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Clinical features and outcomes of tetanus: Analysis using a National Inpatient Database in Japan

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ABSTRACT

Purpose: This study was performed to elucidate the current clinical features and outcomes of tetanus using a national inpatient database in Japan.
Materials and methods: We used the Japanese Diagnosis Procedure Combination inpatient database to retrospectively investigate patients with tetanus from July 2010 to March 2016. We examined the patients' characteristics; the proportions of patients requiring tracheal intubation, mechanical ventilation, and tracheostomy; and the discharge status.
Results: We identified 499 patients who were diagnosed with tetanus. No patient had a diagnosis of tetanus neonatorum or obstetric tetanus. The median age was 74 years. Overall, 53.5% of the patients required intubation and mechanical ventilation. Among patients who required intubation and mechanical ventilation, 80.6% started it within 3 days of admission, and 77.5% required tracheostomy during hospitalization. The median duration of mechanical ventilation was 23 days. The median length of hospitalization was 35 days. The proportions of patients who were discharged to home and to locations other than home were 58.1% and 35.1%, respectively. The in-hospital mortality was 6.8%.
Conclusion: The present study suggests that acute-care physicians should be ready to provide intensive care for patients with tetanus and cooperate with medical social workers and families for subsequent long-term nursing care.

1. Introduction

Tetanus is caused by a neurotoxin released from wounds infected with *Clostridium tetani*, a bacterium transmitted as spores. Tetanus typically follows deep penetrating wounds in which anaerobic bacterial growth is facilitated [1]. Even minor trauma can lead to the disease, and no portal of entry is evident in up to 20% to 30% of patients [2,3]. Symptoms of tetanus include increased muscle tone and muscle spasm, trismus (lockjaw), spasmodic laughter, and dysphagia [4]. The spasms are excruciatingly painful and may be uncontrollable, leading to respiratory arrest and death [1]. Patients with severe tetanus require adequate airway management.

Conventional management strategies for tetanus involve sedation, neuromuscular paralysis and mechanical ventilation combined with wound debridement, antibiotic therapy, and administration of human antitetanus immunoglobulin to neutralize toxins [5]. The most important factor that determines the outcome in patients with tetanus is undoubtedly the quality of supportive care and the rapidity of treatment initiation after a diagnosis has been made [6].

Progression in the prevention of and treatments for tetanus has altered its incidence and mortality. Tetanus can be prevented through immunization with tetanus-toxoid containing vaccines; i.e., the diphtheria-tetanus-pertussis (DPT) vaccine. Vaccination programs have resulted in a marked decrease in the number of patients with tetanus in developed countries [7]. Moreover, the introduction of intensive care units (ICUs) reduced the mortality of tetanus from 43% in 1956–1968 to 15% in 1969–1984 [8]. In particular, mechanical ventilation contributes to reduced mortality in patients with tetanus. A previous cohort study showed an inverse relationship between mortality and the number of ventilated patients. Mortality decreased from 58% in 1993 to 18% in 2002 in patients with tracheostomy [2].

The occurrence of tetanus seems to have become relatively rare; therefore, its clinical features in current clinical practice have not been

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thoroughly examined. Although some case reports showed prolonged mechanical ventilation and hospitalization in elderly patients with tetanus [9], data on patient backgrounds and clinical consequences among the tetanus population are lacking in developed countries.

The aims of the present study were to describe the characteristics of patients with tetanus; proportions of patients requiring tracheal intubation, mechanical ventilation, and tracheostomy; and discharge status using a nationwide inpatient database in Japan.

2. Materials and methods

2.1. Data source

We used the Diagnosis Procedure Combination database in this study. The database includes discharge abstracts and an administrative claims database [10,11] from >1200 acute-care hospitals. It covers approximately 90% of all tertiary-care emergency hospitals in Japan. The database includes the following data for each patient: date of admission; age; sex; diagnoses, comorbidities at admission, and complications after admission recorded using the International Classification of Diseases, Tenth Revision (ICD-10) codes with text data entered in Japanese; procedures; drugs and devices used; length of hospital stay; and discharge status (discharge to home, discharge to other facility, and in-hospital death).

2.2. Patient selection

We retrospectively extracted data on patients discharged from the hospital from July 2010 to March 2016 with the following primary diagnoses: tetanus neonatorum (A33.1), obstetric tetanus (A34.10), or other tetanus (A35). We included patients who had received intravenous tetanus immunoglobulin therapy. We excluded those who were diagnosed with a snake bite or burn because intravenous tetanus immunoglobulin for such patients was considered prophylactic. We also excluded patients who were discharged within 3 days after admission without death because such patients must have been transferred to another acute-care hospital.

2.3. Patient characteristics and outcomes

Patient characteristics included age, sex, diabetes mellitus (ICD-10 codes E10–14), mechanical ventilation, season at admission, and discharge status. Age was categorized into 0–50, 51–60, 61–70, 71–80, and >80 years. Season at admission was divided into spring (March–May), summer (June–August), autumn (September–November), and winter (December–February).

The primary outcome was in-hospital mortality. The secondary outcomes were the length of hospital stay, duration of mechanical ventilation, and tracheostomy.

2.4. Ethical statement

The present study was approved by the Institutional Review Board at The University of Tokyo. Because of the anonymous nature of the data, the requirement for informed consent was waived.

2.5. Statistical analysis

Continuous variables were reported as median and interquartile range (IQR), and categorical variables were reported as count and percentage. The chi-squared test was performed to compare proportions between the groups. The threshold for significance was a p value of <0.05. All statistical analyses were carried out using SPSS version 23.0 (IBM Corp., Armonk, NY, USA).

Table 1
Patient Characteristics at Admission ($n = 499$).

Variables	Number of patients	(%)
Age, years		
0–50	58	(11.6)
51–60	43	(8.6)
61–70	101	(20.2)
71–80	176	(35.3)
≥81	121	(24.2)
Male	258	(51.7)
Diabetes mellitus	52	(10.4)
Seasons		
Spring	116	(23.2)
Summer	171	(34.3)
Autumn	152	(30.5)
Winter	60	(12.0)
Years		
2010[a]	55	(11.0)
2011	81	(16.2)
2012	71	(14.2)
2013	89	(17.8)
2014	99	(19.8)
2015	96	(19.2)
2016[b]	8	(1.6)

[a] 2010 includes July to December.
[b] 2016 includes January to March.

3. Results

Among a total of approximately 40 million inpatients from July 2010 to May 2016, we identified 499 inpatients who were diagnosed with tetanus. No patient had a diagnosis of tetanus neonatorum or obstetric tetanus.

Table 1 summarizes the patient characteristics. The median age of the patients was 74 years (IQR, 63–80 years). The proportion of male patients was 51.7%, and that of patients with diabetes mellitus was 10.4%. The proportion of admitted patients was highest in summer.

Table 2 shows the patients' outcomes. Overall, 53.5% of the patients required intubation and mechanical ventilation. The in-hospital mortality was 6.8% ($n = 34$), while the proportion of patients who were discharged to home was 58.1% and that of patients who were discharged to another facility was 35.1% ($n = 175$). The median length of hospital stay was 35 days (IQR, 18–57 days).

Table 3 shows the age distribution and mortality. Higher mortality was significantly associated with higher age.

Table 4 shows the proportions of patients who required intubation and mechanical ventilation. Of these patients, the proportion requiring tracheostomy was 77.5% ($n = 207$). The median day of starting mechanical ventilation was 2 days (IQR, 1–3 days) of admission, and 80.1% ($n = 173$) started it within 3 days of admission. The median duration of mechanical ventilation was 23 days (IQR, 15–36 days).

4. Discussion

In the current study, we analyzed 499 patients with tetanus using a nationwide inpatient database in Japan. The results showed that most of the patients with tetanus were elderly. Mortality was low, but most patients required tracheal intubation, mechanical ventilation, or

Table 2
Outcomes of All Tetanus Patients (n = 499).

Outcome	Number of patients	(%)
Intubation & mechanical ventilation	267	(53.5)
Death	34	(6.8)
Discharge to home	290	(58.1)
Discharge to other facility	175	(35.1)
Length of hospital stay, days, median (interquartile ranges)	35	(18–57)