Original Article

Clinical and epidemiological profile of food-borne botulism in highland regions of Kyrgyzstan: a retrospective observational study

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ABSTRACT

The Osh region of Kyrgyzstan faces a significant public health threat from botulism because of eating habits and high elevation and insufficient medical care. The research has three main objectives, which includes to describe the epidemiology of the disease, to evaluate the effect of altitude on the incidence and severity of the disease, and to analyze the clinical and laboratory findings to develop appropriate regional management strategies**.** Osh region reported an average of 26.4/100,000 botulism cases annually, with 86.9% of these cases occurring in clustered outbreaks that mostly affected low-altitude areas at a rate of 35.3/100,000. The data showed women were 1.7 times more likely to develop the condition, while 79.7% of cases affected adults between 21 and 50 years old. The most prevalent atypical C. botulinum toxins were found in 52.6% of cases followed by type B in 35.9% and type A in 11.5%. Incubation period showed strong relationship with food type and altitude and age (r=0.9). The combination of advanced age and elevated altitude led to severe disease and delayed hospital admission in 89.4% of patients. The patients who had type A toxin experienced the most severe paralysis among their gastrointestinal symptoms. The elevation level directly affected symptom intensity and all patients needed oxygen therapy because their respiratory function deteriorated into hypoxia. Occurrence of botulism in Kyrgyzstan is influenced by altitude, demographics, and toxin types, with severe cases being more common in women, older adults, and high-altitude areas. It requires targeted prevention, altitude-aware surveillance, and standardized oxygen therapy.

Keywords: Botulism, Diagnosis, Treatment, Poisoning, Intoxication, Low mountains

Introduction

The most dangerous biological toxin in human history causes botulism, which threatens areas where traditional food preservation meets microbial survival. The neurotoxin produced by Clostridium botulinum disrupts neuromuscular signals which leads to progressive flaccid paralysis starting with cranial nerve dysfunction before affecting respiratory function, thus requiring immediate medical response [1]. The Kyrgyz Republic faces increased fatality from botulism because home canning remains deeply traditional in its culinary practices. The traditional food preservation methods in this region protect cultural heritage but simultaneously create conditions where toxin production becomes more likely. The epidemiological patterns in Central Asia show different patterns between Kazakhstan and Uzbekistan because vegetable and fish canning in Kazakhstan leads to

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outbreaks, while Uzbekistan mainly reports adult cases, with women being more frequently affected. The Irkutsk region of Siberia fights against type E toxin, which exists in aquatic environments and shows cold tolerance [2]. The geographical differences between regions demonstrate how botulism adjusts to regional ecological conditions and traditional eating practices. Type B toxin represents the majority globally at 52%, but the specific risk factors in the southern Osh region of the Kyrgyz Republic need further investigation because altitude zones could affect toxin stability and clinical symptoms. Botulism exists as both a medical challenge and a sociocultural paradox because it results from the complex relationship between cultural practices and environmental factors and pathogenic biological processes [3, 4].

Critical care [5-7] advancements have not eliminated botulism mortality, which ranges between 10–70% because delayed diagnosis and variable symptom onset between 12–48 hours and 15 days post-exposure increase the risks. The Kyrgyz Republic deals with two major challenges because it depends on home-preserved foods, and its surveillance systems are fragmented throughout rural Osh. The type A toxin represents 63.8% of regional cases because it is a potent subtype with extended recovery times but there are no existing studies that connect clinical-epidemiological patterns. The diagnostic challenges in this crisis lead clinicians to mistake stroke or Guillain-Barré syndrome symptoms for early botulism signs such as diplopia or dysphagia. The gastrointestinal symptoms of nausea and vomiting make it difficult to diagnose neurological development until patients reach a critical stage of respiratory failure [8]. The condition disproportionately affects individuals aged 30 to 49 years old because of its socioeconomic impact, which undermines both family stability and workforce productivity. The lack of seasonal trends in Kyrgyz outbreaks makes prevention more difficult. Kazakhstan has fish harvest-related peaks in July and September, whereas Kyrgyzstan does not display similar patterns due to diverse contamination sources. There is no particular evidence on how altitude affects spore germination and toxin stability in highland and lowland zones; therefore, public health policies remain generic. The study gives important information for improving emergency response methods and developing preventative programs that correspond with local cultural norms [9, 10].

This research uses a combination of clinical data with epidemiological and geospatial information to study how botulism affects the Osh region based on altitude differences. The research connects toxin types (A/B/E) to dietary sources across elevation gradients from Fergana Valley lowlands to Alay Mountain communities to identify risk behaviors that vary by location. The study will use laboratory testing of locally produced canned foods to identify areas with high contamination rates, while clinical case reviews will show how altitude affects symptom development particularly through delayed paralysis in low-oxygen, high-altitude settings. The detailed approach allows for customized interventions, which include educational programs for specific preservation methods in particular zones and antitoxin administration guidelines adjusted for altitude. The study enables knowledge sharing between countries through its comparison of Kyrgyz data with regional patterns, including Uzbekistan's female-dominated cases and Irkutsk's type E prevalence. The research enables clinicians to detect unusual symptoms at an earlier stage, which reduces death rates, while policymakers obtain evidence to support laboratory infrastructure development in underdeveloped areas. The research connects traditional practices with biotoxin science to protect an area where modernity meets traditional ways of life [11].

Materials and Methods

Data sources and study design

The research used a combination of national health surveillance data with clinical records from the Osh region through a retrospective observational study. The Ministry of Health of the Kyrgyz Republic through its Department of Disease Prevention and State Sanitary and Epidemiological Supervision and the Republican Medical Information Center (RMIC) and the Center for Disease Prevention and State Sanitary and Epidemiological Supervision (DPZiGSEN) in Osh, supplied primary epidemiological data. The institutions granted access to Form No. 1 of the State Statistical Reporting, which contained "Report on Infectious and Parasitic Diseases" data from 2007 through 2019. The dataset contained anonymous case records together with demographic profiles and toxin typing results and altitude-specific incidence rates [12, 13]. The analysis of supplementary data from Osh's DPZiGSEN included altitude zone stratification of botulism cases through geographical mapping of patient residences into lowland (<1,000 m), mid-altitude (1,000–2,000 m), and highland (>2,000 m) zones. The infectious diseases department of the Osh Interregional Joint Clinical Hospital (OMOKB) retrieved clinical [14-17] data from 123 confirmed botulism cases during the period from 2011 to 2019 to match national reporting schedules.

Epidemiological data collection and stratification

The epidemiological analysis aimed to detect altitude-related patterns in toxin exposure origins together with seasonal patterns and population-based risk elements. The researchers used topographic maps together with census data to establish altitude zones while georeferencing cases to patient residential addresses. The analysis linked dietary habits (home-canned vegetables and smoked fish consumption) and storage practices and environmental conditions (temperature changes across elevations) to the toxin types (A, B, E) identified through laboratory confirmations. The analysis of temporal patterns used monthly incidence rates to identify peak periods, which matched local food preservation activities. The validation process combined DPZiGSEN records with hospital admission logs to reduce reporting biases in rural areas with restricted healthcare services.

Clinical data acquisition and parameters

The clinical profiles of 123 hospitalized patients were reconstructed from electronic health records and paper-based archives. The admission procedures included thorough neurological assessments to evaluate cranial nerve problems (e.g., ptosis, dysphagia) as well as motor function and autonomic symptoms (e.g., dry mouth, constipation). The initial 48 hours required hourly documentation of body temperature along with blood pressure and pulse rate vital signs. The laboratory diagnostics included hemogram analysis for leukocytosis and erythrocyte sedimentation rate as well as biochemical tests for troponin levels and creatinine phosphokinase (CK) activity to assess cardiac and skeletal muscle involvement and urinalysis to exclude metabolic issues. The disease progression and therapeutic response were monitored through serial measurements, which started at admission and continued at 24-hour intervals until pre-discharge.

Respiratory function and spirometry assessments

The evaluation of respiratory compromise as a critical disease severity factor used spirometry and pulse oximetry measurements. The portable spirometer measured three spirometry parameters, including forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and Tiffno index (FEV1/FVC ratio), which received comparisons to altitude-adjusted reference values. The vital lung capacity (VEL) and peripheral oxygen saturation (SPO2) were continuously monitored in severe cases. The classification of high-risk respiratory failure patients required FEV1 values below 70% predicted and SPO2 measurements below 92% at rest, which led to mechanical ventilation protocol activation. The interpretation of spirometry results occurred together with clinical signs of respiratory distress, which included accessory muscle use and paradoxical breathing.

Disease severity classification

The researchers applied a composite scoring system to determine case severity in three categories: mild, moderate, and severe. The mild cases presented with cranial neuropathies that included blurred vision and mild dysphagia without any respiratory or bulbar dysfunction. The moderate form of the disease presented with significant neuromuscular symptoms (e.g., limb weakness, dysphonia), but patients could swallow liquids and did not have hypoxemia. The definition of severe botulism included acute respiratory failure (PaO2 <60 mmHg or SPO2 <90% on room air), severe bulbar paralysis (inability to swallow saliva), or hemodynamic instability requiring intensive care. The tripartite classification system determined the treatment approach by deciding when to give antitoxin and when to provide respiratory support.

Ethical considerations

The research followed the ethical standards of the Declaration of Helsinki by protecting patient privacy through dataset anonymization [18]. The Institutional Review Board (IRB) of Osh State University waived ethical approval because the research involved retrospective non-interventional data analysis. The analysis of pre-existing de-identified records qualified for exemption from informed consent requirements. Researchers who worked with the Kyrgyz Ministry of Health data completed confidentiality agreements while strictly following established data access protocols. The results were combined into aggregates to protect individual identities especially in small-altitude communities with few cases.

Results and Discussion

Trends and mortality patterns of food-borne botulism in Kyrgyzstan (2007–2019)

Table 1. Dynamics of the incidence of food-borne botulism in the Kyrgyz Republic according to the data of the DPZ and the GSEN (2007-2019)

Year	n=980		Of these, food -borne botulism n=624		Total deaths from botulism n=32		Laboratory confirmation of botulism n=133	
	Absolute Number	%	Absolute Number	%	Absolute Number	%	Absolute Number	%
2007	60	5,1	29	48,3	4	13,8	6	20,7
2008	51	4,3	24	47,1	3	12,5	5	20,8
2009	74	6,3	46	62,2	0	0	3	6,5
2010	47	4,0	39	83,0	1	2,6	1	2,6
2011	82	7,0	74	90,2	3	4,1	2	2,7
2012	93	7,9	62	66,7	4	6,5	25	40,3
2013	121	10,3	70	57,9	2	2,9	22	31,4
2014	116	9,8	60	51,7	3	5,0	8	13,3
2015	144	12,2	74	51,4	6	8,1	7	9,5
2016	143	12,1	65	45,5	4	6,2	19	29,2
2017	108	9,2	88	81,5	0	0	17	19,3

2018	93	7,9	41	44,1	2	4,9	13	31,7
2019	46	3,9	42	91,3	1	2,8	5	11,9
Total	1178	100,0	714	60,6	33	5,3	133	18,6

The annual registration of botulism cases in the country shows a fluctuating trend, with significant variations from year to year, as shown in **Table 1** and **Figure 1**. These irregular patterns are mainly due to the occurrence of group outbreaks, where several individuals are affected at the same time, often due to the consumption of contaminated food. Thus, some years show a sharp increase in reported cases, while others show a decline, indicating the sporadic nature of botulism incidence and its dependence on the scale and frequency of such collective exposure events **(Figure 1)** [19].

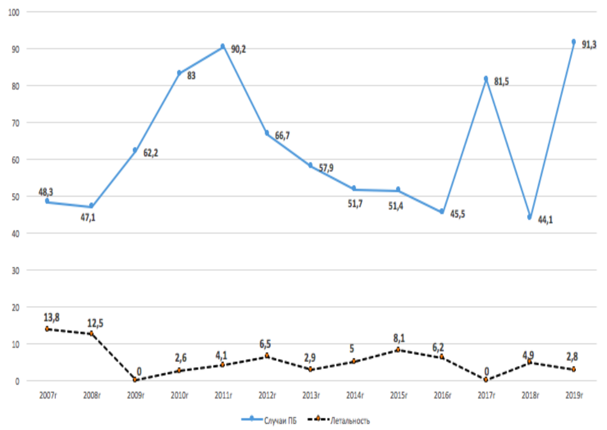

Figure 1. Annual frequency (%) of food-borne botulism cases and associated mortality in the Kyrgyz Republic, based on data from the Center for Disease Prevention and State Sanitary and Epidemiological Surveillance (2007–2019)

The average mortality rate from food-borne botulism was 5.3% ± 0.9%, with annual fluctuations ranging from 0% to a peak of 13.8%. The years with higher mortality rates did not show any correlation with the years of higher incidence. This lack of direct association is supported by statistical analysis: the correlation coefficient (r) was calculated as -0.634, indicating a moderate inverse relationship between incidence and mortality, according to the Chaddock scale. Furthermore, the Student's t-test result of -2.722 confirms the statistical significance of this inverse relationship. These findings suggest that mortality in cases of botulism is not directly dependent on the overall incidence rate and may be influenced more by factors such as the severity of individual outbreaks, the timeliness and quality of medical intervention, or the specific strain of the toxin involved. The distribution of foodborne botulism cases across the northern and southern parts of the republic is shown in **Figure 2**. The southern region recorded 70.2% ± 1.9% of cases over ten years, while the northern region had 29.8% ± 2.9% of cases. The southern region shows a higher incidence of cases because its climate allows for the cultivation and preservation of many vegetable- and fruit-bearing plants. The risk of botulinum toxin contamination increases when home canning and traditional food preservation methods are not performed under proper hygienic and safety standards [20, 21].

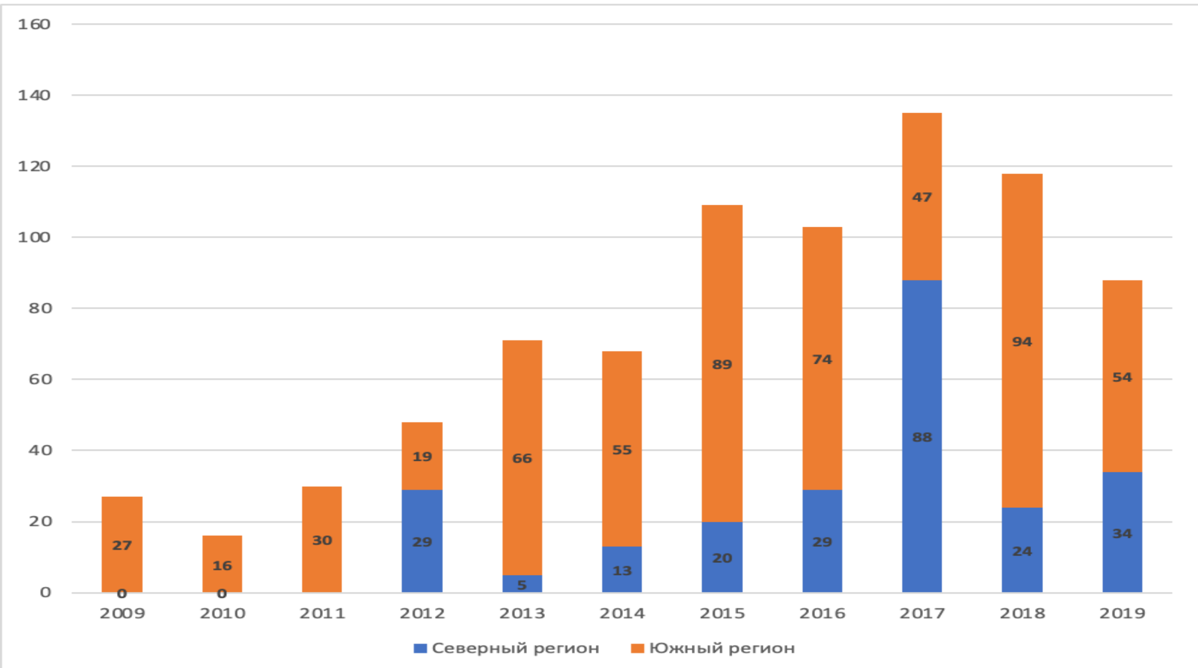

Figure 2. Incidence rates of food-borne botulism in the northern and southern regions of the Kyrgyz Republic according to the Center for Disease Prevention and State Sanitary and Epidemiological Surveillance (2009-2019)

An analysis of the 10-year period of incidence of foodborne botulism in the southern region shows annual registration with a predominance in Osh and Jalal-Abad oblasts. In the northern region, food-borne botulism has been recorded annually since 2012, mainly in Bishkek, while in the Talas and Issyk-Kul regions there were no cases of the disease during this period, and in the Naryn region in 2016 there was one group outbreak with 14 victims. Based on the analysis of the incidence of food-borne botulism by regions of the republic, we conducted its study using the example of the Osh region, taking into account the terrain features—it has a complex combination of high mountains, low elevations (Adyrs), and inside mountain depressions located at various absolute heights above sea level, which will make it possible to identify the clinical and epidemiological features of food-borne botulism in terms of prevalence and the severity of the disease as shown in **Figure 2** [22, 23].

According to the Law of the Kyrgyz Republic "On Mountainous Territories of the Kyrgyz Republic", there are lower mountainous territories—up to 1,500 meters above sea level; middle mountainous territories—from 1,500 to 2,000 meters above sea level; and upper mountainous territories—2,000 meters or more above sea level. In accordance with this gradation, the districts of the Osh region are distributed by altitude zones as follows: the low-altitude zone: Osh, Karasui, Aravan, and Uzgen districts; the middle-altitude zone: Nookat district; and the high-altitude zone: Alai, Kara-Kulzhinsky, and Chon-Alai districts. Based on the above, the activity of the population in the highlands is associated with the development of animal husbandry [24-27], and meat products are the main food product, whereas in low-altitude conditions the economy is focused on the development of agriculture, and, against the background of favorable climatic conditions, vegetable and fruit-berry plants are grown.

Table 2 shows a considerable regional variance in the distribution of foodborne botulism cases throughout the Osh area. The Karasui district recorded 48.0% of all cases this year, giving it the highest case count. Throughout the research period, the Karasui district saw stable near-annual case trends. The Aravan district followed the city of Osh and the Uzgen district in terms of instances, with 19.1%, 13.8%, and 10.9%, respectively. Nookat reported 4.8% of cases, followed by Alai at 2.8% and Kara-Kulja at 0.6%. The examination of botulism frequency by altitudinal zones demonstrates considerable environmental influences in addition to district-level variability. The low-mountain zone contained 327 (91.8% ± 1.5%) of all recorded cases, followed by the mid-mountain zone with 17 (4.8% ± 1.1%) and the high-altitude zone with 12 (3.4% ± 0.9%). The data suggest that lower altitude locations, with their higher human density and agricultural intensity, as well as traditional food preservation practices, provide ideal circumstances for botulinum development and spread. Differences in botulism incidence between altitude levels might be attributed to variances in food management practices and storage methods, as well as public health education and infrastructure availability **(Table 2)** [28, 29].

Table 2. Incidence of food-borne botulism in Osh region according to the Center for Disease Prevention and State Sanitary and Epidemiological Supervision of Osh (2007-2019)

Districts	Years													Total	
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	abs	%
Osh city	-	-	-	-	-	-	-	1	10	16	8	8	6	49	13,8±1,8
Aravansky	3	-	5	3	10	-	14	8	12	5	8	-	-	68	19,1±2,0
Karasu Region	18	17	10	12	17	-	19	15	10	13	15	25	-	171	48,0±2,6
Uzgen Region	1	5	-	-	-	-	-	-	14	-	4	15	-	39	10,9±1,6
Nookat Region	3	-	-	-	-	-	-	2	7	-	1	1	3	17	4,8 ±1,13
Alaiy Region	1	-	-	-	-	-	7	1	-	1	-	-	-	10	2,8 ±0,76
Kara-kul Region	-	-	-	1	-	-	-	-	-	-	1	-	-	2	0,6 ±0,40
Chon-Alai Region	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total for the region	26	22	15	16	27	-	40	27	53	35	37	49	9	356	100

A thorough epidemiological study evaluated foodborne botulism occurrence in Osh region districts through surveillance data from 2007 to 2019. The incidence rates were calculated per 100,000 population . The highest disease burden occurred in the Aravan district, which reported 64.1 cases of botulism per 100,000 population. The Karasui district followed with 49.0 cases, while the city of Osh had 20.1 cases, the Uzgen district had 17.1 cases and Alai district had 13.8 cases, the Nookat district had 7.2 cases, and the Kara-Kulja district had the lowest incidence at 2.3 cases per 100,000 population. The Osh region experienced an average of 26.4 foodborne botulism cases per 100,000 population throughout the 2007–2019 period, which demonstrates a continuous public health issue in this area. The incidence of botulism across different altitude zones in the Osh region shows long-term temporal patterns in **Figure 3**. The data indicates possible geographical and environmental factors affecting disease distribution, which requires additional research into regional food storage practices and climatic conditions and public health interventions [30, 31].

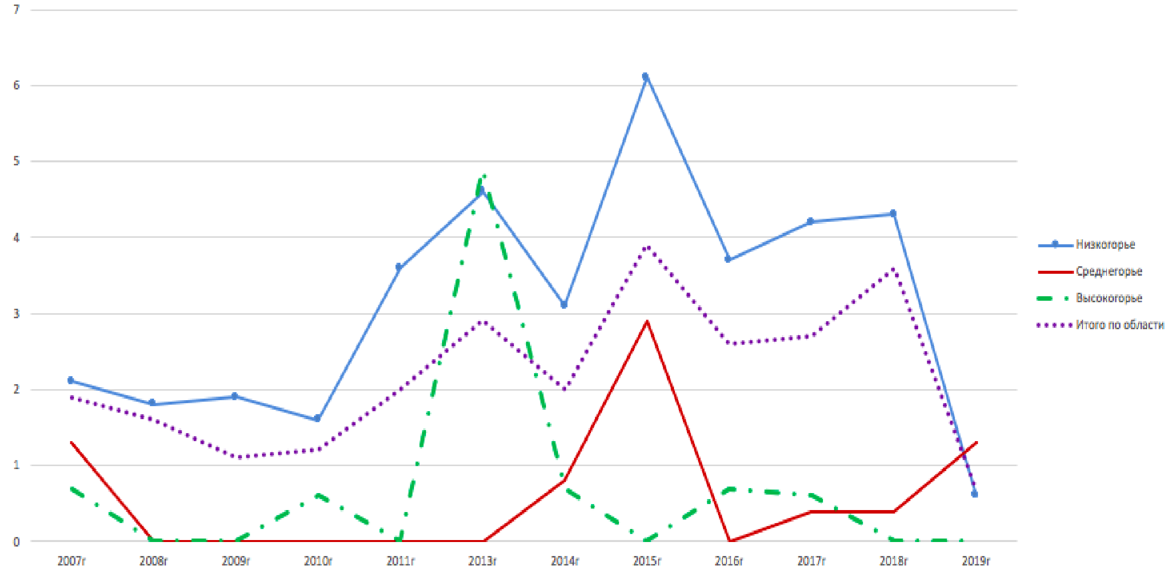

Figure 3. Annual trends across regions (Lowland, Midland, and Highland) and the total for the oblast from 2007 to 2019

The incidence of foodborne botulism in the Osh population from 2007 to 2019 is shown in **Figure 3** for different altitude zones per 100,000 population. The analysis of altitude-based trends over the 13-year period, as depicted in **Figures 3 and 4**, reveals a consistent annual registration of foodborne botulism cases in the low-altitude zones. The low-mountain areas show an incidence curve that matches the overall trend of the Osh region, indicating that these areas are the main drivers of regional epidemiological patterns. The mid-mountain and highland zones showed sporadic and irregular patterns, with some years having no registered cases followed by sudden spikes, indicating localized outbreaks. A notable epidemic outbreak occurred in the mid-mountain zone in 2015, and a similar surge was observed in the highland zone in 2013. These findings highlight the variability in disease dynamics across altitudinal gradients and underscore the importance of tailored public health interventions based on local geographical and environmental conditions **(Figure 3)** [32].

Temporal and seasonal characteristics of botulism incidence

The data showed a clear seasonal pattern through its peak values in November (31.1), January (12.9), May (12.5) and December (13.2) while the lowest values occurred from June to September with July reaching zero. The data shows significant changes that appear to be influenced by environmental factors including temperature and precipitation patterns. The study period showed wide variations in foodborne botulism incidence amplitude because group outbreaks and their associated patient numbers strongly affected the results. The data showed that foodborne botulism cases occurred throughout the entire year, as shown in **Figure 3**. The morbidity rates showed a distinct seasonal pattern, with the highest numbers occurring from October until May. The seasonal peak in morbidity matches the time when people eat more home-preserved and canned food products, which they prepare during harvest season and use during winter months. The number of reported botulism cases decreased substantially during the summer months from June to September because people consumed more fresh produce instead of canned foods. The research shows that dietary patterns during different seasons directly impact foodborne botulism rates, which supports the need for specific public health education about safe home-canning methods and food storage practices before and during the high-risk period [33].

The data shows that foodborne botulism cases primarily affect females at different ages. The study results show that females made up 62.9% ± 3.2% of all reported cases while males comprised 37.1% ± 3.2% ($p < 0.001$). The gender difference in food preparation and home canning activities may explain this gender-based disparity because women in the studied population perform these tasks more frequently. The adult population between 21–40 years old showed the highest vulnerability to foodborne botulism because this age group demonstrates both increased exposure and higher susceptibility. The incidence rate for people aged 15–20 years reached 10.8% ± 2.1%, which remained lower than other age groups. The results indicate that health education and prevention programs should focus on women and young adults who engage in household food preservation activities [34, 35].

The majority of botulism cases emerged from the low mountain zone, where 79.7% ± 3.6% of all reported cases originated. The incidence levels demonstrated an inverse relationship with altitude because disease burden decreased with higher elevations. The middle mountain regions included 11.4% ± 2.7% of all cases, but the highland areas had only 8.9% ± 2.6% of total cases. The distribution pattern of botulism cases can be explained by variations in climate and socioeconomic factors, which impact how people preserve food and access healthcare while also influencing their eating habits. The incidence of botulism showed a significant difference between genders since the disease occurred more often in females than in males by a factor of 1.7 ($p < 0.05$) and this pattern matched previous research about exposure risks between genders. The cases that affected the population most fell within the age group of 21–50 years because they made up 69.1% ± 4.4% of total cases. The cases were distributed as follows: The Infectious Diseases Department of the Osh Interregional United Clinical Hospital documented botulism cases that spanned various age groups with distinct gender patterns. The 21–30 age group showed the highest number of cases with 31.7±4.2% of total patients (15 males and 24 females). The 31–40 age group followed the 21–30 age group with 23.6±3.8% (8 males and 21 females) and the 41–50 age group had 13.8±3.1%. The 15–20 age group made up 12.2±2.9% of cases while patients aged 51–60 years and those older than 61 years accounted for 9.8±2.7% and 8.9±2.5% respectively. The total 123 cases showed a higher incidence of female patients at 66.7±4.3% compared to male patients at 33.3±4.2% [36, 37].

The length of time before symptoms appear from botulism toxin exposure depends on the amount of toxin consumed by the victim. The clinical severity of botulism directly correlates with the time duration between exposure and symptom onset. Medical records show that foodborne botulism causes symptoms to appear between 12 to 72 hours after exposure, and the incubation period can extend from several hours to eight days.

Demographic characteristics and risk factors

We evaluated the incubation period duration through a comparative analysis based on two essential variables, which included the specific food product involved in outbreaks and the altitude region where exposure occurred. The analytical method enabled researchers to explore how environmental conditions along with dietary habits affect disease development and severity.

Our data bring attention to maintaining the consistency of the food product throughout the incubation period in cases of botulism. The incubation period was brief for products with a liquid medium, such as compotes, jams, and pickled cucumbers and tomatoes, averaging 8.0±1.8 hours. In contrast, it was extended for vegetable salads, reaching an average of 17.1±2.9 hours. As a result, a consistent distribution of the toxin is noted in products that have a liquid consistency, resulting in a brief incubation period. The incubation period extended when consuming vegetable salads, resulting in an irregular, "nest" distribution of the toxin within the food item. The data collected reveal statistically significant differences ($p < 0.001$), with a Student's t-test value of 4.48. Furthermore, we have established a correlation between the length of the incubation period and the various altitude zones. Under low-altitude conditions, the incubation period was observed to be prolonged (18.3±0.7 hours) in contrast to the middle altitude (15.6±2.1 hours) and high mountain regions (9.4±0.2 hours). With the rise in altitude, the impact of hypoxia intensified, leading to a reduction in the incubation period duration ($r=-0.982$)

Influence of age, altitude, and environmental factors on the incubation, severity, and clinical course of foodborne botulism

An examination of the incubation period's duration in relation to patient age indicated a trend of elongation with advancing age; specifically, the shortest incubation period was observed in individuals aged 15-20 years, while the longest was noted in those over 50 years old. Consequently, we have established the relationship between the length of the incubation period in botulism and a) the specific food product responsible for the illness, b) variations in altitude zones, and c) different age groups. Upon hospitalization, it was observed that under low-altitude conditions, a significant proportion of patients were admitted within the first day of disease onset (70.4±4.6%), while 13.3±1.4% of cases sought medical assistance after 48 hours. In contrast, in the middle and highlands, there was often a delay in treatment, with percentages of 64.3±12.8% and 72.7±13.4% receiving care after 48 hours, respectively. The examination of hospitalization duration from disease onset indicated a clear correlation with age; as the age category rose, patients experienced later admissions to the hospital ($r=0.89$). Consequently, individuals in the 15-20 year age group were admitted after an average of 17.1±2.9 hours, those aged 21-50 years after 29.1±4.1 hours, and patients older than 51 years after 37.2±4.4 hours.

The most useful system for classifying foodborne botulism severity in clinical practice consists of three categories: mild, moderate, and severe. The study included patients with severe botulism cases which made up 89.4% ± 2.8% of total cases. The diagnosis of moderate severity occurred in 19.5% ± 2.8% of cases, mainly among patients between 21–50 years old who were mostly male. The observed patient cohort showed no cases of mild botulism because foodborne transmission in this population typically results in severe clinical symptoms. Research supports the higher number of female patients with severe botulism because women tend to engage more in food preparation and traditional home-preservation activities [38, 39]. The incidence of severe botulism forms showed a perfect positive correlation ($r = 1.0$) with the altitude zone of the affected areas. The observed relationship between altitude and disease severity indicates that environmental elements together with delayed medical care access in mountainous regions may lead to a worsening of the condition. Foodborne botulism starts abruptly while displaying three primary clinical syndromes, which include gastrointestinal symptoms, paralytic symptoms, and general intoxication symptoms. All patients displayed the gastrointestinal syndrome as their first symptom, which existed at different levels of severity. The gastrointestinal syndrome started with widespread abdominal discomfort followed by vomiting that occurred 3–5 times and short periods of diarrhea, which also occurred 3–5 times. The early symptoms of neurotoxin-induced gastrointestinal irritation occur before the body starts to show signs of systemic neuroparalytic involvement [40].

The research showed that food type directly affected the severity of gastrointestinal syndrome. The clinical [41-43] symptoms became much worse after patients consumed homemade compotes prepared from berries and fruits ($p < 0.001$). The most common gastrointestinal symptoms were nausea and diarrhea, which affected 66.7% of patients while vomiting and abdominal pain occurred in 54.2% of cases. The gastrointestinal symptoms from vegetable-based dishes including salads and pickled cucumbers and tomatoes, were less severe than other foods. Nausea remained the primary symptom in all Clostridium botulinum neurotoxin cases while vomiting and diarrhea appeared briefly with moderate severity. The presence of type A botulinum toxin produced more severe abdominal pain symptoms. All patients experienced neurological symptoms after their gastrointestinal issues disappeared, which indicated that the disease progression followed a pattern from gastrointestinal to neuroparalytic involvement. Foodborne botulism caused paralytic syndrome because botulinum toxin damaged motor nuclei of cranial nerves and parasympathetic neurons located in the brainstem's mesencephalic and bulbar regions [44, 45]. The first neurological symptoms of this condition started with ophthalmoplegic manifestations which included vision blurring described as a "veil" in front of the eyes and unclear object shapes, double vision, poor accommodation, dilated pupils, uneven pupil size, and eye movements. The condition evolved into phagonazoglossoneurological symptoms, which included swallowing difficulties and nasal reflux and choking and tongue deviation, together with phonolaryngological signs of dysphonia and dysarthria. Acute respiratory insufficiency syndrome (ARIS) emerged as a dangerous complication in some patients who experienced dyspnea and air hunger followed by worsening respiratory distress. The neuromuscular symptoms started appearing during the first phase of the illness and became more severe as the disease progressed. The patients commonly experienced widespread muscle weakness together with fatigue, lethargy and physical exhaustion. The symptoms described in the literature as "bulbar myasthenic syndrome" match the myasthenic response of bulbar musculature to botulinum toxin [46, 47].

Impact of altitude on clinical severity, vital signs, and epidemiology of botulism in the osh region

The severity of the paralytic syndrome in botulism patients demonstrated a significant correlation with altitude **(Figure 4)**. The clinical manifestations in low-mountain residents were mostly of moderate intensity and were observed in 69.4 ± 4.7% of cases ($p < 0.001$). The specific neurological symptom complexes in this group were distributed as follows: ophthalmoplegic symptoms were observed in 73.7 ± 4.4%, phagonazoglossoneurological in 71.1 ± 4.6%, phonolaryngological in 54.4 ± 5.1%, and acute respiratory insufficiency (ODN) in 66.8 ± 4.7% of patients. The middle-mountain zone residents had more severe paralytic syndrome cases, which were reported in 63.3 ± 12.9% of cases ($p < 0.001$). The phagonazoglossoneurological and phonolaryngological symptoms were observed in 71.4 ± 12.1% of patients, and ophthalmoplegic in 62.3 ± 12.9% and ODN in 60.7 ± 13.1% within this group. The most severe paralytic manifestations were found in patients from high-altitude areas where neurological symptoms reached 87.0 ± 10.1% of cases. The combination of hypoxia effects at high altitudes likely contributes to the increased severity of the condition. The neurological impairment showed a strong inverse correlation with altitude ($r = -1.0$) indicating that elevation increases the severity of the paralytic syndrome **(Figure 4)**.

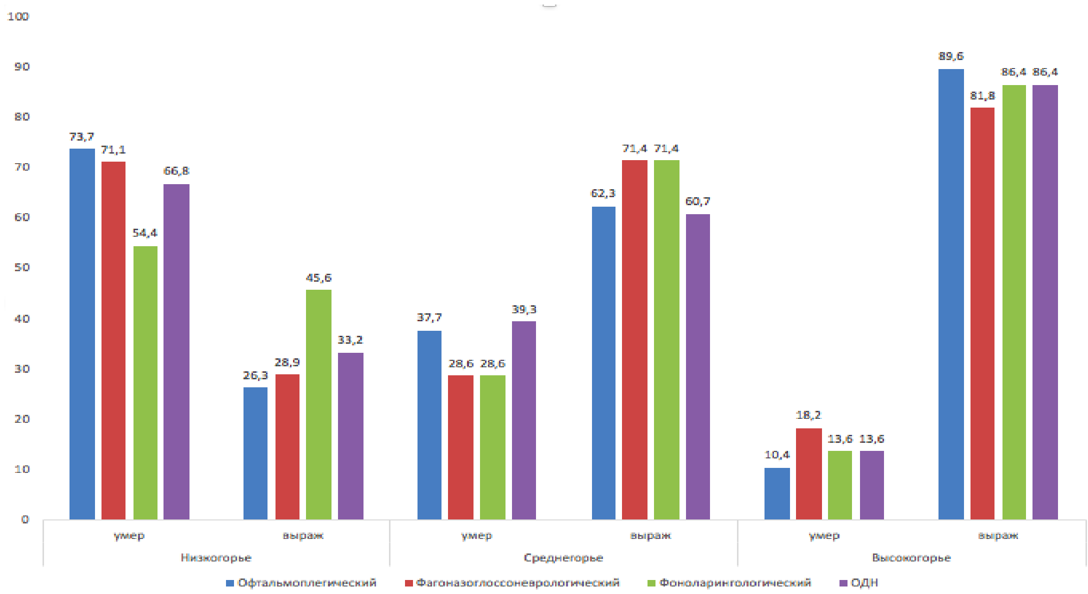

Figure 4. The frequency (%) of clinical manifestations of paralytic syndrome in botulism, depending on the altitude zone and severity (n=123)

The vital signs of patients with severe botulism showed different patterns based on their altitude zone location. The patients located in low mountain regions (n=98) showed respiratory rates of 21.5±3.8 breaths per minute and heart rates of 88.6±3.0 beats per minute and systolic blood pressure of 90.9±3.3 mmHg and diastolic pressure of 62.3±1.5 mmHg and body temperature of 37.1±0.2°C. Middle mountain patients (n=14) exhibited slightly elevated respiratory and heart rates of 23.6±3.8 and 94.8±2.8 while their blood pressure readings were slightly lower (88±4.7 systolic and 61±3.2 diastolic) with a body temperature of 37.3±0.3°C. The high-altitude zone patients (n=11) displayed respiratory rates of 24.4±3.9 and heart rates of 100.6±2.7 with decreased blood pressure readings of 86.3±5.3 systolic and 60.2±2.6 diastolic and a body temperature of 37.5±0.2°C. The data shows that respiratory and heart rates increase with altitude while blood pressure decreases slightly and body temperature rises slightly.

Tachypnea and tachycardia appear as essential clinical indicators when botulism causes respiratory failure. The disease initially produced elevated blood pressure readings but patients developed decreased blood pressure levels as the condition worsened. Botulism typically shows no fever in its uncomplicated form. The presence of low-grade fever (subfebrility) occurs in moderate to severe cases of botulism but high-grade fever (Nikiforov V.N., 1985) develops when secondary bacterial infections occur. The vital sign patterns across different altitude zones showed that respiratory rate and heart rate and body temperature increased together (correlation coefficient r = 0.9). Blood pressure measurements showed a negative correlation with increasing altitude (r = −0.9). The research results demonstrate how highland hypoxic conditions worsen botulism symptoms. Bacteriological investigations showed Clostridium botulinum presence in 78 patients (63.4 ± 4.3%). The pathogen was detected in blood samples from 12 patients (15.4%) while vomit samples tested positive in 29 cases (37.2%) and feces samples in 30 cases (38.5%) and urine samples in 9 cases (11.5%). The Cl. botulinum toxin was detected in 20 food residue samples (25.6%). The pathogen was simultaneously found in clinical specimens (vomit, blood, feces, urine) and corresponding food samples in 8 patients (10.3%). The OGTSPZIGSEN laboratory performed toxin neutralization assays that revealed toxin type A in 9 patients (11.5%) and type B in 28 patients (35.9%) and atypical variants in 41 patients (52.6%). Type A toxin has emerged as a new finding in this region during the last few years [2, 3]. The epidemiological profile of botulism in the Osh region shows a shift because atypical toxin variants now represent the most common form of the disease. Type B used to cause 91.3% of cases during the 1980s but now represents only 2.5% of current cases.

The clinical indicators of respiratory failure caused by botulism include tachypnea and tachycardia. The disease starts with high blood pressure but the condition leads to a decrease in blood pressure as it advances. Botulism remains without fever in its uncomplicated form. The disease shows low-grade fever (subfebrility) in moderate to severe cases but develops high-grade fever when secondary bacterial infections occur (Nikiforov V.N., 1985). The study of vital signs at different altitude levels showed a strong positive relationship between respiratory rate and heart rate and body temperature (r = 0.9). Blood pressure demonstrated a negative relationship with rising altitude (r = −0.9). The research shows that botulism symptoms become more severe when patients experience hypoxic conditions at high elevations. Bacteriological analysis revealed Clostridium botulinum in 78 patients (63.4 ± 4.3%). The pathogen was detected in blood samples of 12 patients (15.4%) while vomit samples contained it in 29 cases (37.2%) and feces samples in 30 cases (38.5%) and urine samples in 9 cases (11.5%). The laboratory detected Cl. botulinum toxin in 20 food residue samples which made up 25.6% of the total samples. The pathogen was detected in clinical specimens (vomit, blood, feces, urine) and corresponding food samples in 8 patients (10.3%).

The OGTSPZIGSEN laboratory performed toxin neutralization tests that showed type A toxin in 9 patients (11.5%) and type B toxin in 28 patients (35.9%) and atypical toxin variants in 41 patients (52.6%). The toxin type A has been registered in this area only during the last few decades. The epidemiological profile of botulism in the Osh region has changed because atypical variants now make up the majority of cases. Type B toxin used to make up 91.3% of cases during the 1980s but now represents only 2.5% of cases **(Table 3)**.

Table 3. Indicators of respiratory function in patients with botulism (n=42)

Indicators	Control Group n=11	Age Groups			Altitude Zone	
		15-20 Years	21-50 Years	>50 Years	Low-altitude	High-altitude
VC, L (Vital Capacity)	3,3±0,5	2,7±1,1	2,3±0,6	2,4±0,5	2,5±0,8	2,2±0,2
VC, % of predicted	81,2±1,2	71,3±4,2	68,4±4,1	65,7±4,4	68,5±4,3	57,3±4,6
FEV1, L (Forced Expiratory Volume in 1 sec)	2,9±0,5	2,8±0,2	2,3±0,3	2,4±0,5	2,5±0,3	1,9±0,2
FEV1, % of predicted	86,7±1,2	85,7±2,1	78,5±3,8	75,0±4,0	79,7±3,7	64,2±4,4
FVC, L (Forced Vital Capacity)	3,3±0,5	3,2±0,6	2,5±0,3	2,6±0,4	2,7±0,4	2,1±0,3
FVC, % of predicted	94,1±3,7	87,5±2,6	72,1±4,1	64,5±4,4	74,7±4,0	60,1±4,5
FEV1/FVC ratio	1,1±0,2	1,1±0,6	1,05±0,4	1,0±0,2	1,05±0,4	1,0±0,3

There was no ischemic myocardial necrosis but potential posthypoxic myocardial injury, as seen by the 0.2 ng/ml increase in troponin levels at a rate of 0.1 ng/ml and the more than 1.5-fold increase in CK activity across all groups. The study found no correlation between the outcomes and age group. Compared to patients from the high-altitude region, the CPK levels in the low-altitude region were marginally higher.

Conclusion

The Osh region shows food-borne botulism as an endemic condition with 26.4 cases per 100,000 inhabitants annually which mainly occurs in group outbreaks (86.9%) and most commonly affects low-altitude areas (35.3 per 100,000). The disease affects women more than men since their incidence rate is 1.7 times higher and primarily affects people between 21–50 years old (79.7 ± 3.6%). The epidemiological data shows that atypical Clostridium botulinum toxin type is the most common (52.6%) followed by type B (35.9%) and type A (11.5%). The low level of public awareness (32.5%) indicates the requirement for stronger sanitary measures and educational programs. The incubation period shows a strong relationship with food consistency and altitude zone and age ($r = 0.9$) and older patients and middle- and high-altitude zone residents experience delayed hospitalization. The severity of disease cases, especially severe ones (89.4 ± 2.8%), directly correlates with altitude levels ($r = 1.0$) and affects women and people from both younger and older age groups. The onset of gastrointestinal symptoms occurred in all patients, but paralytic symptoms were more severe in type A toxin infections and moderate in type B and atypical toxin infections. The severity of symptoms increased with altitude from moderate in low mountains (74.7 ± 4.4%) to most severe in highland populations. The respiratory function parameters LVEF, FEV1 and VC showed restrictive impairment mainly in older patients and highland residents. The biomarkers showed minimal posthypoxic myocardial damage, while blood oxygen saturation levels decreased from 92.4% to 91.7% which proved hypoxia, thus requiring supplemental oxygen therapy.

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