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ORIGINAL RESEARCH

# Clinical features and outcomes of tetanus: a retrospective study

This article was published in the following Dove Press journal:  
*Infection and Drug Resistance*

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**Background:** Tetanus is a serious disease resulting in muscle spasm, and even death.

**Methods:** A retrospective, single-center study was conducted by analyzing demographic and clinical parameters.

**Results:** The study included 12 males (70.6%) and 5 females (29.4%). The mean age of the patients was  $56.71 \pm 9.05$  years. Patient occupations included farming (47.0%), retired (23.5), homebound (23.5), and workers (6.0%). The causes of patient injuries were as follows: metal injury (52.9%), deep injury (29.4%), electrical injury (5.9%), maxillofacial region and knee injury (5.9%), and skin ulceration (5.9%). The disease duration ranged from 3 to 36 days, and the mean incubation period was  $12.65 \pm 10.17$  days. Four patients had co-morbidities. The infected patients were given tetanus antitoxin (TAT) and antibiotics treatment. One patient was given continuous renal replacement therapy (CRRT) and only one patient died.

**Conclusions:** In our department, although tetanus is a serious disease, with effective treatment, patients have reasonable cure and low death rates.

**Keywords:** tetanus, intensive care unit, retrospective study

## Introduction

Tetanus is an acute infectious disease caused by the bacterium, *Clostridium tetani* (*C. tetani*), as defined by the WHO,<sup>1</sup> which generates a neurologic toxin.<sup>2</sup> Because of the high mortality rate, tetanus is still a significant issue worldwide, especially in developing countries.<sup>3,4</sup> In developed countries, tetanus has a low incidence; specifically, there were 43 cases per year between 1998 and 2000.<sup>5</sup> In addition to the disease process, a lack of experience in diagnosing tetanus contributes to the high mortality rate.<sup>6</sup> Tetanus often leads to death, with a reported 213,000–293,000 deaths worldwide.<sup>7</sup> The incidence of tetanus is about 1 case per 10,000,000 in the US.<sup>8</sup> There are no guidelines with respect to tetanus immunization for adults in China; however, in 2012, China was validated to have eliminated maternal and neonatal tetanus.<sup>9</sup> The tetanus bacillus generates tetanospasmin and tetanolysin; the former toxin causes local inflammation by acting on gangliosides within local nerve terminals, resulting in the clinical syndrome.<sup>5,10</sup> Muscle spasm is the main characteristic of tetanus; trismus affects 95.7%, neck stiffness affects 89.3%, body spasms/stiffness affect 73%, and dysphagia affects 38.9% of the patients.<sup>11</sup> The present study investigated the demographic data, prognosis, and mortality of patients with tetanus.

Tetanus is a preventable infection that results in severe problems worldwide, especially in developing countries.<sup>12</sup> It is believed that poor wound care and lack of immunization awareness leads to a high prevalence of tetanus in developing

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countries.<sup>13</sup> The incidence of tetanus is low in high-income countries, which has been attributed to a robust immunization program.<sup>14</sup> In China, the government has offered diphtheria–pertussis–tetanus vaccines to children since 1978. Therefore, tetanus-infected people are >33 years of age. In the present study, the youngest tetanus-infected patient was 46 years of age as a result of the aforementioned government program. It has been reported that there are 35–70 people infected with tetanus each year, and most of the patients are >65 years of age in the USA, which is thought to represent waning immunity.<sup>15</sup>

## Patients and methods

We retrospectively analyzed 17 patients infected with tetanus from the intensive care unit (ICU) of the Second Affiliated Hospital of Dalian Medical University. The diagnosis satisfied the World Health Organization (WHO) definition for tetanus. Consent was obtained from all of the patients. The research was approved by the Ethics Committee of the Second Affiliated Hospital of Dalian Medical University.

The patient records were collected from January 2011 to December 2017. When admitted to the hospital, because of different levels of local injury, all patients received antibiotic treatment; because of muscle spasm, all patients were administered TAT. The following data were collected: age, sex, occupation, etiology, incubation period, comorbidities, onset of symptoms, degree of dyspnea, Sequential Organ Failure Assessment (SOFA), whether or not mechanical ventilation was used, dosage of tetanus immunoglobulin, continuous renal replacement therapy (CRRT), antibiotic; length of hospital stay, pneumonia (defined by the findings on chest computed tomography), and death. Patient consent was obtained by written informed consent, and this study was conducted in accordance with the Declaration of Helsinki.

## Results

The study included 12 males (70.6%) and 5 females (29.4%), for a male-to-female ratio of 2.4:1. The mean age of the patients was  $56.71 \pm 9.05$  years (range, 46–70 years) and 76.5% of the patients were >50 years of age. The patients' occupations included farming (47.0%), retired (23.5), homebound (23.5), and worker (6.0%). The causes of patient injuries were as follows: metal injury (52.9%), deep injury (29.4%), electric injury (5.9%), maxillofacial region and knee injury (5.9%), and skin ulcer

(5.9%). None of the patients received DTP, Td, Tdp, or Tdap vaccinations (Table 1).

The duration of disease ranged from 3 to 36 days, and the mean incubation period was  $12.65 \pm 10.17$  days. Four patients had comorbidities. When the patients presented to the hospital, onset of symptoms differed: trismus was the most common presentation accounting for 70.6%, followed by dysarthria (35.3%), and muscle spasm (17.6%). There were varying degrees of dyspnea based on the oxygenation index ( $\text{PaO}_2/\text{FiO}_2$ ), reflecting the severity of the disease, as follows: severe degrees of dyspnea ( $\text{PaO}_2/\text{FiO}_2 \leq 100$  mmHg; 11.8%), moderate degrees of dyspnea (100 mmHg <  $\text{PaO}_2/\text{FiO}_2 \leq 200$  mmHg; 17.6%), mild degrees of dyspnea (200 mmHg <  $\text{PaO}_2/\text{FiO}_2 \leq 300$  mmHg; 58.8%), and no dyspnea (11.8%). Patients with severe and moderate dyspnea were treated in the ICU; the other patients were observed in the general ward with supervision by the ICU staff as needed.

The mean SOFA grade was  $5.29 \pm 4.37$  (range, 2–19; Table 2).

Upon admission to the hospital, positive treatment was initiated, including open wound, tetanus antitoxin (TAT), antibiotics, improving breathing, and continuous renal replacement therapy (CRRT), if necessary. The patients were given different O<sub>2</sub> treatments based on the different degrees of dyspnea, as follows: intubation for severe dyspnea (2 patients); nasal cannula for moderate dyspnea (3 patients [2 of the 3 patients were intubated using transient nasal intermittent positive pressure ventilation {NIPPV}]); and nasal cannula for mild dyspnea (10 patients). All infected patients were given TAT treatment, and the mean dosages were  $11,294.12 \pm 8970.54$  IU/day (range, 1,500–30,000 IU). The patients were administered penicillin or piperacillin-tazobactam empirically based on the presentation of the injury as inpatients because it was more likely for the injury to be associated with coccal infections. Secretion of the

**Table 1** Demographic characteristics of the patients

Parameters	
Age (years)	$56.71 \pm 9.05$
Male gender	12/17 (70.6%)
Female	5/17(29.4%)
Occupation	
Farmer	8(47.0%)
Retired	4(23.5%)
Homebound	4(23.5%)
Worker	1(6.0%)

**Table 2** Disease characteristics of the patients

Parameters	
Etiology	
Metal injury	9(52.9%)
Deep injury	5(29.4%)
Electric injury	1(5.9%)
Maxillofacial region and knee injury	1(5.9%)
Skin ulcer	1(5.9%)
Incubation period (days)	12.65±10.17
Comorbidity	
Diabetes mellitus	1(5.9%)
Hypertension	1(5.9%)
Sequelae of cerebral infarction	1(5.9%)
Lumbar disc herniation	1(5.9%)
Onset of symptoms	
Difficulty swallowing	6(35.3%)
Muscle spasm	3(17.6%)
Trismus	12(70.6%)
Degree of dyspnea	
Severe ( $\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$ )	2(11.8%)
Moderate ( $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$ )	3(17.6%)
Mild ( $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ )	10(58.8%)
None	2(11.8%)
Intubation	
Yes	4
No	13
Sequential Organ Failure Assessment	5.29±4.37

wound was collected for guiding and administrating the administration of antibiotics. When local infection was controlled, the antibiotics were terminated. Sputum cultures were collected routinely from all of the patients, and the results were as follows: normal throat bacteria (4), none (11), and *C. baumanii* (1). The patient with a *C. baumanii* infection was administered tigecycline for treatment. Antibiotics were administrated for remedying the infection; piperacillin-tazobactam and penicillin were both effective. Because of respiratory muscle fatigue, there were four patients who were placed on mechanical ventilation. Because of multiple organ dysfunction syndromes, one patient was given CRRT. Pneumonia was the main complication of tetanus-infected patients and was diagnosed based on clinical symptoms and chest computed tomography (CT). In the present study, there were four patients with pneumonia; one patient had a *C. baumanii* infection and was treated with tigecycline, while the antibiotics were not changed in the other three patients (treated with piperacillin-tazobactam according to the sputum cultures). After aggressive treatment, only one patient died (Table 3).

**Table 3** Treatment characteristics of the patients

Parameters	
Dosage of tetanus immunoglobulin (IU/day)	11,294.12±8970.54
Antibiotic	
Piperacillin-tazobactam	9(52.9%)
Penicillin	8(47.0%)
Sputum cultures	
Normal throat bacteria	5
<i>Clostridium baumanii</i>	1
None	11
Mechanical ventilation	4(23.5%)
Continuous renal replacement therapy	1(5.9%)
Length of hospital stay (days)	11.88±6.57
Complication	
Pneumonia	4(23.5%)
None	13(76.5%)
Death	1(5.9%)

## Discussion

In the present research, the percentage of males (70.6%) was greater than the percentage of females (29.4%), which differs from other research: Fawibe<sup>20</sup> reported 85.7% males and 14.3% females and Chukwubike and God'spower<sup>16</sup> reported 58.1% males and 41.9% females in their studies. Males often do outdoor jobs, such as farming or skilled jobs, that have an increased probability of injuries. In our study, the patients had metal and deep injuries when they did heavy work, while females often did light work with fewer injuries. Females may have a low incidence of tetanus because of immunization during pregnancy.<sup>17</sup> Patient occupation is an important risk factor for tetanus. Farmers have a tetanus incidence of 47.0% in the present tetanus cases, while the retired and homebound have an incidence of 23.5% in the present tetanus cases. Chukwubike et al<sup>16</sup> reported that 46.5% of the patients with tetanus were students and civil servants, while artisans and commercial motorcyclists accounted for 25.6% of the infections and farmers represented 4.7%.<sup>16</sup> Other studies have shown the dominance of farming among tetanus-infected patients,<sup>18</sup> which is in agreement with our study. The cause may be that the elderly have less medical knowledge and less health consciousness. In the USA, the Centers for Disease Control and Prevention advise people to receive a dose of tetanus vaccine every 10 years to remain immunized.<sup>19</sup>

The pathogenesis of tetanus consists of several cases in which there is contamination of the wound by tetanus. It is well known that tetanus originates from puncture wounds,

abrasions, burns, injections, surgery, compound fractures, animal bites or scratches, gastrointestinal infections, abortion, and childbirth.<sup>5</sup> In the present research, metal and deep injuries separately account for 52.9% and 29.4% of the cases, respectively. Tetanus is a gram-positive bacillus and obligates anaerobe. Rusted metal is full of anaerobes, therefore metal injuries have a high infection rate. The disease has characteristic regions similar to snake bites or scorpion stings in Nigeria.<sup>20</sup>

The incubation period ranged from 3 to 36 days with a mean period of 12.65 days, which is similar to the results by Zielinski and Rudowska<sup>21</sup> Because of a lack of health consciousness, the entire patient cohort in our study had not been previously vaccinated. The incubation period was not so short that patients did not have time to accept immunotherapy. There were four patients with comorbidities. Rogers and Frykberg<sup>22</sup> reported that diabetic foot could result in tetanus because immunopathy, vasculopathy, and ulceration increase the risk. Therefore, diabetes mellitus may be a relevant factor with tetanus. Hypertension, sequelae of cerebral infarction, and lumbar disc herniation are not associated with tetanus.

Trismus was the more frequent initial symptom, accounting for 70.6% of the patients because the muscles of the jaw with shorter axonal pathways facilitate the toxin effect on inhibitory neurons.<sup>5,10</sup> The initial presentation of tetanus lockjaw includes stiff neck, dysarthria, and abdominal muscle stiffness, which are usually affected by noise and light. Other symptoms follow, such as fever, sweating, and high blood pressure. Muscle stiffness also extends from the jaw to the limb muscles.<sup>21</sup> There were different degrees of dyspnea, but mild symptoms occurred in the majority of patients. The SOFA score reflected the severity of ICU patients. Vora et al<sup>23</sup> concluded that a mean SOFA score <2.15 was safer than for patients who expired (SOFA score of 2.89).<sup>23</sup> In the present study, the mean SOFA was 5.29, which was higher than reported by Vora et al.<sup>23</sup> Patient death was associated with a high SOFA score of 19. Treatment for tetanus includes the following: stop further toxin release, neutralize toxins, and reduce toxicity.<sup>24</sup> In our study, the infected patients underwent debridement to clean the wound and were administered antibiotics to reduce inflammation; TAT was used to neutralize toxins; mechanical ventilation supported respiratory failure. Formal research suggests that penicillin and metronidazole are two effective antibiotics.<sup>10,24</sup> Our experience showed that piperacillin-tazobactam and penicillin were effective as well.

Neutralizing toxins can be achieved with equine/human tetanus immunoglobulin by passive immunization. The suggested dose of adults is 3,000–6,000 IU<sup>17</sup> In our study, the minimal dose of tetanus immunoglobulin was 1,500 IU, and the maximal dose was 30,000 IU. Most patients enrolled in the study recovered.

When the respiratory muscles are affected by tetanus toxin, mechanical ventilation must be performed. Among the infected patients on mechanical ventilation, there were three affected by pneumonia and one developed renal failure, who underwent CRRT treatment. Loan et al<sup>25</sup> reported >90% of the patients with severe tetanus had pneumonia. Nobrega et al<sup>26</sup> concluded that 84.8% of the patients had pneumonia. The incidence of pneumonia in our study was low. Spasm was the main symptom, often lasting 1–2 weeks, while stiffness persisted a long time.<sup>10</sup> One report advised that patients required 11–30 days of treatment in the hospital.<sup>27</sup> Our study indicated a mean of 11.88 days of treatment, which was less than the previous reports. A report found that 45% of the deaths occurred in south Asia.<sup>28</sup> Only one patient (5.9%) died of multiple organ dysfunction syndrome (MODS) in our study; however, because of the small sample size, a large sample, multi-center study should be conducted.

Although the number of tetanus infections from the single center was small, there was an absence of vaccines. There are two recommendations for settling the present issue. First, it is vitally important for the general population and health staff to realize the necessity of tetanus vaccines. Second, there should be more effort supported by the government regarding an adult vaccine policy.

## Conclusion

Tetanus is a critical disease and often has a high mortality rate. When injury occurs, it is important to acquire immunity. In a retrospective single-center study, most patients were cured by stopping further toxin release, neutralizing toxins, and reducing toxicity. The mortality of patients infected by tetanus was low. A vaccination policy and program should be implemented by our government.

## Acknowledgments

We thank International Science Editing (<http://www.internationalscienceediting.com>) for editing this manuscript. The present study was supported by National Natural Science Foundation of China (NO. 81701965, 81872255,

81501699); Natural Science Foundation of Liaoning Province (No. 20180550116); Dalian Medical Science Research Project (No. 1711038).

## Disclosure

The authors have no conflicts of interest in this work.

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