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Microbiological contamination of commercial enteral feeding and blenderized tube feeding: A systematic review

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Abstract

Background: All types of enteral feeding (EF) formulations, whether blenderized tube feeding (BTF) at hospital kitchen, or commercial enteral feeding (CEF), contains nutrients. The nature of these foods (in terms of pH, nutrient contents, water activity, etc.) is so that if they become contaminated, would immediately grow pathogens inside and put the patient at the risk of infection. This systematic review aimed to investigate the microbial safety of BTF and CEF used in hospitals.

Methods: Literature search was conducted in four English databases, including Scopus, PubMed, Science Direct, and Google Scholar, using multiple keywords, such as enteral nutrition, blenderized formulas, home enteral nutrition, enteral formula, EF, blenderized enteral formula, blended feeds, blenderized home-made food, CEF, microbial contamination, and bacterial contamination. Finally, 16 eligible studies were selected for the systematic review.

Results: Out of 132 retrieved articles, 16 were selected and reviewed CEF was mostly exposed to contamination with total coliforms, *Staphylococcus aureus*, mesophilic bacteria, and *Escherichia coli*. In addition, contamination with gram-negative bacteria, *Bacillus cereus*, mold, and yeast was detected. Most BTF contamination was caused by total coliforms, mesophilic bacteria, *Listeria* spp., *B. cereus*, mold, and yeast.

Conclusion: Due to the nonconformity of hygienic guidelines, the microbial safety of EF solutions in hospitals and homes are relatively low, which may lead to foodborne diseases. Therefore, a hazard analysis and critical control point (HACCP) system is essential in every hospital kitchen.

Keywords: Enteral nutrition, Hazard analysis and critical control points, Foodborne diseases, Hospitals, Nutrients

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Introduction

Enteral feeding (EF) is essential to the management of the patients who are unable to use oral nutrition. EF is the preferred route of nutritional supplementation in such cases (1). EF formulas could be developed as blenderized tube feeding (BTF) and commercial enteral feeding (CEF) (2). EF solutions are the major concern of physicians as they increase the risk of infection (3). Although CEF has been available for over two decades, BTF remains a popular measure in several countries, including Iran, Philippines, Brazil, the United States, and Saudi Arabia (4-8). There is a growing interest in the use of BTF given its multiple advantages, such as the handover of a complete variety of foodstuffs for upgrading a healthy microbiome and reduction of added sugar, artificial flavors, and additives (e.g., emulsifiers), reduction of gagging/retching, flatulence, nausea and vomiting, diarrhea, constipation, and oral aversion and could also improve bowel function. Commercial EF contains large amounts of processed carbohydrates and highly saturated fats, and free of fruits, protein, fruits, vegetables, fiber, and other beneficial foodstuffs that play a role in the pathogenesis of cardiovascular and pulmonary diseases (9-13). The main reason for nutritionists to avoid BTF is its microbial contamination, which increases the risk of infection (8). Food contamination by food pathogens is a serious public health concern that can lead to foodborne diseases (14). According to the World Health Organization (WHO) report in 2015, approximately 600 million cases of contaminated food were observed in 2010, 350 million of which were related to pathogenic bacteria (15). According to the European Food Safety Authority (EFSA, 2010) reports, approximately 48.7% of foodborne diseases are associated with foodstuff services in the foodstuff premises

(16). Furthermore, studies attribute 70% of the prevalence of bacterial poisoning in foodstuffs to the catering sector, while 70% of the food poisoning is due to the inappropriate timing and temperature of food processing, and the remaining 30% is caused by cross-contamination (17). Food safety concerns in hospitalized patients have been noted in several countries, particularly in regards to the prevention of food poisoning mortality, provision of effective treatments for the patients, and reducing the risk of foodborne diseases (18,19). EF formulations invariably contain proteins, carbohydrates, and lipids in multiple combinations. Notably, the nature of these foods in terms of pH, nutrient contents, and water activity provides a suitable environment for microorganism growth. The rapid growth of pathogenic or spoilage microorganisms in these substances poses the risk of infection in patients (5,20-22). Additionally, the microbial contamination of these formulas reduces the recovery rate of patients and may cause various hazardous conditions, such as pneumonia, nosocomial infections, salmonellosis, abdominal pain, leukocytosis, tachycardia, sepsis, and even death (6,21,23,24). In clinical cases, infections could also reduce nutrient absorption and cause nutrient loss (20,23). Since patients with a weakened immune function require regular, nutritious, and safe dietary regimens as a major part of their hospital treatment, hospital foodstuffs should be prepared with care and great hygiene. Therefore, it is essential to observe the principles of food hygiene to prevent foodborne diseases in public places, such as hospitals (8).

Given the importance of EF in hospitalized patients, especially the elderly and those with weakened immune systems, who have lower immunity than normal individuals and lower doses are needed for starting a poisoning and infection, the present study aimed to investigate the microbiological quality of CEF and BTF in hospitals.

Materials and Methods

Data sources and literature search

Literature search was conducted for the articles published during 2000-2020 regarding the prevalence of microbial contamination in EF in four English databases, including Scopus, PubMed, Science Direct, and Google Scholar. The keywords used in the systematic search included Enteral nutrition OR Blenderized formulas OR home enteral nutrition OR enteral formula OR Enteral feeding OR blenderized enteral formula OR blended feeds OR Blenderized OR Enteral tub feeding home-made food OR Commercial Enteral Feeding AND microbial contamination OR bacterial contamination.

Eligibility criteria, article selection, and data collection

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol (25). Then, quantified evidence on microbiological contamination of CEF and BTF was identified.

The eligibility criteria in the present review were the studies using CEF (powder/ready-to-use), BTF with sample numbers and contamination percentages. The exclusion criteria were as follows: 1) lack of access to full-text articles; 2) failure to report the number or percentage of the samples contaminated with microorganisms, 3) contamination of the enteral nutrition system, 4) contamination of enteral nutrition formulations (BTF and CEF) at home, 5) conference abstracts, editorials, errata, letters, review articles and notes. The number and percentage of the samples with microorganism contamination were extracted and summarized. The process of searching and data extraction were performed by three authors. The first reviewer (B.B) assessed all titles, abstracts, and full texts for inclusion, the second reviewer (E.N) assessed 50% of all titles, abstracts, and full texts, and the third and fourth reviewers (M.S) assessed 25% of each of the remaining titles, abstracts, and full texts. In the event of a disagreement, a senior researcher (M.R), independent of the three reviewers, was consulted. After final study selection, duplicates were removed by identification of the same Ovid ID alongside manual searching. Following the identification of the full texts, one reviewer (B.B) assessed the quality of all papers and another reviewer (E.N) independently checked 12 randomly selected articles.

Results

In addition, the references of the retrieved articles were searched for related studies. In the systematic literature search, 132 articles were obtained from Scopus, PubMed, Science Direct, and Google Scholar, as well as the relevant studies identified in cross-references. After the elimination of the duplicates, 132 articles were considered eligible for title/abstract screening, 46 of which were retrieved for full-text assessment. Finally, 16 eligible studies were selected for the systematic review. In total, 132 articles were identified, and 16 were selected for this systematic review (Figure 1). Tables 1 and 2 show the selected studies on the microbial contamination of EF in different countries. According to the findings, most CEF diets show contamination with coliforms, *Staphylococcus aureus*, mesophilic bacteria, and *Escherichia coli*. However, only few of these formulas have been reported to be contaminated with yeast, mold, *Bacillus*, coagulase-positive staphylococci, *Acinetobacter*, *Streptococcus*, *Staphylococcus epidermidis*, *Enterobacter cloacae*, *Serratia marcescens*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Enterococcus faecium*. Some findings have also indicated that the contamination of CEF diets is directly associated with the preparation steps. On the other hand, BTF has mostly shown contamination with coliforms and

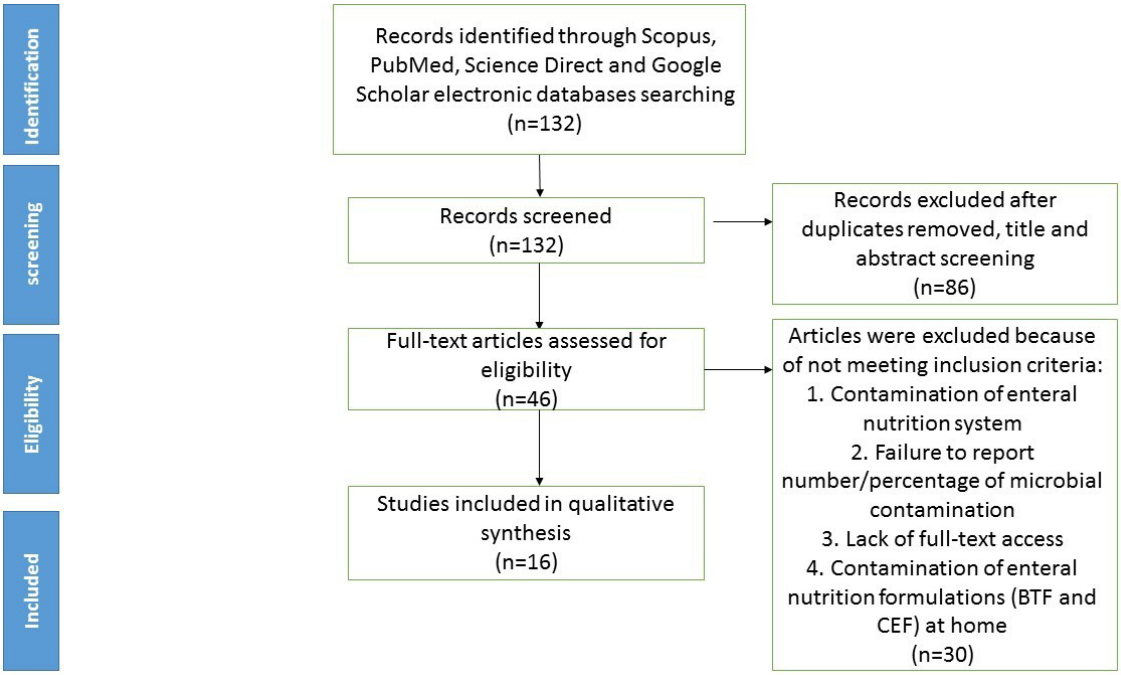

Figure 1. Flow diagram of the results of searches

Table 1. Contamination of commercial enteral nutrition in different countries

Country	Sample size	Prevalence rate (%)	Ref.
USA 2019	16 Solution	*Staphylococcus aureus*: 0%; coliforms: 0%; *Escherichia coli:* 0%	(4)
Iran 2017	18 Powders	Coliforms: 33.33%; *S. aureus*: 0%; *Salmonella*: 0%; *Listeria monocytogenes*: 0%	(6)
Brazil 2015	12 Solutions	Mesophilic bacteria: 8.5%; total coliforms: 0%; thermo-tolerant coliforms: 0%; coagulase-positive *Staphylococcus*: 0%; *Salmonella* spp.: 0%; *L. monocytogenes*: 0%	(8)
Brazil 2015	227 Solutions	Mesophilic microorganisms: 1.76%; coliforms: 4.40%; *S. aureus*: 0%; *Salmonella*: 0%	(26)
Brazil 2015	30 Solutions	*Klebsiella*: 20%	(27)
Iran 2014	28 Solutions	S. *aureus*: 86%; coliforms: 96%	(20)
Iran 2014	Hospital 1, 10 solutions Hospital 2, 10 solutions	Hospital 1: Coagulase-positive staphylococci: 10% Hospital 2: Coagulase-positive staphylococci: 0%	(2)
Brazil 2013	8 Solutions	Coagulase-positive staphylococci: 12.5%; coliforms: 12.5%; *Bacillus cereus*: 25%; mesophilic bacteria: 12.5%; molds and yeasts: 12.5%; sulfite-reducing clostridia: 0%; *Salmonella* spp.: 0%; *L. monocytogenes*: 0%	(28)
Brazil 2011	Hospital 1, 40 powders Hospital 1, 80 solutions Hospital 2, 40 powders Hospital 2, 80 solutions	Hospital 1; powder: mesophilic bacteria: 0%; yeasts and molds: 2.5%; coliforms: 5%; *Escherichia coli*: 0% Hospital 1; solution: mesophilic bacteria: 25%; yeasts and molds: 6.2%; coliforms: 58.8%; *E. coli*: 1.2%; *S. aureus*: 2.5% Hospital 2; powder: mesophilic bacteria: 0%; yeasts and molds: 0%; coliforms: 0%; *E. coli*: 0%; *S. aureus*: 0%; Hospital 2; solution: mesophilic bacteria: 27.5%; yeasts and molds: 0%; coliforms: 37.5%; *E. coli*: 2.5%; *S. aureus*: 0%	(29)
Brazil 2010	Hospital 1, 80 Solutions and 40 Powders Hospital 2; 80 solutions and 40 powders	Hospital 1; solution: *S. aureus*: 2.5%; *E. coli*: 1.2%; powder: *S. aureus*: 0%; *E. coli*: 0% Hospital 2; solution: *E. coli*: 2.5%; *S. aureus: 0%* powder: *S. aureus*: 0%; *E. coli*: 0%	(30)
Brazil 2005	10 Solutions 10 Powders	Total coliforms: 25%; *E. coli*: 10%; aerobic mesophilic bacteria: 20%; *B. cereus*: 0%, *Salmonella* spp.: 0%; sulfite-reducing *Clostridium*: 0%; coagulase-positive staphylococci: 0%	(31)
France 2005	The first study: 26 The second study: 14 T0: immediately refrigerated until analysis T1: other sample taped to feeding bottle before administration and to EN bag during administration	The first study: *Acinetobacter* spp.: 3.84%; *Streptococcus* spp.: 3.84%; *Staphylococcus epidermidis*: 11.53%; *Enterobacter cloacae*: 7.69%, *Serratia marcescens*: 3.84%; *Bacillus* spp.: 7.69%; *Proteus mirabilis*: 3.84%; *Pseudomonas aeruginosa*: 3.84%; *Enterococcus faecium*: 3.84% The second study: T0; *Bacillus* spp.: 14.28% T1: *Bacillus* spp.: 21.42%; *Acinetobacter* spp.: 7.14%	(32)

Table 2. BTF contamination in different countries

Country	Sample size	Ingredients	Prevalence rate (%)	Ref.
USA 2019	48	BTF whole food: whole milk, broccoli, cauliflower, chicken breast, cod liver oil, olive oil, raw banana, blueberries, salt, and water BTF baby food: whole milk, baby food chicken, baby food peas, baby food apple and blueberry, olive oil, and cod liver oil	*Staphylococcus aureus*: 0%; coliforms: 0%; *Escherichia coli*: 0%	(4)
Iran 2017	T0: 18 Preparation Time T1: 18 18 Hours after Preparation	Lactose-free powder milk, low-fat yogurt, cheese, cooked chicken, egg, lentil, boiled potatoes, rice flour, wholegrain biscuit, cucumber, cooked carrot, cooked tomato, peeled apple, tangerine, orange, banana, olive oil, and corn oil	T0; coliforms: 0% *S. aureus*: 0%; *E. coli*: 0%; *Salmonella*: 0%; *Listeria monocytogenes*: 0% T1; coliforms: 0%; *S. aureus*: 0%; *E. coli*: 0%; *Salmonella:* 0%; *L. monocytogenes*: 0%	(6)
Brazil 2015	13	UHT (long-life) whole milk, protein supplement (Nutren Active®, Nestlé, Brazil), pureed fruits, and vegetable soup (potato, chayote, carrot, and ground beef)	Mesophilic bacteria: 69%; total coliforms: 54%; thermotolerant coliforms: 8%; *Listeria* spp.: 7.69%; *Staphylococcus:* 0%; *Salmonella* spp.: 0%	(8)
Iran 2014	T0: 21 Time of Preparation T1: 21 18 Hours after Preparation	Dry milk, green beans, carrot, orange juice, and chicken	T0; *S. aureus:* 24%; coliforms: 52% T1; *S. aureus*: 62%; coliforms: 76%	(20)
Iran 2009	T0; 76 Samples (each at preparation) T1; 76 Samples 18 Hours after Preparation	Egg, milk, and meat	T0; *S. aureus*: 90%; coliforms: 70%; *Salmonella*: 0%; *Listeria*: 0%; T1; *S. aureus*: 95%; coliforms: 90%; *Salmonella*: 0%; *Listeria*: 0%	(33)
Brazil 2009	18	Skinned ground chicken chest, rice flour, corn oil, calcium carbonate, glucose, sodium chloride, and water	Mesophilic bacteria: 83.33%; coliforms: 16.66%; fecal coliforms: 11.11%; *S. aureus*: 11.11%; *Bacillus cereus*: 11.11%	(34)
Brazil 2008	15	Pasteurized cow milk, boiled apple, boiled beets, boiled chicken breast, powdered gelatin, powdered milk, Water, Mucilon® rice, Isoy®, chicken broth, cooked vegetables, refined sugar, salt, and corn oil	Mold: 20%; yeast: 60%; coliforms: 86.66%; *B. cereus*: 13.33%; mesophilic bacteria: 20%; *Salmonella*: 0%; coagulase-positive *Staphylococci*: 0%	(35)

mesophilic bacteria, *S. aureus*, while fewer formulas have been reported to be contaminated with *Bacillus cereus*, mold, yeast, and *Listeria*. Although only few studies have investigated BTF contamination, concerns remain significant regarding this type of contamination.

Discussion

Microbiological rules in medical foods

The American Food and Drug Administration (FDA) instructions have mandated the evaluation of foodstuffs in terms of the total colony count of aerobic microorganisms, coliform count, *E. coli*, and *B. cereus*, as well as the further detection of *Salmonella* spp. and *Listeria monocytogenes* and determining staphylococcal enterotoxins. In conformity with this instruction, food products that are contaminated with aerobic microorganisms at the level of $>10^4$ CFU/g in one sample or more than 10^3 CFU/g in three or more samples, those with the coliform count of more than three microorganisms per gram, and the products that are positive for *L. monocytogenes* or *Salmonella* spp. are considered to have low microbiological standards and are not suitable for consumption (20,33,36). According to the British Dietetic Association (BDA) Parenteral and Enteral Nutrition specialist group, the acceptable total microbiological counts in enteral nutrition formulas is lower than 10^1 and 10^3 CFU/mL at the outset and end of administration, respectively (2). In Spanish and Brazilian guidelines, the acceptable count of *S. aureus* has been set at 10^1 CFU/mL (2,33).

Sources of contamination in enteral feeding solutions

In the powder samples used in the reviewed studies, no data was available regarding the sterility of packaging. Upon contact with the manufacturers of these commercial formulas, it became clear that these powders were not produced under sterile conditions, and microbial contamination could not be zero (20).

Mesophilic bacteria, coliforms and *E. coli*, are the microorganism indicators used to evaluate the microbial quality of foodstuffs given their ecological specifications, which are similar to pathogenic microorganisms; these indices indicate that foodstuffs have been exposed to the conditions that facilitate the growth of microorganisms. These indicators are also used to confirm the effectiveness of foodstuff treatments to ensure the safety of food products (e.g., heat treatment) (21). Contamination with mesophilic bacteria may indicate that temperature has been overlooked during preparation, storage or

distribution (26). Mesophilic bacteria do not pose a direct hazard to consumer health, while they affirm disinfection, improper storage or inappropriate distribution/ transportation. On the other hand, these microorganisms could be used to monitor food processing and sanitation conditions (26).

Coliforms may affect the safety and maintenance of foodstuffs as these microorganisms signify fecal pollution (37). The pollution caused by total coliforms may not necessarily be associated with the presence of pathogenic microorganisms, while *Enterococcus* spp. and coliforms in enteral nutrition indicate a poor hygienic status during the preparation and processing of the contaminated feed. *Enterococcus* spp. could tolerate a wide range of temperatures (low and high) and is mostly applied in dry foodstuffs (3).

Escherichia coli is a gram-negative coliform bacterium of the genus *Escherichia*. Although most *E. coli* strains are harmless, some serotypes could cause severe food poisoning in the host and are occasionally responsible for food contamination as well. *E. coli* O157:H7 is a potentially fatal bacterium, which could cause bloody diarrhea, dehydration, and even kidney failure in severe cases. The youth, seniors, and those with a poor immune function are more susceptible to foodborne diseases. Therefore, the presence of this bacterium in the infant feeding solution may be hazardous (38).

S. aureus could survive in stress and dry conditions, such as surfaces and clothing (39). The presence of *S. aureus* in EF formulas may indicate the poor hygienic status of the production staff and food handlers (33). Improper food preparation by staff may contribute to the contamination of enteral nutrition with *S. aureus*, while these bacterial *strains* and the other coagulase-positive *Staphylococcal* species may also release enterotoxin (2). The temperature range for the growth and formation of the toxins produced by *S. aureus* is 6-46°C. Therefore, the optimal cooking and refrigerator temperatures should be above 60°C and under 5°C, respectively (40).

Microorganisms could survive on the contact surfaces of foodstuffs for a considerable amount of time, thereby, increasing the risk of cross-contamination among the foodstuff handlers, products, and contact surfaces (41). For instance, eggs may be contaminated with *Salmonella enteritidis,* and the cross-contamination occurring in the kitchen could also contaminate the kitchen surfaces and dishes (42). As such, consumers must only use pasteurized and hard-boiled eggs (43).

The other causes of EF solution contamination are the involvement of a personnel with respiratory infections, addition of a new formula to the used feeding container, addition of other nutrients or modular materials to the EF solution, dilution, long-term maintenance, suction apparatus, delayed transfer to the fridge-free section (added opportunity for bacterial growth), mixers, poor personal health, worn-out disposable gloves, failure to monitor product temperature, containers/surfaces, poor ventilation, unclean can openers, lack of a separate area for formula preparation, and addition of medicines and vitamins to the EF solution (3,5,6,26,39,44,45).

According to the literature, foodstuff service personnel at hospitals are mostly unaware of the principles of food hygiene, such as the proper temperature of foodstuff storage, prevention of cross-contamination, hand washing, and the acceptable temperature range of the cold chain and freezers (46). Hands are an important pathway for the transmission of nosocomial infections as they may become contaminated even after washing by touching towels, clothes, handles or scratching the skin, hair, and nose due to the residing capability of *S. aureus* in skin, nose, mouth, and throat and transferring to the feed during preparation. Therefore, even healthy individuals could be a potential source of *S. aureus, Salmonella, Clostridium perfringens*, and fecal *Streptococcus* contamination (44,47). Hand washing is accomplished by using hand-held antibacterial soaps (e.g., soaps containing chlorhexidine gluconate), hand sanitizers, and paper towels for drying (48). Hand drying is the critical last step in the hand washing process that should be carried out to decrease the risk of cross-contamination, and using disposable paper towels is considered to be the optimal solution in this regard (49).

Some researchers believe that hand hygiene plays a more significant role in the control of pathogenic microorganisms than cleaning and disinfecting foodstuff contact areas (46). Moreover, it has been reported that parts of food manipulation areas could be contaminated by *E. cloacae, Pseudomonas fluorescens, Burkholderia cepacia*, and *Staphylococcus* spp. (26). When a dish becomes contaminated with *S. marcescens*, the bacteria secretes a substance to protect itself against drying and scrubbing (45). Steps such as proper training, using disposable gloves, clean and separate rooms, dietary monitoring by specialists, and recruiting trained personnel for food preparation may effectively reduce microbial contamination (20,50).

Previous findings have indicated that using mixers may be the major source of the contamination of BTF solutions. The mixers that are widely used in this regard are basically in a way that cannot be thoroughly cleaned, disinfected or dried. Therefore, it is essential to clean all parts of the blenders that are in contact with feed (3,20). In selecting mixers, it must be assured that the gasket and blade are detachable because a mixer's gasket is a source of bacterial contamination (51). Numerous mixers cannot be placed in the dishwasher; if a commercial dishwasher is not available, the bleach sanitation method is recommended (51). If the water available for washing the dishes is not hygienic, it may also contaminate food, and boiling water must be utilized (3).

While cleaning kitchen utensils with sponges and cloth, food sticks to the sponges and provides a suitable environment for bacterial growth, thereby further contaminating dishes, surfaces, and food. Studies of sponges and cloth have exhibited contamination with *Pseudomonas* (16.9%), *Bacillus* (11.1%), *Micrococcus* (10.6%), *Streptococcus* (7.8%), and *Lactobacillus* (6%) (52). *Pseudomonas* spp. and a few other gram-negative psychrotrophic microorganisms dominate the foodstuffs containing protein, which are stored aerobically under cold conditions (53). Therefore, a thorough kitchen staff training is highly recommended for the hygienic protocols and frequent change of sponges (54). After the preparation of an EF solution, it should be stored within the temperature range of 2-8°C. Personnel should wash, dry, and disinfect hands frequently and use masks before preparing EF for non-sterile, blended, diluted or decanted foods. Notably, the administration time should not exceed four hours (32). During the handling process, EFs should not be exposed to hazardous temperatures (10-60°C) for more than 30 minutes, and the storage time should be less than 12 hours (55). Furthermore, producers recommend that commercial EF dishes should be preserved in a cool and dry place out of direct sunlight where the temperature does not fluctuate by more than 5°C and 25°C in order to reduce the risk of bacterial contamination (54). Commercial feed cans must also be cleaned with an alcohol-soaked cloth before opening (23). Parents and hospitals could follow the guidelines provided on www.homefoodsafety.org and www.foodsafety.gov, which have been published to minimize microbial contamination.

Implementation of the hazard analysis and critical control point system of an enteral feeding system at hospital

The optimal and safest approach to minimize microbial contamination is the implementation of a *hazard analysis critical control point* (HACCP) system. The wide variety of microorganisms that have been detected so far may be due to inappropriate manufacturing practices and storage conditions. Efficient manufacturing practices and the contentious control of processing lines could reduce the rate of contamination, especially in the case of pathogenic species. In addition, the strict implementation of microbial recipes (e.g., HACCP), good manufacturing practices, and good hygiene practices proposed by the WHO and the FDA could reduce the microbiological contamination of enteral nutrition (40).

The HACCP system is globally known as the ideal approach to assuring food safety by monitoring foodborne risks (33). The Codex HACCP system is also considered as the most efficient system to indemnify food safety worldwide and is mandatory in some countries. The system lays the basis for optional standardized approaches to food safety management, including the standard ISO 22000, BRC, and IFS (56). Since 1978, the HACCP system has been applied in the foodstuff service systems of medical centers. The original studies of the HACCP system are mainly focused on foodstuff service systems, such as breast milk, entrée production, fresh/frozen foodstuffs, sandwiches, foodstuff handlers, and enteral nutrition in hospitals (57).

The most effective method to prevent the contamination and spoilage of a food product is to identify the critical points of its production line and implement a control system in these areas. Due to the rising trend of BTF and the role of a wide range of microorganisms (e.g., coliforms, pathogenic microorganisms) in the contamination of these products, identifying the pollution sources by determining the critical points of the production line plays a pivotal role in enhancing the marketing and shelf life of these products. Another approach to reducing contamination is to implement the HACCP principles in hospitals to decrease foodborne diseases and provide safe food (41,57).

The seven approved principles of the HACCP are as follows:

1. Risk identification at each stage of the process to prevent or reduce the risks at an acceptable level;
2. Implementation of the points where control over an identified risk could be achieved, which are referred to as critical control points (CCP);
3. Setting crucial limits for each CCP;
4. Establishing and implementation of efficient monitoring methods at CCPs within each step of the process;
5. Taking corrective measures for the cases outside of a safe range;
6. Determining methods to assure that the mentioned stages are implemented effectively;
7. Documenting and recording paragraphs 1-6 (43,58).

Jin et al implemented the HACCP system of an EF at a private local hospital in Taiwan (Figure 2). According to the findings, the total microbial count, coliforms, and *E. coli* of the EFs of the patients before the implementation of the HACCP were 0.68, 0.6, and 0.66 Log CFU/mL, respectively. After HACCP implementation, the total microbial counts decreased to 0.11 Log CFU/mL, while coliforms and *E. coli* were not detected (57).

In a study conducted in 2001, the HACCP system was applied to prepare the powder feed for enteral nutrition. After identifying hazards and CCPs (personal cleanliness, assembly of feed components and utensils, reconstituting feed in mixer, transmission to stainless steel dishes, package into plastic dishes, storage in kitchen, warming in water bath to serve, distribution, administration), control/preventive measures and monitoring methods were performed. According to the findings, the bacterial counts of EF decreased from 10^5 CFU/mL to $< 10^1$ CFU/mL after the implementation of the HACCP system (59).

In another study conducted by Oliviera et al, the HACCP system was implemented to assess the microbial quality of enteral nutrition in a hospital. Before the implementation of the HACCP system, the microbial investigation of the EF formula indicated the presence of index microorganisms (e.g., coliforms and *Enterococcus* spp.), as well as the unacceptably high levels of mesophilic aerobic microorganisms (10^4 CFU/mL). To implement

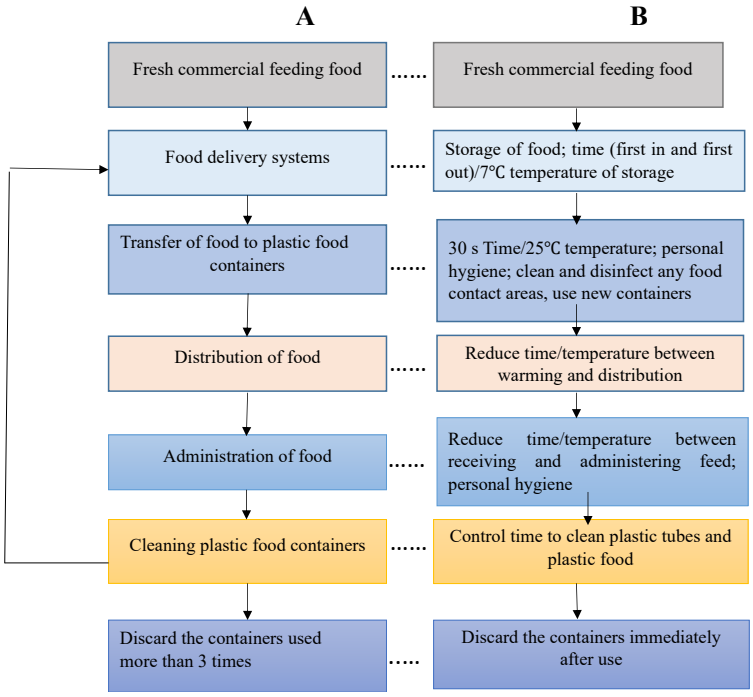

Figure 2. Flow diagram of (A) before and (B) after HACCP implementation in food

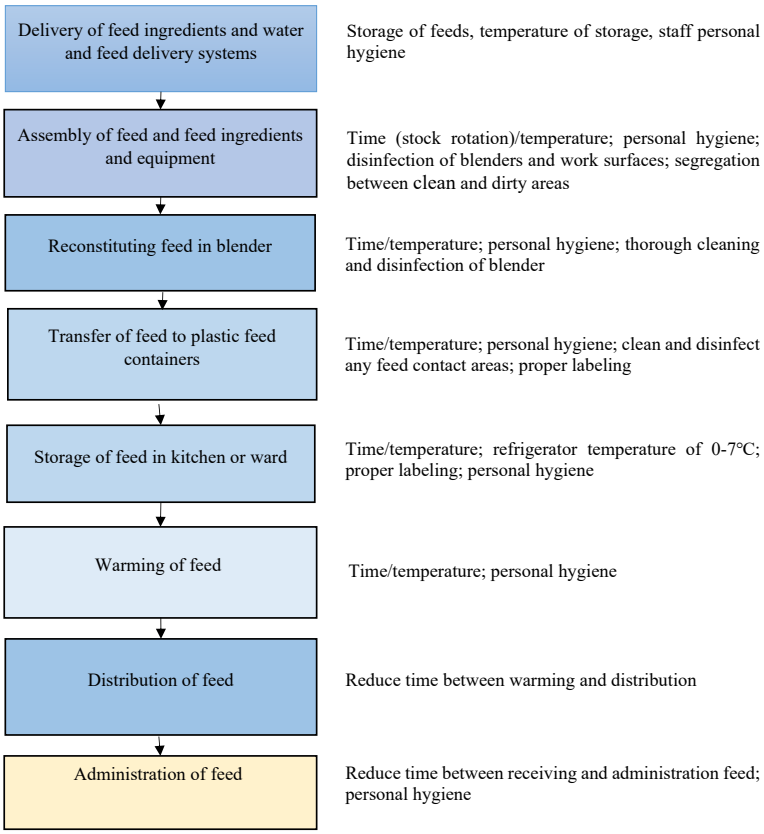

Figure 3. Flow diagram of feed preparation, storage, administration to patients, and CCPs

the HACCP system in the mentioned study, CCPs were defined using control measures for each stage, and monitoring was also defined based on the preventive measures (Figure 3). Despite the control measures, the microbiological quality of the powder feed reduced to $< 10^1$ CFU/mL (3).

Conclusion

The present systematic review confirmed the high rate of feed contamination and the non-observance of hygienic protocols in various stages of the preparation, storage, and transmission of enteral nutrition solutions in hospital kitchens. The microbiological safety of enteral nutrition solutions at homes and in hospitals have been reported to be low, which increases the risk of foodborne diseases, infections, and intoxication in patients. Therefore, food safety training at home and in hospitals seems crucial, and such interventions should be performed under the supervision of nutritionists and food safety experts. Moreover, food safety courses should be provided regularly at health centers and hospitals pertaining the mandatory attendance of kitchen staff. The HACCP system is among the safest approaches to the reduction of food contamination to an acceptable level and must be implemented in hospital kitchens.

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Ethical issues

The study protocols were approved by the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran (Ethical code: IR.MUMS.MEDICAL.REC.1399.085)

Competing interests

The authors declare that they have no conflict of interests.

Authors' contributions

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Formal Analysis: Behnam Bahramian and Elyas Nattagh-Eshtivani.
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Supervision: Mitra Rezaie.
Validation: Mitra Rezaie and Mahboobe Sarabi-Jamab.
Visualization: Behnam Bahramian.
Writing – original draft: Behnam Bahramian.
Writing – review & editing: Behnam Bahramian, Mitra Rezaie and Mahboobe Sarabi-Jamab.

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