OPEN

Nontyphoidal Salmonella Outbreaks Associated With Chocolate Consumption

A Systematic Review

Zacharie Patà, MD,* Pietro B. Faré, MD,†‡ Sebastiano A. G. Lava, MD,§¶ Gregorio P. Milani[®], MD,||** Mario G. Bianchetti, MD,* Simone Janett, MD,†† Isabella Hunjan, MD,*, and Lisa Kottanattu, MD‡‡§§

Background: A large, cross-border outbreak of nontyphoidal salmonellosis connected to chocolate product consumption was recently reported. This occurrence motivated us to conduct a comprehensive review of existing literature concerning outbreaks of nontyphoidal salmonellosis associated with chocolate consumption.

Methods: We performed a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PROSPERO CRD42022369023) in 3 databases: U.S. National Library of Medicine, Web of Science and Excerpta Medica. Google Scholar and the bibliography of each identified report were also screened. Eligible were articles published after 1970, describing outbreaks of more than 10 patients with a nontyphoidal salmonellosis associated with chocolate consumption.

Results: Twenty-three articles were included, which described 12 outbreaks involving a total of 3266 patients. All outbreaks occurred in high-income countries: 1 was limited to 1 city, 6 involved 1 country and the remaining 5 involved 2 or more countries. Six outbreaks peaked in winter, 3 in autumn, 2 in spring and 1 in summer. Children were mainly affected. No predominant serotype was identified.

Conclusions: Our data documents that chocolate is an optimal medium for the transmission of nontyphoidal salmonellosis. A connected worldwide reporting system including high-income, middle-income and low-income countries is crucial to detect infectious diseases outbreaks in an early phase and avoid their spread.

Key Words: child, chocolate, nontyphoidal salmonella, outbreak

Accepted for publication December 16, 2023

*From the Family Medicine Institute, Faculty of Biomedical Sciences, Università della Svizzera Italiana; †Department of Internal Medicine, Ente Ospedaliero Cantonale, Lugano, Switzerland; †Department of infectious diseases, University Hospital Zurich, Zurich, Switzerland; §Pediatric Cardiology Unit, Department of Pediatrics, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland; ¶Clinical Pharmacology and Therapeutics Group, University College London, London, United Kingdom; ||Pediatric Unit, Fondazione IRCCS Ca¹ Granda Ospedale Maggiore Policlinico, Milan, Italy; *Pepartment of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy; ††Sleep Center, Neurocenter of the Southern Switzerland, Ente Ospedaliero Cantonale; ‡‡Faculty of Biomedical Sciences, Università Della Svizzera Italiana, Lugano, Switzerland; and §§Pediatric Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland.

The study was partially funded by the Italian Ministry of Health (Ricerca Corrente).

The authors have no conflicts of interest to disclose.

Z.P. and P.B.F. contributed equally to the work as co-first authors.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.pidj.com).

Address for correspondence: Gregorio P. Milani, MD, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, via della Commenda 9, Milan, Italy. E-mail: milani.gregoriop@gmail.com.

Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ISSN: 0891-3668/24/435-420424

DOI: 10.1097/INF.00000000000004252

(Pediatr Infect Dis J 2024;43:420–424)

Domestic and wild animals, including mammals, poultry and reptiles, are the natural hosts of nontyphoidal Salmonella (hereafter referred to as Salmonella, for simplicity), which is one of the most frequently reported causative agents for foodborne outbreaks worldwide. 1-3 Traditionally, foodborne Salmonella infections have been associated with eggs and poultry. 1-3 Nowadays many other foods are implicated, such as dried fruits and vegetables, nuts, spices, cereal-based and confectionery products. 1-4

The link between chocolate consumption and nontyphoidal salmonellosis has been established since the 1950s, with several documented outbreaks in the literature.¹

Over the past 5 decades, considerable progress has been made in optimizing the food supply chain, including improvements in production and distribution processes. These advances have been mainly developed in high-income countries (HICs). Surveillance systems at national and supranational levels, such as Pulse NET (in the US) and the European Centre for Disease Prevention and Control in Europe, play a crucial role in monitoring the epidemiology of nontyphoidal Salmonella infections. Rapid disease cluster detection, sharing of molecular subtyping data via surveillance reports or online platforms like Enterobase and close collaboration with the Food and Drug Administration in the US and the European Food Safety Authority in Europe are essential in reducing the likelihood of widespread outbreaks. Such structured networks are less common in middle-income countries and low-income countries, although efforts to improve the situation, such as the PulseNet International network, are underway in a subset of countries.

The increasing globalization has amplified the potential for a single outbreak to spread rapidly, thus affecting a very large number of subjects.^{2-4,5}

In spring 2022, a large outbreak of nontyphoidal salmonellosis linked to chocolate products from a factory in Belgium affected more than 450 patients in 16 countries.⁶

The existing literature lacks a comprehensive epidemiologic analysis of the characteristics, patterns and outcomes of outbreaks of nontyphoidal Salmonella infections linked to the consumption of chocolate.

METHODS

Data Search

The protocol for this systematic review has been registered on PROSPERO (CRD42022369023). The principles underlying the UK Economic and Social Research Council guidance on the conduct of narrative synthesis and the 2020 version of the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were employed.7

A literature search with no language restrictions using the terms ("salmonella" OR "salmonellosis") AND "chocolate" was carried out using the US National Library of Medicine, Excerpta Medica and Web of Science databases in November 2022 and repeated before submission (August 10, 2023). Google Scholar and the bibliography of each identified report were also screened.8 Because reports published until 1970 were poorly documented, only reports published thereafter were considered.9

Eligibility Criteria, Data Extraction and Quality Assessment

For the final analysis, we retained exclusively outbreaks of more than 10 patients diagnosed with an intestinal Salmonella infection following the consumption of any sort of food containing chocolate (such as confectionery products, cakes, pastries and ice cream). Chocolate-containing food had to have been considered as the source of infection according to one of the following 3 conditions: (1) microbiologic studies revealing the presence of the same Salmonella strain in both fecal specimens and food samples; (2) epidemiologic evidences indicating that all infected individuals consumed the same food; (3) a combination of both microbiologic and epidemiologic evidences.

The following data were extracted from the included papers: timeframe and geographic area of the outbreak, chocolate vehicle, microbiologic studies in fecal samples and/or in the vehicle of infection, number of cases, demographics, hospitalization rate, complications and outcome. If 2 or more reports provided information on the same outbreak, the corresponding data were cumulated. The Newcastle-Ottawa Quality Assessment Scale was employed to assess the risk of bias in the included studies.10

Two authors (Z.P. and P.B.F.) performed in duplicate the literature search, the selection of eligible reports, data extraction and quality assessment. Disagreements between individual judgements were solved by consensus meetings with a third author (L.K.). The data were input into a predefined worksheet by one author (Z.P.) and the accuracy of the data entry was verified by the second author (P.B.F.).

RESULTS

Search Results and Quality of Studies

The literature search process is summarized in Figure, Supplemental Digital Content 1, http://links.lww.com/INF/F396. Twentythree articles published between 1972 and 2022 were retained for the final analysis: 20 were written in English, 1 in Italian, 1 in Norwegian and 1 in Swedish. 6,11-32 The mentioned articles describe 12 outbreaks of nontyphoidal salmonellosis linked with chocolate consumption. The risk of bias assessment score could only be calculated for 7 studies (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/F397) that were classified as case-control studies. Only 2 studies were of good quality. 18,25 The remaining studies could not be analyzed because they did not meet the criteria for classification as either case-control or cohort studies.

Findings

The characteristics of the 12 outbreaks, involving a total of 3266 patients, are presented in Table 1. Two outbreaks took place in the 1970s, 3 in the 1980s, 1 in the 1990s, 3 in the decade 2000– 2009 and 3 thereafter. Six outbreaks peaked in winter, 3 in autumn, 2 in spring and 1 in summer.

One outbreak was limited to 1 city. Six outbreaks involved 1 country and the remaining 5 outbreaks involved 2 or more countries. On 3 occasions, the outbreak spread across 2 continents.

No predominant Salmonella serotype was identified. Between 1970 and 1989, conventional microbiologic laboratory techniques were applied to identify the responsible strain. 11-19 Subsequently, pulsed-field gel electrophoresis, 20,24,27,28 multilocus variable-number tandem repeat analysis²⁷ and whole genome sequencing^{6,30,31} were also employed. The number of cases in each outbreak ranged from 29 to 1111, median 115 cases (interquartile range: 77–385 cases). In 4 studies, the median age of the patients was not provided. Among the remaining studies, the median age ranged from 3 to 15 years. The hospitalization rate ranged between 3% and 41%, median 16% (interquartile range: 10%-29%). No infections involving the bloodstream or other normally sterile sites and fatalities were reported as a direct consequence of the Salmonella infection.

DISCUSSION

Chocolate has peculiar characteristics that make it an optimal medium for the spread of Salmonella. Three factors account for that. First, the low water content and the high fat level of chocolate increase the thermal resistance of Salmonella. Second, higher temperatures during chocolate production, despite eliminating Salmonella, would worsen its taste. Third, Salmonella may persist for more than 1 year in chocolate. These factors, combined with the very small amount of Salmonella required to initiate an infection, illustrate the challenge of preventing outbreaks of this infection.^{33–37}

This systematic literature review describes the characteristics of 12 human nontyphoidal salmonellosis outbreaks associated with chocolate consumption in the past 50 years. Between 1 and 3 outbreaks occurred during each decade. All the reported outbreaks were observed in HICs. This finding may be related, on one hand, to the large availability of industrially produced food and, on the other hand, to the presence of effective outbreak detection and control networks in these countries. It is also conceivable that outbreaks detected in middle-income and low-income countries have not been reported.

techniques Conventional culture-based diagnostic are time-consuming and labor intensive. Today's molecular methods offer rapid and precise detection, enabling early identification and management of foodborne illnesses.³⁸

The results of this review confirm that nontyphoidal salmonellosis occurs most often in children. However, the factors underlying this tendency are elusive. First, it has been suggested but never proven that children might be more susceptible to intestinal infections because the immune system is still developing. Second, person-to-person transmission of Salmonella might likely be more common in children due to behaviors that increase germ exposure (such as putting hands contaminated with bacteria into mouth and having less developed hygiene practices). Additionally, the allure of chocolate in children could also play a contributing factor. 1-3,32-34,39

Nontyphoidal salmonellosis outbreaks typically occur during warm season. The majority of Salmonella outbreaks temporally associated with chocolate consumption were observed in the cold season. We speculate that very popular seasonal products such as chocolate Santa Clauses and chocolate Easter bunnies might account for this observation.

No cases of death were reported, likely because nontyphoidal Salmonella disease is self-limiting and does not require treatment other than hydration. Furthermore, extraintestinal complications are uncommon in immunocompetent individuals living in HICs. 40

Characteristics of 12 Outbreaks of Nontyphoidal Salmonella Infections Associated to Chocolate Consumption, Between 1970 and 2022 (N = 3266 Patients)TABLE 1.

Year	${\rm Region}^*$	Vehicle	Salmonella Serotype Peak of Outbreak	Peak of Outbreak	Number of Cases	Median Age (Years)	Hospitaliza- tion Rate (%) References	References
1970–1971	Sweden	Chocolate balls	Durham	November- December	110	15	NA	11,25
1973–1974	United States, Canada	Chocolate balls	Eastbourne	November- December	119†	က	34	12,13
1982	United Kingdom, Italy	Chocolate bars	Napoli	June-July	272	15	19	14–16
1985 - 1986	Canada, Belgium, England, United States	Chocolate coins	Nima	December	29	4	NA	17,18
1987–1988	Norway, Finland	Various products containing chocolate	Typhimurium	March–April	361	‡9	NA	19,20
1998	United Kingdom	Chocolate mousse	Enteritidis	September	54	œ	9	23
2001-2002	Germany, Austria, Belgium, Canada, Croatia, Czech Republic, Denmark, Finland, Netherlands, Sweden	Various products containing chocolate	Oranienburg	October-November	538	15	38	21,22,24,25
2006	United Kingdom	Various products containing chocolate	Montevideo	March–April	42	NA	12	26,27
2007	United Kingdom	Chocolate coated nuts	Schwarzengrund	November- December	06	NA	NA	27
2018	Busan Metropolitan City (South Korea)	Chocolate cake	Thompson	September	1111	NA	14	28
2018–2019	Canada	Chocolate French pastries Enteritidis	Enteritidis	November- December	85	NA	26	29
2021–2022	12 European Union countries¶, Canada, Switzerland, United Kingdom, United States	Switzer- Various products containing chocolate	Monophasic Typhi- murium	January– February–March	455	10	41	6,30–32

*When several countries are involved, that with the highest number of recorded cases is shown in bold, while the others are listed in alphabetical order.

†D'Aoust et al¹³ mentioned 95 cases; Craven et al¹² mentioned 119 cases.

 \ddagger Kapperud et al²⁰ reported a median age of 15 years for the cases recorded in Finland (N = 12).

¶Austria, Belgium, Denmark, France, Germany, Ireland, Italy, Luxembourg, Netherlands, Norway, Spain and Sweden. || Data available only for European Union and United Kingdom (N = 324). NA indicates information not available. \$Data available only for Germany (N = 426).

This study has limitations. An outbreak is a sudden increase of infections linked to a common source. It is important to note that the definition of an outbreak can vary depending on specific jurisdictions and circumstances. Local authorities often have own guidelines and protocols for identifying an outbreak.

These assumptions likely underlie the high heterogeneity and variability observed in the outbreaks included in this analysis. It is tempting to speculate that some reports may have predominantly focused on documenting severe cases rather than mild ones. On the other hand, some studies may have included only primary cases while other studies did not differentiate between primary and secondary cases. Since the serotypes identified in sporadic cases do not differ from those identified in outbreaks, certain small outbreaks may go undiagnosed. The age of patients was not homogeneously provided in all included studies. A further limitation is that only a minority of reports were of good quality.

CONCLUSIONS

This systematic review of outbreaks of nontyphoidal salmonellosis induced by chocolate consumption highlights a recurring pattern of outbreaks occurring every decade over the past 50 years. The outbreaks primarily occurred in HICs. Children were most affected. Despite the high number of cases, no fatalities were reported, indicating a mild disease severity.

Surveillance reporting systems have a pivotal role in detecting foodborne outbreaks. In particular, prompt timing and coordination with stakeholders at an international level is crucial. The example from the 2022 nontyphoidal Salmonella outbreak is impressive: on March 27, 2022 the United Kingdom notified a cluster of cases with Salmonella typhimurium infection with an unidentified source. The outbreak was quickly linked by investigators to a chocolate firm in Belgium, and a global product recall was initiated on April 10, 2022.

ACKNOWLEDGMENTS

Dr. Lava is the current recipient of research grants from Fonds de perfectionnement, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; Fondation SICPA, Prilly, Switzerland; Fondazione Dr. Ettore Balli, Bellinzona, Switzerland; Fondazione per il bambino malato della Svizzera italiana, Bellinzona, Switzerland; and Frieda Locher-Hofmann Stiftung, Zürich, Switzerland

REFERENCES

- Prost E, Riemann H. Food-borne salmonellosis. Annu Rev Microbiol. 1967;21:495–528.
- Bula-Rudas FJ, Rathore MH, Maraqa NF. Salmonella infections in childhood. Adv Pediatr. 2015;62:29–58.
- Chousalkar K, Gole VC. Salmonellosis acquired from poultry. Curr Opin Infect Dis. 2016;29:514–519.
- Williams MS, Ebel ED. Temporal changes in the proportion of Salmonella outbreaks associated with 12 food commodity groups in the United States. *Epidemiol Infect*. 2022;150:e126.
- Ebel ED, Williams MS, Cole D, et al. Comparing characteristics of sporadic and outbreak-associated foodborne illnesses, United States, 2004-2011. Emerg Infect Dis. 2016;22:1193–1200.
- Samarasekera U. Salmonella typhimurium outbreak linked to chocolate. Lancet Infect Dis. 2022;22:947.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *J Clin Epidemiol*. 2021;134:178–189.
- Haddaway NR, Collins AM, Coughlin D, et al. The role of Google Scholar in evidence reviews and its applicability to grey literature searching. *PLoS One*. 2015;10:e0138237.

- Spillmann A, Browayes J, Dunez A, et al. A propos de 200 cas de toxiinfections d'origine alimentaire par chocolats glacés survenus dans la région
 de Saint-Germain-en-Laye [Two hundred cases of toxi-infections of alimentary
 origin due to chocolate-coated ice cream in Saint-Germain-en Laye: contribution to the study of salmonellosis]. Rev Hyg Med Soc. 1953;1:687–696.
- Stang A. Critical evaluation of the Newcastle-Ottawa Scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603–605.
- Gästrin B, Kämpe A, Nyström KG, et al. Salmonella durham-epidemi spridd genom kakaopulver [Salmonella Durham epidemic caused by contaminated cocoa]. *Lakartidningen*. 1972;69:5335–5338.
- Craven PC, Mackel DC, Baine WB, et al. International outbreak of Salmonella eastbourne infection traced to contaminated chocolate. *Lancet*. 1975;305:788–792.
- D'Aoust JJ, Aris BJ, Thisdele P, et al. Salmonella eastbourne outbreak associated with chocolate. Can Inst Food Sci Technol J. 1975;8:181–184.
- Gill ON, Sockett PN, Bartlett CL, et al. Outbreak of Salmonella napoli infection caused by contaminated chocolate bars. *Lancet*. 1983;321:574– 577
- Gizzarelli S, Salmaso S, Toti L, et al. Indagini microbiologiche su cioccolata contaminata da Salmonella napoli [Microbiologic investigation of chocolate contaminated with Salmonella napoli]. Nuovi Ann Ig Microbiol. 1983;34:347–352.
- Greenwood MH, Hooper WL. Chocolate bars contaminated with Salmonella napoli: an infectivity study. Br Med J (Clin Res Ed). 1983;286:1394.
- Jessop JH, Khanna B, Black WA, et al. Salmonella nima in British Columbia. CMAJ. 1986;135:1286.
- Hockin JC, D'Aoust JY, Bowering D, et al. An international outbreak of Salmonella nima from imported chocolate. J Food Prot. 1989;52:51–54.
- Kapperud G, Lassen J, Aasen S, et al. Sjokoladeepidemien i 1987 [The contaminated chocolate epidemic of 1987]. *Tidsskr Nor Laegeforen*. 1989;109:1982–1985.
- Kapperud G, Gustavsen S, Hellesnes I, et al. Outbreak of Salmonella typhimurium infection traced to contaminated chocolate and caused by a strain lacking the 60-megadalton virulence plasmid. *J Clin Microbiol*. 1990;28:2597–2601.
- Ethelberg S. International outbreak of Salmonella oranienburg, October-December 2001, part 2: Denmark. Euro Surveill. 2002;6:2006.
- Fisher IST, de Jong B, van Pelt W, et al. International outbreak of Salmonella oranienburg, October-December 2001, part 3: other countries. Euro Surveill. 2002;6:2007.
- Linnane E, Roberts RJ, Mannion PT. An outbreak of Salmonella enteritidis phage type 34a infection in primary school children: the use of visual aids and food preferences to overcome recall bias in a case control study. *Epidemiol Infect*. 2002;129:35–39.
- Werber D, Ammon A, Dreesman J, et al. International outbreak of Salmonella oranienburg, October-December 2001, part 1: Germany. Euro Surveill. 2002;6:2005.
- Werber D, Dreesman J, Feil F, et al. International outbreak of Salmonella oranienburg due to German chocolate. BMC Infect Dis. 2005;5:7.
- Elson R; Outbreak control team collective. National increase in human Salmonella montevideo infections in England and Wales: March to June 2006. Euro Surveill. 2006;11:2985.
- Harker KS, Lane C, Gormley FJ, et al. National outbreaks of Salmonella infection in the UK, 2000-2011. Epidemiol Infect. 2014;142:601–607.
- Eun Y, Jeong H, Kim S, et al. A large outbreak of Salmonella enterica serovar Thompson infections associated with chocolate cake in Busan, Korea. Epidemiol Health. 2019;41:e2019002.
- Rao M, Tamber S. Microbiological analysis of frozen profiteroles and mini chocolate eclairs implicated in a national salmonellosis outbreak. Food Microbiol. 2021;100:103871.
- European Centre for Disease Prevention and Control, European Food Safety Authority. Multi-country outbreak of monophasic Salmonella typhimurium sequence type 34 linked to chocolate products – first update – 18 May 2022. EFSA Support Publ. 2022;19.
- Larkin L, Pardos de la Gandara M, Hoban A, et al. Investigation of an international outbreak of multidrug-resistant monophasic Salmonella typhimurium associated with chocolate products, EU/EEA and United Kingdom, February to April 2022. Euro Surveill. 2022;27:2200314.
- Lund S, Tahir M, Vohra LI, et al. Outbreak of monophasic Salmonella typhimurium sequence type 34 linked to chocolate products. *Ann Med Surg* (Lond). 2022;82:104597.

- Riva G, Keller H. Diagnostische und therapeutische Aspekte der Salmonellosen: I [Salmonellosis - diagnostic and therapeutic aspects: I]. Schweiz Rundsch Med Prax. 1978;67:1767–1773.
- Riva G, Keller H. Diagnostische und therapeutische Aspekte der Salmonellosen: II [Salmonellosis - diagnostic and therapeutic aspects: II]. Schweiz Rundsch Med Prax. 1978;67:1835–1842.
- Blaser MJ, Newman LS. A review of human salmonellosis: I. Infective dose. Rev Infect Dis. 1982;4:1096–1106.
- Tamminga SK, Beumer RR, Kampelmacher EH, et al. Survival of Salmonella eastbourne and Salmonella typhimurium in milk chocolate prepared with artificially contaminated milk powder. J Hyg (Lond). 1977;79:333–337.
- Podolak R, Enache E, Stone W, et al. Sources and risk factors for contamination, survival, persistence, and heat resistance of Salmonella in lowmoisture foods. *J Food Prot.* 2010;73:1919–1936.
- Elnekave E, Hong SL, Lim S, et al. Comparing serotyping with wholegenome sequencing for subtyping of non-typhoidal Salmonella enterica: a large-scale analysis of 37 serotypes with a public health impact in the USA. *Microb Genom.* 2020;6:mgen000425.
- Qamar FN, Hussain W, Qureshi S. Salmonellosis including enteric fever. Pediatr Clin North Am. 2022;69:65–77.
- Marchello CS, Birkhold M, Crump JA; Vacc-iNTS consortium collaborators. Complications and mortality of non-typhoidal Salmonella invasive disease: a global systematic review and meta-analysis. *Lancet Infect Dis*. 2022;22:692–705.