



Epidemiological and Clinical Evaluation of Botulism Cases Whom Referred to Imam Reza Hospital through May 2016 to May 2020 and their 3 Years Follow Up

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Abstract

Background: Botulism is a rare severe neuroparalytic disease that is imposing great danger to the health system.

Materials and Methods: The data of all botulism cases admitted in toxicology wards of Imam-Reza Hospital of Mashhad University of Medical Sciences (March 2016 to March 2019) were extracted. In August 2020, the type and duration of remaining symptoms of patients were evaluated by call.

Results: Thirteen hospitalized cases (males/ females = 14/16), with the mean age = 30.97 ± 11.56 years, were included. The most prevalent infection sources were local yogurt (10 cases, 34.5%) and strained yogurt (6 cases, 20.7%). The mean number of observed symptoms in patients was 4.26 ± 1.41 and diplopia (83.3%), ptosis (73.3%), blurred vision (70%), and dysphagia (46.7%) were the most common symptom. Ptosis and diplopia were more common in men. The mean of incubation period 2.46 ± 1.50 days with no relation to sex. Mydriasis (2.85 ± 0.89 days), lower extremity paralysis (2.50 ± 2.12 days) and speech disorder (4.75 ± 2.60 days) were the sooner recovered symptoms after hospitalization, however dyspnea (8.65 ± 6.65 days) and dysphagia (7.35 ± 2.89 days) were the last. Seven patients (23.3%) required tracheal intubation. The average of hospitalization length was 6.23 ± 3.84 days that was shorter in patients with mydriasis. 60% of cases had ptosis when they returned to home. Decreased daily function (83.3%), blurred vision (83.3%), weakness (80%) and speech disorders (76.7%) were the most common reported complain in follow-up. 30% of patients had at least one symptom to 12 months, and 7% up to 36 months after discharge.

Conclusion: Two year follow-up of the patients is suggested.

Keywords: Botulism; Blepharoptosis; Deglutition Disorders; Diplopia; Activities of Daily Living

Introduction

Botulism is a severe neuroparalytic disease, provoked by neurotoxin-producing bacteria of the genus *Clostridium*; especially *botulinum*, *barati*, *sporogenes*, and *argentinense* species [1]. *Clostridia* are Gram-positive, spore-forming bacilli frequently found in soil and marine sediments, contaminating food sources [2,3]. In the case of anaerobic milieu with a pH above 5, these are capable of producing seven serologically recognizable exotoxins named from A to G, among which types A, B, E, and seldom F are reported to cause morbidity and mortality in humans [1,4]. *Clostridia* spores lose their activity when heated above 100°C, yet they may remain intact in conventional cooking methods which provide the spores with the conditions necessary for toxin production [5].

Botulism is divided into several forms based on the entryway of the toxin, including food-borne, intestinal toxemia, wound, inhalation, and iatrogenic botulism [3]. The most prevalent form of the disease is food-borne or classic botulism, evoked by consumption of nutrients containing Botulinum Neurotoxin (BoNT) [4,6]. BoNT imposes presynaptic inhibition on cholinergic synapses by obstructing acetylcholine release from motor nerve terminals, resulting in flaccid paralysis of muscles [3]. Other signs and symptoms may include general weakness, xerostomia, dysphagia, dysarthria, blurred vision, ptosis, urinary retention, and constipation. This condition can potentially lead to paralysis of the respiratory muscles and subsequently death if not immediately treated [3]. Management of the condition relies mostly on supportive treatments and antitoxin administration [7]. Hereby the early onset of treatment is crucial. However, cases are frequently misdiagnosed or identified only after death, which can be partly attributed to the relatively low incidence of the disease. Diagnosis of botulism is mainly based on clinical manifestations, and also the epidemiology of the disease is taken into consideration [7,8].

Considering the high mortality of the disease and the probability of outbreak via contaminated food, botulism is considered a serious matter in public health. Herewith a thorough analysis of epidemiology of botulism is recommended, enabling us to recognize associated risk factors and eliminate clusters as soon as possible. In this regard, the Centers for Disease Control and Prevention (CDC) have implemented surveillance policies and botulism registries to reduce the burden of the disease. Also in Iran, the national surveillance system for botulism provides a database for the epidemiologic state of the disease since 2003 [5]. Each year, an

average of 1000 cases of botulism are confirmed worldwide, which is estimated to cover only 5% of the actual statistics [9].

Botulism is a rare, but still concerning disease, imposing great danger to the health system. Although some studies have previously been conducted in this regard in Iran, a lack of sufficient follow-up is present to our knowledge. Thus, we aimed to clinically investigate the epidemiologic state of botulism in a cross-sectional study, with follow-up evaluation after the initial investigation.

Materials and Methods

This retrospective cross-sectional included data of patients with a confirmed diagnosis of botulism hospitalized in toxicology wards of Imam-Reza hospital, affiliated with Mashhad University of Medical Sciences (MUMS). Data of all eligible patients in the time period between March 2016 and March 2019 were extracted from the Hospital Information System (HIS). In general, data of 30 patients were inserted in the study. In case of a lack of enough relevant data available in HIS or Hospital Records, additional information was obtained via telephone calls. In August 2020, the type and duration of remaining symptoms of all patients were evaluated by telephone call.

The study was in line with the Declaration of Helsinki and confirmed by the Ethics Committee of MUMS, with the Ethics Code IR.MUMS.MEDICAL.REC.1398.272. Patients' data were included in the study with their written informed consent; and their personal information, entailing their name, remained undisclosed.

Demographic data of patients, such as age, gender, and occupation were obtained. Information related to the course of the disease, including incubation period, clinical signs and symptoms, and the duration of symptoms were analysed. Also, results of laboratory tests of patients, including Complete Blood Count (CBC) and liver function tests, were evaluated.

Participants' data were analysed with SPSS (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). The normal distribution of data was assessed with the Kolmogorov-Smirnov test. The mean \pm SD of parametric and nonparametric quantitative data were compared using independent sample T-test and Mann-Whitney U test, respectively. Fisher's exact test was used to evaluate qualitative values. *p*-values smaller than 0.05 were considered significant.

Results

Our study involved 30 hospitalized patients diagnosed with botulism, among them 14 males (46.7%) and 16 females (53.3%). The mean age of patients was 30.97 ± 11.56 years, and there was no significant difference between the mean age of male and female (33.36 ± 13.26 years and 28.88 ± 9.81 years old, respectively).

In regards to patients' careers, the most frequently mentioned occupation was housekeeping (12 people, 40%), followed by free-lance jobs (8 people, 26.7%). Most patients (16 patients, 55.2%) had primary education or less.

The most prevalent source of infection in patients was local yogurt (10 cases, 34.5%), with strained yogurt standing in the second

position (6 cases, 20.7%). Other sources of infection were canned corn (4 cases, 13.8%), canned green peas (4 cases, 13.8%), local yogurt drink (3 cases, 10.3%), and fruit compote (2 cases, 6.9%).

Table 1 demonstrates the signs and symptoms of participants. The most common symptoms that patients presented with were diplopia (83.3%), ptosis (73.3%), blurred vision (70%), and dysphagia (46.7%) in descending order. Except for ptosis (13; 92.9% male and 9; 56.2% female, p -value = 0.039) and diplopia (14; 100.0% male and 11; 68.8% female, p -value = 0.045), the distribution of the rest of the symptoms was not significantly different between the two sexes. The mean number of symptoms observed in patients was 4.26 ± 1.41 that was not statistically significant difference between to sexes (4.71 ± 1.58 in men and 3.87 ± 1.87 in women).

| Sign or symptom | Frequency (%) at admission | Time of onset | Time of exacerbation | Time of recovery |
|---------------------------|----------------------------|-----------------------------|-----------------------|------------------------|
| Diplopia | 25 (83.3%) | -1.64 ± 1.52 (-5, 0; -1) | 0.18 ± 0.61 (-1,2 ;0) | 5.29 ± 3.18 (2,17;4) |
| ptosis | 22 (73.3%) | -1.68 ± 1.42 (-5, 0; -1) | 0.14 ± 0.48 (0, 5 ;0) | 5.47 ± 3.40(2,17;5) |
| Blurred vision | 21 (70.0%) | -1.38 ± 1.35 (-4, 0; -1) | 0.14 ± 0.48 (-1.1 ;0) | 4.90 ± 3.40 (2,17;4) |
| Dysphagia to liquids | 14 (46.7%) | -3.13± 1.18 (-4, 0; -3) | -0.11± 0.84 (-1,0 ;0) | |
| Dysphagia to solids | 14 (46.7%) | -2.21 ± 1.52 (-5, 0; -2) | 0.29 ± 0.99 (-2,2 ;0) | 7.35 ± 2.89 (4,15;7.5) |
| Mydriasis | 8 (26.7%) | -0.42 ± 0.53 (-1, 0; 0) | 0.142 ± 0.38 (0,1 ;0) | 2.85 ± 0.89 (2,4;3) |
| Speech disorders | 8 (26.7%) | -3.25 ± 1.48 (-5, -1; -4) | | 4.75 ± 2.60 (2,9;4.5) |
| Weakness | 4 (13.3%) | -2.50 ± 1.00 (-4, -2; -2) | | |
| Diarrhea | 2 (6.7%) | -1.50 ± 0.70 (-2, -1; -1.5) | | |
| Dyspnea | 5 (6.7%) | -0.6 ± 2.19 (-4, +2; 0) | 0.800 ± 0.83 (0,2;1) | 8.40 ± 6.65 (2,17;5) |
| Lower extremity paralysis | 2 (6.7%) | -2.50 ± 2.12 (-4, -1; -2.5) | | 2.12 ± 3.50 (2,5;3.5) |
| Constipation | 2 (6.7%) | +3.00 ± 1.40 (+2,+4; +3) | 4.00 ± 1.41 (3, 5;4) | 6.50 ± 3.53 (4,9;6.5) |
| Facial paralysis | 1 (3.3%) | -5.00 (-5, -5; -5) | | 4.00 (4,4;4) |
| Upper extremity paralysis | 1 (3.3%) | -1.00 (-1,-1; -1) | 2.00 (2,2; 2) | 7.00 (7,7;7) |
| Urinary retention | 1 (3.3%) | +1 (+1, +1; +1) | | |

Table 1: Frequency of signs and symptoms at admission and times of onset, exacerbation and recovery of signs and symptoms (in reference to admission day,) in patients diagnosed with botulism in Imam Reza hospital from March 2016 to March 2019 data reported as: Mean ±SD (Minimum, Maximum; Median).

The mean of reported incubation period 2.46 ± 1.50 days (min = 0.5, max = 7; median = 2 days) and there was no significant difference between incubation period of two sexes (male = 2.57 ± 1.68 days and female = 2.36 ± 1.39 days, $PV = NS$).

Table 1 also summarizes the onset time of signs and symptoms. Regarding the time of onset of symptoms, facial paralysis with 5.00 days (only one case), speech disorders with 3.25 ± 1.48 days, dysphagia to liquids with 3.13 ± 1.18 days and weakness with $2.50 \pm$

1.00 days prior to hospital admission were the earliest symptoms and constipation with an average of 3.00 ± 1.40 days after hospitalization was the latest symptom to appear. It was also found that the time range of onset of symptoms could vary from 5 days before hospitalization (symptoms such as ptosis, diplopia, facial paralysis, dysphagia, and speech disorder) to 4 days after hospitalization (constipation).

Regarding the time of exacerbation of symptoms (table 1), diplopia with an average of 0.17 ± 0.61 days, blurred vision with 0.14 ± 0.47 days, and ptosis with 0.142 ± 0.47 days were the first symptoms that worsened after hospitalization, and upper extremity paralysis with 2.00 ± 0.00 days had the latest time of exacerbation compared to other symptoms. Also, the time range of symptom exacerbation varied from 1 to 2 days before hospitalization (dysphagia, diplopia, and blurred vision) to 5 days after hospitalization (ptosis and constipation).

In terms of symptom recovery time during hospitalization, mydriasis with an average of 2.85 ± 0.89 days, lower extremity paralysis with 2.50 ± 2.12 days and speech disorder with 4.75 ± 2.60 days after admission had a faster recovery time than other symptoms, dyspnea with 8.65 ± 6.65 days and dysphagia with 7.35 ± 2.89 days had the latest recovery time (Table 1). Symptom recovery time ranged from a minimum of 2 days to a maximum of 17 days after admission.

Regarding changes in laboratory tests, shown in Table 2, only three parameters of white blood cells (WBC), polymorphonuclear cells (PMN), and Alanine transaminase (ALT) were statistically meaningful. The mean amount of the first day of WBC was $9.033 \pm 2.76 \times 1000$ cells/ μ l, which reduced to $7.66 \pm 2.36 \times 1000$ cell/ μ l through 2 to 3 days after admission (p-value = 0.001). The mean of PMN was $67.33\% \pm 10.1\%$ of total WBC, which was significantly reduced to $63.74\% \pm 9.90\%$ of total WBC (p-value < 0.05).

| Laboratory test | Mean \pm SD at admission | Mean \pm SD of changes | p-value |
|---|----------------------------|--------------------------|---------|
| White blood cells ($\times 10^9$ cells / L) | 9.03 ± 2.76 | 7.66 ± 2.36 | 0.001 |
| Polymorphonuclear cells (% of total WBC) | $67.33\% \pm 10.10\%$ | $63.74\% \pm 9.90\%$ | 0.057 |

| | | | |
|---------------------------------------|----------------------|----------------------|--------|
| Lymphocytes (% of total WBC) | $25.30\% \pm 9.36\%$ | $27.10\% \pm 8.73\%$ | 0.174 |
| Platelets ($\times 10^9$ cells/L) | 2.22 ± 40.10 | 2.29 ± 50.35 | 0.251 |
| Hemoglobin (g/dl) | 13.54 ± 1.40 | 13.63 ± 1.18 | 0.402 |
| Sodium (mmol/L) | 139.00 ± 2.47 | 138.00 ± 2.10 | 0.891 |
| Potassium (mmol/L) | 3.92 ± 0.37 | 3.93 ± 0.24 | 0.984 |
| Blood sugar (mg/dl) | 97.66 ± 18.07 | 97.85 ± 13.31 | 0.956 |
| Blood Urea Nitrogen (mg/dl) | 24.78 ± 9.71 | 25.07 ± 8.70 | 0.664 |
| Creatinine (mg/dl) | 0.81 ± 0.23 | 0.78 ± 0.17 | 0.493 |
| Aspartate transaminase (Units/L) | 21.38 ± 11.82 | 22.83 ± 11.42 | 0.076 |
| Alanine transaminase (Units/L) | 22.00 ± 14.75 | 24.44 ± 15.13 | <0.001 |
| Alkaline phosphatase (IU/L) | 39.33 ± 1.57 | 34.71 ± 1.59 | 0.749 |

Table 2: Laboratory tests of patients diagnosed with botulism in Imam Reza hospital from March 2016 to March 2019. P-value less than 0.05 considered significant (SD: Standard Deviation, WBC: White Blood Cells, L: Litre, mmol/l: millimoles per litre, g/dl: gram per decilitre, mg/dl: milligram per decilitre, IU/L: International Units per Litre).

Also, the mean Alanine transaminase (ALT) level at the time of admission was 22.00 ± 14.75 IU/L and the mean of remarkable changes during hospitalization was 24.44 ± 15.13 IU/L which showed statistical significance (p -value <0.001). However, the amount of raised ALT was not clinically significant.

During the hospitalization, 7 patients (23.3%) required treatment in the Intensive Care Unit (ICU), whereas 23 patients (76.7%) recovered without intensive therapy. The mean number of days with mechanical ventilation was 3.96 ± 1.60 days, with a minimum of 0 days and a maximum of 18 days.

The mean number of antitoxin vials consumed in patients in this study was 14.03 ± 9.25 vials per patient. This research showed no relationship between the number of antitoxin vials and age, sex, number of symptoms, length of hospital stay or incubation period. The number of vials consumed was 22.42 ± 12.81 in ICU admitted patients and 11.47 ± 6.22 in other patients, which was significantly different (p -value = 0.004). There was a positive correlation between the number of infused antitoxin and the number mechanical ventilated time ($R_2 = 0.41$, $PV < 0.0001$).

In this study, the mean duration of hospitalization was calculated as 6.23 ± 3.84 days. Table 3 demonstrates the relationship between the presentations of certain signs or symptoms and the duration of hospital stay. Patients with weakness and Dysphagia to liquids had the longest hospital stay, whereas participants presenting with mydriasis had the shortest duration of hospitalization. The mean duration of hospitalization in patients with mydriasis was 3.12 ± 0.83 days, and 7.36 ± 3.36 days in patients without mydriasis, which was significantly different (p -value = 0.005).

The most common remained symptoms at discharge was ptosis (60%). On average, about one-third of patients were symptomatic up to 12 months after discharge, 20% up to 24 months, and 7% up to 36 months after discharge (Figure 1).

The number of patients' symptoms in the first month after discharge was much higher than in the following months, so that in the second month the number of patients' symptoms was very low and from 12 months onwards the number of symptoms was almost less than one case (Figure 2).

Decreased daily function (25 patients, 83.3%), blurred vision (25 patients, 83.3%), weakness (24 patients, 80%) and speech

| Sign or symptom | Mean \pm SD | | p-value |
|---------------------------|--------------------------------------|---|---------|
| | In patients with the sign or symptom | In patients without the sign or symptom | |
| Ptosis | 6.05 ± 3.77 | 6.75 ± 4.26 | 0.665 |
| Diplopia | 5.72 ± 3.64 | 8.80 ± 4.20 | 0.103 |
| Blurred vision | 5.57 ± 3.74 | 7.78 ± 3.83 | 0.153 |
| Weakness | 8.25 ± 1.70 | 5.92 ± 4.00 | 0.267 |
| Mydriasis | 3.12 ± 0.83 | 7.36 ± 3.89 | 0.005 * |
| Facial paralysis | 4.00 ± 0.00 | 6.31 ± 3.89 | 0.564 |
| Dysphagia to liquids | 7.79 ± 2.96 | 4.88 ± 4.09 | 0.036 * |
| Speech disorders | 5.25 ± 2.60 | 6.59 ± 4.20 | 0.408 |
| Lower extremity paralysis | 4.00 ± 1.41 | 6.39 ± 3.92 | 0.405 |

Table 3: Association between duration of hospitalization and signs or symptoms present in patients diagnosed with botulism in Imam Reza hospital from March 2016 to March 2019. P-value less than 0.05 considered significant (SD: Standard Deviation).

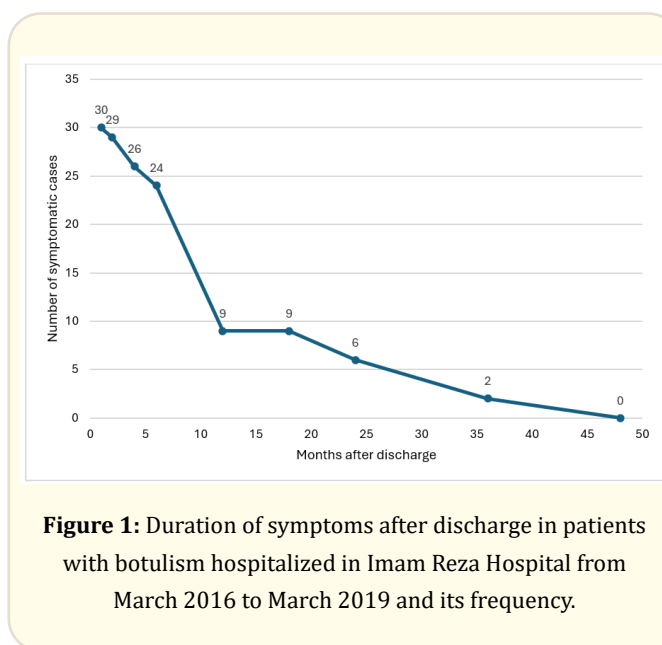
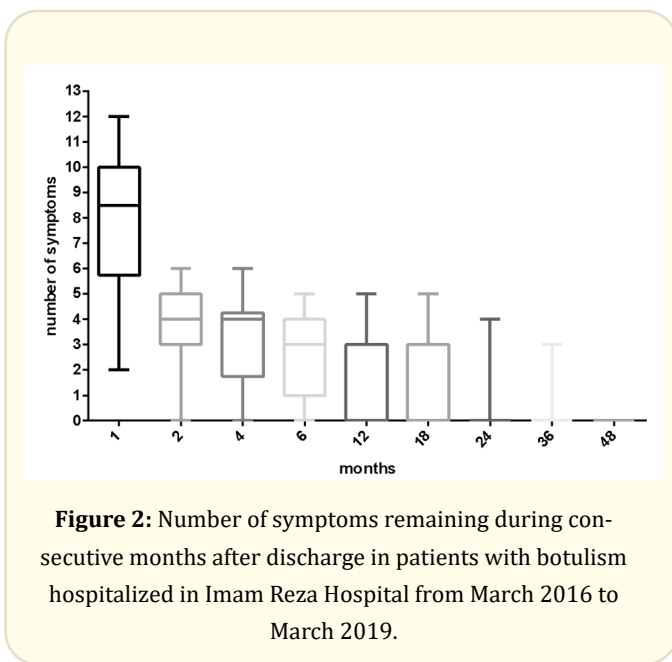


Figure 1: Duration of symptoms after discharge in patients with botulism hospitalized in Imam Reza Hospital from March 2016 to March 2019 and its frequency.



disorders (23 patients, 76.7%) had the highest frequency among post-discharge symptoms (Table 4). No serum sickness was reported. Edginess, shortness of breath, and dizziness also had the longest duration of persistence among symptoms. On the contrary; constipation, diplopia, blurred vision, and weakness disappeared sooner (Table 4). No case mortality was recorded during the study.

Discussion

Despite global endeavors, botulism has remained a major public health affair, capable of engendering severe morbidity and mortality. The most common form of the disease is reported the food-borne variation, which can be spread through nourishments containing Botulinum toxin [10]. Although some studies have addressed the epidemiology of botulism, the high-risk nature of the disease calls for more research on the topic to identify the conditions correlating with botulism. Hence, we aimed to assess the epidemiologic situation of botulism in Mashhad, Iran.

| Sign or Symptom | Frequency (%) | Mean ± SD (months) | Median | Minimum | Maximum |
|---------------------------|---------------|--------------------|--------|---------|---------|
| Blurred Vision | 25 (83.3%) | 0.38 ± 0.19 | 0.27 | 0.20 | 1.00 |
| Reduced daily performance | 25 (83.3%) | 14.00 ± 10.61 | 10.00 | 1.00 | 36.00 |
| Weakness | 24 (80%) | 15.75 ± 13.59 | 10.00 | 1.00 | 48.00 |
| Speech disorders | 23 (76.6%) | 0.47 ± 0.23 | 0.50 | 0.20 | 1.00 |
| Diplopia | 23 (76.6%) | 0.38 ± 0.19 | 0.30 | 0.20 | 1.00 |
| Edginess | 21 (70%) | 14.80 ± 10.54 | 10.00 | 4.00 | 36.00 |
| Dysphagia | 18 (60%) | 0.58 ± 0.56 | 0.30 | 0.25 | 2.00 |
| Walking disorders | 16 (53.3%) | 0.52 ± 0.29 | 0.50 | 0.25 | 1.00 |
| Dizziness | 15 (50%) | 14.00 ± 13.41 | 10.00 | 1.00 | 48.00 |
| Inability to lift objects | 14 (46.7%) | 11.67 ± 9.28 | 6.00 | 1.00 | 48.00 |
| Dry mouth | 13 (43.3%) | 14.94 ± 13.38 | 6.00 | 1.00 | 48.00 |
| Constipation | 13 (43.3%) | 0.25 ± 0.08 | 0.25 | 0.20 | 0.50 |
| Mild dyspnea | 6 (20%) | 13.01 ± 14.50 | 10.00 | 1.00 | 36.00 |

Table 4: Duration of signs and symptoms persistence after discharge in patients diagnosed with botulism in Imam Reza hospital from March 2016 to March 2019 (SD: Standard Deviation).

Most studies performed on patients with botulism have examined the demographic data of patients and presented clinical signs. For example, in 2010, Afshari *et al.* [11] reviewed all of the patients 'signs and symptoms according to outpatients' clinical findings and inpatients' medical records, who were admitted to the poison-

ing ward of Imam Reza Hospital, MUMS daily from 27 September to October 4, 2006. They included 23 patients in this study. The mean age of patients was 39.5 ± 17.0 years, with a minimum age of 14 years and a maximum age of 60 years and equal sex ratio (male/female = 57%/43%). The results of Afshari's study [11] were rela-

tively consistent with the present study. In our study, patients' ages ranged from 5 to 56 years, with an average of 30.97 ± 11.56 years; and almost the same sex ratio (male/female = 46.7%/53.3%). However, another study has estimated the mean incidence of botulism in Iran as 7.1 cases in males and 3.3 cases in females per 100,000 individuals annually, showing a significant difference between genders [5].

Afshari's research [11] demonstrated a remarkable variation in the clinical picture of patients. While most patients developed diplopia and speech disorders; dizziness, mydriasis, ptosis, and general weakness were recorded in approximately half of the patients. The symptoms, nonetheless, did not necessarily overlap. Gastrointestinal symptoms, nausea, and vomiting were also seen in 71% of patients. Unlike the mentioned observations, our study revealed speech disorders, mydriasis, general weakness, and gastrointestinal symptoms to be present in solely a small fraction of participants. Diplopia was recorded in all of male patients, and in two-thirds of the female patients in our study. However, diplopia and ptosis were the most common symptoms among patients involved in both studies.

Afshari's study showed an average length of hospital stay of 3.7 days. That was much shorter than the current research (6.23 ± 3.84 days). None of the patients included in Afshari's study [11] required intensive care. On the other hand, 4 cases (13%) in our analysis were admitted to the Intensive Care Unit (ICU) as a result of serious clinical presentations. Another retrospective study performed in Germany between 1975 and 2005 on 49 cases of botulism, 6% of patients had severe clinical manifestations and required mechanical ventilation [12]. Additionally, another study conducted in 2000 in France on 9 patients with botulism, showed a 33% need for intensive care, roughly double as our study [13].

In 1994, 24 people with botulism were hospitalized in Texas, USA. The age range of patients ranged in age from 12 to 59 years and are somewhat similar to the present study. General weakness in more than 80% of patients was reported, while in our study this number was 13.3% [14]. Another controversy is detected hereby in the incidence of limb paralysis, which in the Texas investigation is estimated to be nearly 4 times current cases [14]. This difference could be due to the early diagnosis and treatment of patients in our research.

We could justify the variation with the lack of timely referral and diagnosis of patients, which implies the necessity of early recognition of the disease and its magnificent role in eliminating severe complications associated with it. As elucidated earlier, botulism could be presented with a relatively wide range of signs and symptoms, adding difficulty to correct diagnosis. Since the timely diagnosis and management of botulism is challenged through its relatively low incidence and non-pathognomonic clinical presentation, it is recommended for health care workers to be acquainted with the clinical manifestations and probable poison entryways, thereby minimizing delays in treatment initiation and symptoms exacerbation. The scarcity of botulism makes it possible that physicians frequently misdiagnose the condition with other neurological disorders, inter alia Guillain-Barré Syndrome, Miller-Fisher Syndrome, and myasthenia gravis. Such a situation is linked with antitoxin administration postponement and higher mortality and morbidity [15].

Our results showed that 9 patients were still symptomatic 12 months after discharge. Decreased daily function, blurred vision, weakness and speech disorders were the most frequent post-discharge complications. In 24 months, six patients were experiencing post-discharge symptoms, reducing to two in 36 months. Another research, studying 14 botulism affected patients in five outbreaks in the United States, revealed no signs of residual neurological disorder in the follow-up examinations months to years after the acute disease. However, total recovery could take a longer time. The mild cases recovered within two or three months, whereas more severe cases needed a year or more to recover. Post-discharge symptoms were recorded in two patients four years after the acute phase, including xerostomia and fatigue. The neurological examinations were normal, whatsoever [16]. Wilcox and his colleagues evaluated the remained symptoms of 13 cases survived from a botulism outbreak after 2 years. As current finding, they reported that the dyspnea and fatigue were the most common remained symptoms however the pulmonary function tests were normal [17]. In our study there was no relationship between the number of antitoxin demonstration and duration of symptoms after discharge.

Our study also addressed the possible contaminated meals related to food-borne botulism. Although we observed a strong correlation between traditional yogurt consumption and botulism, Montazer Khorasan *et.al* reported fish products and industrial canned

foods as the principal cause of the disease in Iran [5]. Similarly, the Pasteur Institute of Iran has also reported an association between botulism and traditional cheese consumption [18]. In another study performed from 2002 to 2007, 88 out of overall 260 cases diagnosed with botulism were due to salted fish, whereas 38 cases had a history of local dairy products [19,20]. Reports show a correlation between botulism cases and homemade nourishment; including dairy products, salted fish, and canned foods [21,22]. Considering the data derived from these studies, it is suggestable to control the consumption of traditional seafood and milk products; for instance through better hygienic protocols, pasteurization, and boiling canned foods [23].

Conclusion

There is an association of traditional dairy products consumption with botulism, intensifying the impact of sanitation and pasteurization on reducing prevalence of the disease. The present study encompasses a one-year follow-up of the patients, which contributes to the validity of the results.

Author Contributions

Conceptualization, Mohsiri, M.; Atae Z and Etemad L.; Methodology, Mohsiri, M.; Atae Z and Etemad L.; Investigation and data collection: Mohsiri, M. and Golmohammadi R. Writing – Original Draft: Mohsiri, M and Sharifan Y.; Writing – Review and Editing, all authors; Funding Acquisition, Atae Z. Supervision, Atae Z. and Moshiri M.

Conflict of Interest

None declared.

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