



## *Cronobacter sakazakii*: An Emerging Foodborne Bacterial Pathogen of Public Health Significance

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### Abstract

Foodborne pathogens have a great impact on health and economy of the country. *Cronobacter sakazakii* is an important foodborne pathogen associated with outbreaks of life-threatening necrotizing enterocolitis, meningitis, and sepsis in neonates and infants. It is an emerging bacterial foodborne pathogen that is reported from many countries of the world including India. There has been increasing interest among the whole public community and food industry, especially in the production of powdered infant formula. Hitherto, the natural habitat of *C. sakazakii* is unidentified. Clinical manifestations of disease include septicemia, meningitis and necrotizing enterocolitis. The contaminated powdered infant formula serves as an important vehicle of the bacteria. *Cronobacter sakazakii* has been isolated from various food products, such as mixed salad vegetables, meat, milk, and cheese. The organism is widely prevalent in the environment, plant materials, powdered infant formulas, cereal foods, fermented beverages, fruits, and vegetables. Contamination is caused by poor handling and added raw ingredients. As infants and young children are more vulnerable to foodborne infections, the microbiological safety of infants and powdered infant formula is more important. *Cronobacter sakazakii* can be controlled during the initial production of powdered infant formula, and avoiding post processing contamination, using suitable microbiological approaches. Further, regulatory standards for infant food manufacturers need to be improved.

**Keywords:** *Cronobacter sakazakii*; Emerging Pathogen; Foods; Infants; Life Threatening Infection; Mortality

### Introduction

Foodborne diseases have emerged as an important growing public health and economic problem in many countries of the world during the last two decades. It comprises a broad group of illnesses concerning to public health problems. Among them, gastroenteritis is the most frequent clinical syndrome, which can be attributed to a wide range of microorganisms, including bacteria, viruses, and parasites [1]. Currently, over 250 foodborne diseases of varied etiologies have been described [2]. In USA, five pathogens, namely *Staphylococcus aureus*, *Clostridium perfringenes*, *Salmonells*, *Campylobacter*, and *Norovirus* are most commonly implicated in foodborne diseases. Further, infections caused by *Listeria*

*monocytogenes*, *Clostridium botulinum*, *Escherichia coli*, and *Vibrio* is more likely to lead to hospitalization of the patient [2]. Recent decades have witnessed the emergence of many foodborne bacteria, which include *Aeromonas hydrophila*, *Arcobacter butzleri*, *Campylobacter jejuni*, *Clostridium difficile*, *Cronobacter sakazakii*, *Escherichia coli* 0157: H7, *Listeria monocytogenese*, *Plesiomonas shigelloides*, *Vibrio parahaemolyticus*, and *Yersinia enterocolitica* [3]. There seems to paucity of statistical data on the exact incidence and prevalence of foodborne diseases in most of the countries of world. In this context, CDC [2] estimated that foodborne illnesses are responsible for 48 million cases, 128,000 hospitalization and 3,000 deaths annually in the United States.

*Cronobacter* species are emerging and opportunistic foodborne pathogens, which cause infections in neonates, infants, adults and immunocompromised individuals [4]. The primary reservoirs of *Cronobacter* are not well defined due to the ubiquitous nature of this bacterium. *Cronobacter* strains have been isolated from a wide range of foods including milk, cheese, dried foods, meats, water, vegetables, rice, tea, herbs, and spices, besides various food production environments [5].

Currently, seven are main internationally recognized species of *Cronobacter*, namely, *C. sakazakii*, *C. turicensis*, *C. malonaticus*, *C. muytjensii*, *C. universalis*, *C. dublinensis* and *C. condiment* [6]. Three of these namely, *C. sakazakii*, *C. malonaticus*, and *C. turicensis*, are human opportunistic pathogens [7] and the rest of them have not been associated with human disease until recently [8].

*Cronobacter sakazakii*, previously known as *Enterobacter sakazakii*, is an important foodborne pathogen, which is implicated with outbreaks of life-threatening necrotizing enterocolitis, meningitis, and sepsis in neonates and infants [9]. Bowen and Braden [10] mentioned that case definition for invasive *E. sakazakii* infections in infants have been met in only 46 cases worldwide. The infection caused by *C. sakazakii* can occur in sporadic and epidemic form. Ray and co-investigators [11] are credited to delineate the first report of *E. sakazakii* infections in infants from India. It is an emerging foodborne pathogen that causes life-threatening meningitis [12], septicemia, and enterocolitis in infants [13].

It is a Gram-negative, oxidase positive, catalase positive, non-spore-forming bacterium that belongs to the *Enterobacteriaceae* family [14,15]. This pathogen is receiving increasingly raised interest among the whole public community and food industry, especially in the production of powdered infant formula. The natural habitat of *C. sakazakii* is presently unknown. However, the organism has been recovered from water, sediment and soil. In a large survey of over 500 foodstuffs and ingredients, a large proportion (~25%) of herbs and spices were shown to contain *C. sakazakii* [14]. It is pertinent to mention that *E. sakazakii* has been isolated from milk powder manufacturing facilities and household vacuum cleaners [16] and also from baby foods, milk powders, cheese products, sausage meat, minced beef, and vegetables [14]. A recent study undertaken by Mahindroo and co-workers [17] indicated that the incidence of *C. sakazakii* in humans, goat meat, goat feces, pork, pig stool, chicken stool, and environment was 3.37%,

9.4%, 11.1%, 5.9%, 7.0%, 6.7%, and 11.5%, respectively. Antibiotic susceptibility profile revealed that of the 63 isolates of *C. sakazakii* tested, maximum resistance was noticed against ampicillin (50.8%) followed by ciprofloxacin (20.6%), and meropenem (17.2%) [17].

Symptoms of *Cronobacter sakazakii* infection are severe, including meningitis, septicemia and necrotizing enterocolitis [18]. The original reservoir of *C. sakazakii* is still not known [19]. The bacterium has been isolated from various food products, such as mixed salad vegetables, milk, cheese, and meat [20]. The present communication delineates the growing significance of *Cronobacter sakazakii* as an emerging foodborne pathogen of public health concern.

### Clinical spectrum

Neonates having <2.5 kg weight and infants of <28 days age are at heightened risk compared to more mature infants [18]. Symptoms include meningitis leading to ventriculitis, brain abscess, hydrocephalus and cyst formation as well as necrotizing enterocolitis characterized by intestinal necrosis and pneumatosis intestinalis, pulmonary, urinary, and blood stream infections [21]. Infants that survive *C. sakazakii* infection often suffer delayed neurological symptoms, e.g., delayed brain development, brain abscesses or hydrocephalus [22]. The mortality rate for neonatal infections has been reported to be as high as 80% [23] and survivors often suffer from severe irreversible neurological disorders. Food other than infant formula has been rarely investigated for the presence of *C. sakazakii*. Nevertheless, this microorganism could be isolated from a wide spectrum of food and food ingredients. The International Commission on Microbiological Specification for Foods has classified *C. sakazakii* as a severe hazard for restricted populations, life-threatening or with substantial chronic sequelae over long duration [24].

### Transmission

The sources of *C. sakazakii* and its vehicles of transmission are not clearly documented. It is distributed and frequently contaminated in the environment [25], plant materials [26], powdered infant formulas [27], cereal foods [28], fermented beverages [29], fruits, and vegetables [26]. In particular, contamination on powdered infant formula occurs more easily because it is a non-sterilized product. Contamination can be caused by poor handling and added raw ingredients. The information on environmental source, transmission routes, and human carriage of *C. sakazakii* in India is grossly lacking [17].

### Public health implications

Infants and young children are particularly vulnerable to food borne infections. As result, the microbiological safety of infant and follow-up formula is very essential [30]. Because powdered infant formula (PIF) is not a sterile product, it is an excellent medium to support bacterial growth. As we know bovine milk is a vital ingredient of PIF and a potential source of bacteria that are pathogenic to humans [31]. The World Health Organization recommends that infants should be exclusively breast-fed for the first 6 months of life. Infants who are not breast-fed should be provided with a suitable breast milk substitute, formulated in accordance with Codex Alimentarius Commission standards. To reduce the risk of infection in infants fed PIF, recommendations have been made for the preparation and storage of PIF. Manufacturers of PIF is being encouraged to develop a greater range of commercially sterile alternative formula products for high-risk groups. In addition, formula manufacturers must implement strategies aimed at reducing the risks of product contamination [32].

### Prevention and control

*Cronobacter sakazakii* can be controlled during the initial production of PIF and avoiding post processing contamination, using suitable microbiological approaches, will have a positive effect. Standardized analytical approaches are necessary to ensure the safety of the product [33].

Effective environmental monitoring programs, good manufacturing practice guidelines, and hazard analysis and critical control point systems to control the risk of microbiological contamination along the entire production chain, from the starting raw materials, throughout the entire process, until the final product is ready for distribution, should be implemented [34]. In addition, health education should be imparted to the mothers to give breast feeding to child for at least 6 months.

### Conclusion

*Cronobacter sakazakii* is an emerging foodborne bacterium that can cause life threatening infections particularly in neonates and infants. The infection can occur in sporadic as well as in epidemic form. The fatality rate in neonates may reach to 80%. The infection caused by *C. sakazakii* is not well reported in many countries of the world including India. The pathogen has been isolated from a wide range of foods including, milk, meat, cereals and vegetables. Laboratory help is mandatory to make an unequivocal diagnosis of *C.*

*sakazakii* infection. *Cronobacter sakazakii* can be controlled during the initial production of PIF and avoiding post processing contamination, by employing suitable microbiological approaches. It is emphasized that regulatory standards for infant food manufacturers need to be enhanced. Comprehensive and systematic research is required to elucidate the natural habitat, source, reservoir, and epidemiology of this emerging pathogen of public health significance.

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### Conflict of Interest

None.

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