge about TF, and living in a refugee camp or in the neighborhood. However, the consumption of contaminated food [27, 31, 39], and untreated drinking water [27, 31, 37, 39], were associated with higher probability of contracting TF, four and six times more than other factors, respectively. In Tanzanian citizens TF was common in all ages, and it was associated with contaminated food and untreated drinking water ($p < 0.05$) [49].

In 2017 and 2018, TF was high related to contaminated food compared to untreated drinking water in tropical Africa. Similarly, in studies on children and younger than 16 years, between 2013 and 2017 in Kenya [50], and in India in 2017 [51]. In an older study, performed between 1992 and 1994 in Indonesia on people older than 14 years, similar findings were observed. Untreated drinking water was consumed as ice cubes in beverages, resulting in a five times higher chance of contracting TF [52].

Two studies [27, 28], found similar outcomes for Vietnamese and Turkish citizens, and in one study [26], a higher prevalence of TF was observed in people who had consumed untreated drinking water compared to those who had consumed contaminated food. However, based on our findings, the prevalence of TF was higher in people that had consumed contaminated food.

Studies published or published research between 2018 and 2019 and in 2021 in India, targeting children and younger under 16 years, also reported an association of TF with contaminated food [53]. Importantly, the treatment of drinking water, such as via filtration, reverse osmose, or boiling, can decrease TF occurrence. In our results, we don't find the outcomes the effect of use treated drink water from these procedures, but we observed that the author referred the use well water associated with all techniques of the treatment of the drink water how being best to prevent for TF occurrence.

These scenarios are supported with other outcomes found in our results. For example, inadequate hygiene practices [33, 36, 37] can lead to *S. typhi* infections in co-occupied spaces because of the secretion of urine or feces from a person with TF or a high level of *S. typhi* [27, 28, 31, 33, 35, 37]. Infections with *S. typhi* are also higher among people with a low socio-economic status, people without knowledge of TF [28, 31, 33, 35–37], and people living in refugee camps or nearby [27, 31, 37]. These findings are supported by previous studies [50, 52].

Children between five and 15 years, were more susceptible to TF [26, 29, 30, 33, 41, 45, 49]. Probably, this age young consumed more food from street food and do not observe good hygiene practices. Another author found a high TF prevalence in children between 5 and 8 years old ($p < 0.05$) [50]. Children are generally easily infected with S. typhi, with a higher chance of complications; also, males are more often affected than females [27, 31, 33, 39, 45]. Other studies also found a higher prevalence in males, mostly linked with issues in good hygiene and sanitation [50, 54].

In many cases, *Salmonella* was present on surfaces, water, or food or was contracted from someone who had TF. Such scenarios are frequently observed for people with a low socio-economic status, no or little schooling, and travelers. We were not expected to find such results in our outcomes. To ensure a substantial typhoid reduction by 2035 [6], strong policies regarding sanitation, health education, and good hygiene practices are necessary, along with education about the sources of *Salmonella typhi* transmission.

Improved diagnosis practices are also required, such as the Widal test. Diagnoses and intervention are ideally made in the months between April and August or in warmer months with higher rainfall. It is also recommended to perform more original studies to diagnose TF in people that live in environments where *Salmonella typhi* is present. Finally, new technologies for the elimination of *Salmonella typhi* from food and water are needed.

5. Conclusions

The probability of contracting TF ranges between two- and six-fold in cases of: contact with an infected person, the consumption of contaminated food and water, poor hygiene practices, the living in a refugee camp, and lacking knowledge about TF. Consequently, contaminated food and water as well as inadequate living conditions are the main reasons for contracting TF.

In development countries the main causes of the occurrence communicable diseases are microbiologic contamination from inadequate hygiene practices associated with poverty and low living conditions the people that majority of whom are low social economic status.

The sub-Saharan countries living with this reality. On the basis of this is important to develop strategies to guarantee safe food and water sources and to improve sanitation in urban areas. Further studies on TF prevalence are needed to determine the current exposition in consideration of this outcomes.

Conflicts of Interest

The authors declare no conflicts of interest.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

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