

# Clinical Profile and Prognostic Factors of Mortality among Adult Tetanus Patients in Cagayan Valley Medical Center: A Cross-sectional Study

Evervic Joy G. Dalanao, M.D.\*; and Jose Carlo B. Valencia, M.D.\*

## Abstract

**Introduction:** Tetanus remains a public health threat in developing countries and is associated with a high morbidity and mortality rate. There is paucity of published data regarding the management of tetanus in the Philippines, hence, the study was conducted to determine the demographic, clinical profile, and prognostic factors that are associated with mortality among adult tetanus patients admitted in Cagayan Valley Medical Center (CVMC).

**Methods:** This is a retrospective study of patients who presented with a clinical diagnosis of tetanus, above 19 years old at CVMC between September 1, 2012 to October 31, 2018.

**Results:** A total of 194 patients were studied. The male to female ratio was 11:1. Majority of patients were aged > 40 years (68.56%), rural dwellers (88.66%), farmers (84.02%) and males (91.75%). Only 3.09% of patients had prior tetanus immunization. Most common antecedent injury is trauma (84.53%), most commonly due to punctured wounds (63.40%). All patients had generalized tetanus, and majority were admitted in moderate grade (68.56%). Most common

manifestations were trismus (92.78%), spasms (84.02%), dysphagia (80.93%) and rigidity (68.04%). Complication rate is 64.43%. Mortality rate is 38.66%. Most common cause of death is acute respiratory failure. Poor prognostic factors determined by univariate analysis were age more than 40 years (OR=2.24,  $p$ -value=0.0160), incubation period less than seven days (OR=2.65,  $p$ -value=0.0027), period of onset less than three days (OR=2.52,  $p$ -value=0.0150), severity of disease (OR=17.35,  $p$ -value=<0.0001), need for ventilatory support (OR=22.20,  $p$ -value=<0.0001) and presence of complications (OR=2.96,  $p$ -value=0.0013). In multivariate analysis, only need for ventilatory support is associated with mortality (OR=31.57,  $p$ -value=0.000).

**Conclusion:** Mortality rate of adult tetanus in Cagayan Valley Medical Center is high. Therefore, health education is highly encouraged to promote awareness, specifically in immunization and basic wound management.

**Keywords:** tetanus, clinical form, complications, treatment outcome, prognostic factors of mortality, philippines

## Introduction

Tetanus is an acute disease manifested by skeletal muscle spasm and autonomic nervous system disturbance caused by tetanospasmin produced by the bacterium *Clostridium tetani*, a gram-positive, obligate anaerobic rods and is completely preventable by vaccination.<sup>1</sup> Tetanus is the only vaccine-preventable disease that is infectious but not contagious.<sup>2</sup> Globally, there are around one million cases of tetanus annually or an incidence rate of 18/100,000 population and mortality rate is as high as 28 per 100,000.<sup>3</sup> The Philippines is ranked number nine among Asian countries with an annual mortality rate of 0.5 per 100,000 and cases has decreased by 69.6% since 1990, an average of three percent

\* Department of Internal Medicine, Cagayan Valley Medical Center, Tuguegarao City, Cagayan Valley, Philippines

Corresponding author: Evervic Joy G. Dalanao, M.D., Cagayan Valley Medical Center, Tuguegarao City, Cagayan Valley, Philippines  
Email: evervicjoydalanao@gmail.com

a year.<sup>4</sup> At the Research Institute for Tropical Medicine, an average of 22 cases of tetanus per year or 1.8 per month was seen from 2001 to 2011 with overall case fatality rate for all ages of 11.7%.<sup>5</sup>

Tetanus typically presents with trismus, dysphagia, muscle pain, rigidity and more ominously, opisthotonos.<sup>1</sup> The incubation period ranges from three to 21 days, usually about eight days. In general, the further the injury site is from the central nervous system, the longer is the incubation period. Shorter incubation periods are associated with a higher chance of death.<sup>2</sup> The diagnosis is entirely based on clinical findings and does not depend upon bacteriologic confirmation. *C. Tetani* is recovered from the wound in only 30% of cases and can be isolated from patients who do not have tetanus.<sup>2</sup> There are four clinical forms of tetanus recognized, and they include generalized, localized, cephalic and neonatal tetanus. The most common type, about 80% of reported tetanus is generalized tetanus.

The disease usually presents with a descending pattern.<sup>2</sup> In developing countries, where access to high intensity care may be a challenge, the mortality rate of tetanus ranges from 32.7%<sup>6</sup> to 43.1%.<sup>7</sup> This can be due to the lack of immunization, poor wound management and personal hygiene. In addition, high incidence of tetanus admissions in developing countries has been attributed to low levels of health awareness in terms of vaccination and availability of human and material resources to manage the disease.<sup>8</sup> In contrast to developed countries like France with a mortality rate of 14%, the enduring incidence of tetanus is mainly due to a lack of vaccination coverage of the elderly.<sup>9</sup> The following were identified predictors of mortality: area of residence,<sup>6</sup> age more than 40 years,<sup>7,10,11,12</sup> presence of complications,<sup>6,10,12</sup> severity of tetanus,<sup>6,7,12,13,14</sup> incubation period less than seven days,<sup>7,12,14,15</sup> period of onset less than three days,<sup>11,12</sup> need for ventilatory support,<sup>7</sup> as predictors of mortality. On the other hand, predictors like tetanus anti-toxin prophylaxis,<sup>6</sup> sex,<sup>7, 8, 10, 11</sup> clinical form,<sup>7</sup> admission pattern,<sup>7</sup> and presence of co-morbidities,<sup>10,12</sup> did not significantly affect the outcome.

There is a scarcity of studies on adult tetanus, not only in Cagayan Valley but nationwide. Thus, this study was a maiden attempt to identify the demographic, clinical profile and prognostic factors influencing the survival of patients with Tetanus. The result of the study may be useful for early diagnosis, proper wound management, planning appropriate effective immunization and health education programs to create awareness among the public and establishing an ICU facility in the hospital thereby decreasing morbidity and mortality.

The general objective is to determine prognostic factors of mortality among adult tetanus patients admitted in Cagayan Valley Medical Center (CVMC) over a six-year period from October 1, 2012 to September 31, 2018. More specifically:

1. To determine the association of the following demographic characteristics of adult tetanus patients to mortality:
  - a. Sex
  - b. Age
  - c. Place of residence
  - d. Pre-existing co-morbidities
  - e. Antecedent injury
  - f. Tetanus vaccination history
2. To determine the association of the following clinical profile of adult tetanus patients to mortality:
  - a. Tetanus anti-toxin post-exposure prophylaxis
  - b. Type of wound
  - c. Incubation period
  - d. Period of onset
  - e. Clinical form
  - f. Severity (Ablett's Classification)
  - g. Clinical manifestation
  - h. Management

- i. Complications
  - j. Length of hospital stay
  - k. Admission pattern
3. To determine the causes of death of adult tetanus patient seen at CVMC
  4. To determine mortality rate of adult tetanus patient seen at CVMC

## Methods

This is a cross-sectional study conducted in CVMC. CVMC is situated in Carig Sur, Tuguegarao City, a Level III Tertiary Teaching, Training and Research Medical Center with 500-bed authorized capacity. The study is not done in a laboratory. A total of 204 tetanus cases were documented over a six-year period.

All adult tetanus patients admitted as service or pay, at CVMC aged 19 years old and above from October 1, 2012-September 31, 2018 were included in this study. Patient who transferred to other institution and those who were discharged against medical advice were also included in the analysis but were considered "died" as per outcome.

A sample size of 181 was computed based on the odds ratios of the independent risk factors for mortality among tetanus patients from the studies reviewed (See Appendix II). The highest sample size from the computed odds ratios was used in this study with an assumed 25% mortality in the unexposed patient, 80% power and 5% type I error rate of a two-sided test. Openepi was used to calculate the desired number of tetanus patients using a cross-sectional study design.

Clinical records were searched manually and data extraction sheet was used to collect the following data: sex, age, place of residence, pre-existing co-morbidities, antecedent injury, tetanus vaccination history, tetanus anti-toxin post- exposure prophylaxis, type of wound, incubation period, period of onset, clinical form, severity, clinical manifestation, management given, complications, length of hospital stay, admission pattern, cause of death and treatment outcome at hospital discharge.

The diagnosis of tetanus was based on clinical findings. Incubation period (time from wound to first symptoms) and period of onset (time from first symptoms to the first generalized spasm) were determined. Patients were classified into localized (painful spasm of muscles at the site of inoculation, which may be mild or persistent, no systemic signs and spontaneously resolves without sequelae), cephalic (a lower motor neuron lesion, frequently producing facial nerve weakness, is often apparent) and generalized type (painful, progressive increase in stiffness of voluntary muscles).

The severity was graded using Ablett's classification into mild (mild trismus, general spasticity, no respiratory

compromise, no spasms, no dysphagia), moderate (moderate trismus, rigidity, short spasms, mild dysphagia, moderate respiratory involvement, ventilatory frequency more than 30), severe (severe trismus, generalized rigidity, prolonged spasms, severe dysphagia, apneic spells, pulse more than 120, ventilatory frequency more than 40) and very severe (grade III with severe autonomic instability).

The patients were divided into two groups (survived or died) according to the clinical outcome at the time of hospital discharge. The “survived” group was defined as patients who were cured and discharged from the hospital or patients whose symptoms of tetanus had significantly improved. The “died” group was defined as patients who died in the hospital after systemic therapy or patients whose condition had deteriorated further, those who were discharged on the wishes of family members and those who transferred to other institutions. (Figure 1)

After data has been collected, data was encoded in Microsoft Excel and was transferred to Stata 14 for further statistical treatment and analysis. All hypothesis tests used 5%

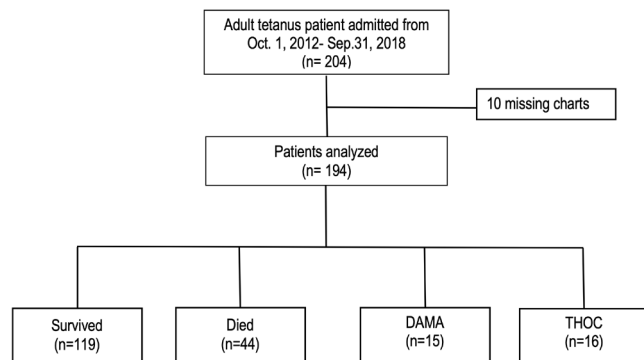


Figure 1. Study flow

level of significance. Cross tabulation was done to describe the dataset of study.

The mean and ranges were calculated for continuous variables whereas proportions and frequency tables were used to summarize categorical variables. Continuous variables were categorized.

Moreover, univariate logistic regression analysis was done to evaluate the relationship of each possible predictor variable to mortality of tetanus patients. All variables yielding significant relationship with mortality were included in fitting a multiple logistic regression model to predict odds of dying among tetanus patients. Interpretation of odds ratio was done for each significant predictor controlling for other variables after fitting the final model.

The study was started after obtaining an ethical approval from the ethics board of review. Anonymity and confidentiality were assured by assigning each patient record a unique number during data collection.

## Results

From the data, a total of 194 patients were included in the sample. Among all tetanus patients, 75 (38.66%) died during the study period. Age, incubation period, period of onset, severity upon admission, need for ventilatory support, and presence of complications were found to be statistically associated with mortality of tetanus patients based on univariate logistic regression analysis. (Table I)

Multiple logistic regression analysis was done between the survival outcome and all significant predictors from

Variables		Survived (N=119)	Died (N=75)	Total (N=194) Odds ratio (95% C.I.)	Univariate analysis	
					P-value	
Sex	Male (1)	108	70	178	1.4259 (0.48-4.28)	0.5269
	Female (0)	11	5	16		
Age	>40 (1)	74	59	133	2.2424 (1.12, 4.68)	0.0160
	≤40 (0)	45	16	61		
Residence	Rural (1)	109	63	172	0.4815 (0.18, 1.30)	0.1042
	Urban (0)	10	12	22		
Presence of co-morbidities	Yes (1)	10	12	22	2.0762 (0.85, 5.08)	0.1095
	No (0)	109	63	172		
Incubation Period	< 7 days (1)	25	31	56	2.6491 (1.40, 5.00)	0.0027
	≥ 7 days (0)	94	44	138		
Period of onset	< 3 days (1)	15	20	35	2.5212 (1.20, 5.31)	0.0150
	≥ 3 days (0)	104	55	159		
TAT Prophylaxis	Yes (1)	10	8	18	1.3015 (0.49, 3.46)	0.5975
	No (0)	109	67	176		
Admission Pattern	ICU (1)	14	11	25	1.2891 (0.55, 3.01)	0.5576
	Ward (0)	105	64	169		
Severity upon admission	Severe to Very severe (1)	9	44	53	17.3477 (7.24, 44.19)	<0.0001
	Mild to Moderate (0)	110	31	141		
Debridement done	Yes (1)	22	14	36	1.0119 (0.44, 2.25)	0.9750
	No (0)	97	61	158		
Need for ventilatory support	Yes (1)	11	52	63	22.1976 (10.06-48.96)	<0.0001
	No (0)	108	23	131		
Presence of complications	Yes (1)	66	59	125	2.9612 (1.53-5.73)	0.0013
	No (0)	53	16	69		

**Table II. Significant variables from multiple logistic regression analysis with backward elimination**

Variable	Odds ratio controlling for other variables	p-value
Age (>40)	1.80	0.165
Incubation Period (<7 days)	0.78	0.682
Period of Onset (<3 days)	1.18	0.810
Severity upon admission (severe to very severe)	1.27	0.783
Presence of complications (had complications)	0.40	0.064
Need for ventilatory support(had ventilatory support)	31.57	0.000

the univariate logistic regression analysis. The result of the mentioned analysis was given below. (Table II)

Only variable need for ventilatory support was significantly associated with mortality ( $p < 0.001$ ).

## Discussion

Despite recognized effectiveness of tetanus vaccines and its availability, tetanus is still ubiquitous especially in developing countries which constitutes significantly to high morbidity and mortality. The overall actual mortality rate of 22.68% was documented. However, the value increased to 38.66% when patients who went on DAMA and transferred to other institution were included. This is possibly because of lack of or inadequate intensive care facilities and services in our setting, and financial constraints that often hamper successful management of such patients. However, the mortality rate in the study is comparable with that obtained in other studies done in developing countries wherein mortality rate can be as low as 32.7%-35.3%<sup>8</sup> and as high as 42.2%-46%.<sup>12</sup> Nonetheless, mortality rate in a developed country like France can be as low as 14%.<sup>9</sup>

The profile of the adult patients with tetanus in the study was similar to other reported large studies. Sex is one of the studied predictive factors for mortality. In agreement with other studies in developing countries,<sup>6,7,8,10,11,12,14,15</sup> there was a male preponderance of cases reflecting a probable greater exposure to tetanus prone injuries. This is because men tend to spend more time outdoor, in farming activities and other types of fieldwork and high proportion of admission among males in this study also reflects the low vaccination rates among males in the community as compared to females and children who gets their vaccination during pregnancy and childhood respectively.<sup>7</sup> Although in the affected female patients, only 37.5% had prior tetanus immunization. Age standardized mortality from tetanus was higher among males than females globally.<sup>16</sup> There was no significant difference in outcome between sexes<sup>11</sup> and there was no significant association with mortality.<sup>7,8,10,11</sup> These findings were consistent with the result of the study. The study also shown that mortality rate is much higher in those above 40-years of age. In a population-based serologic survey of immunity to tetanus in the United States, the prevalence of protective levels of tetanus antibody declined rapidly starting at the age of 40 years, and that most cases of tetanus occurred

in the older age group.<sup>17</sup> Furthermore, a person more than 60 years of age are at greater risk of tetanus because antibody levels decrease over time.<sup>1</sup> Majority (80.41%) of the patients in the present study was between the ages of 20 and 59 years. This age group constitutes the working force of the society. This is in sound agreement with the studies done in Ethiopia, India, USA and Nigeria.<sup>6,9,10,12</sup> The result can be attributed to low level of immunity against tetanus as they would never have received immunization. Though this observation contrasts with other studies done in Tanzania<sup>7</sup> and India<sup>11</sup> which reported higher incidence of tetanus in age below 40. This is because in developing countries, tetanus is common in the young due to lack of effective immunization program and inappropriate treatment of injuries whereas in developed countries tetanus occurs mainly in elderly due to decline in protective antibodies.<sup>7,12</sup>

Consistent with other studies, majority of tetanus patients in the study were rural dwellers<sup>6,10</sup> and farmers.<sup>7,10,12</sup> Farming is the major occupation in Cagayan Valley, and most of them live in the rural areas. The farming activities and other forms of field work result in higher exposure to *C. tetani*, which is ubiquitous in soil, and the penetrating injury necessary for the organism to enter the body.<sup>12</sup> One or more co-morbidities were recognized to twenty-two patients, and the most frequent co-morbidities identified were hypertension (6.70%), diabetes mellitus (3.61%) and coronary artery disease (2.06%). No association between co-morbidities and outcome was documented and this finding is in congruent with other studies.<sup>10,12</sup> Similar to others<sup>6,7,10,11</sup> the most common portal of entry was trauma (84.53%), majority of which is due to punctured wound (63.40%). Other patients developed tetanus secondary to dental carries (5.67%), foreign body in penile area (1.55%) and chronic otitis media (1.03%). There were nine patients (4.64%) with no clinically identifiable portal of entry, which is comparable to other studies ranging from 10.3%<sup>8</sup> to 21.7%<sup>10</sup>-33.6%.<sup>7</sup> This reflects that the injuries were very trivial for the patients to be educated. In congruent with the study done in Tanzania<sup>7</sup> and India,<sup>10</sup> there is high percentage of patients with unknown vaccination history (70.10%) and with no prior tetanus immunization (27.83%). Post-exposure prophylaxis in the study was given to 18 (9.28%) of study population, wherein, 10 of them survived. However, there is no association between TAT prophylaxis and outcome, agreeing to one study.<sup>6</sup> Constraints related to financial and human resources and difficulty vaccinating people in hard to reach rural areas were among the factors influencing tetanus toxoid vaccine coverage.<sup>16</sup> This can also be explained by low levels of health awareness in terms of vaccination and availability of human and material resources to manage the disease. Majority (76.80%) of the wound causing tetanus in the study was dry or healed, reflecting the delay of consultation by the patient. In assessing prognosis, the speed at which tetanus develops is important. The incubation period and period of onset are of particular significance; shorter times are associated with worse outcomes.<sup>1</sup> In the study, the incubation period and period of onset were identified in

all patients. Of these, majority had an incubation period of more than seven days (71.13%) and period of onset greater than three days (81.96%). Both were identified as significant predictors of mortality by univariate analysis in the study, however, not significant by multivariate analysis. The finding is consistent with the study done in Ethiopia.<sup>8</sup> All patients had generalized tetanus in keeping with other studies<sup>10,12</sup> and majority were of moderate grade (68.56%). This contrasts with other studies wherein majority of patients were in severe form.<sup>6,7,8</sup> Presence of autonomic disturbances characterized severe form of tetanus and manifested as tachycardia, labile blood pressure and diaphoresis and in very severe cases, as bradycardia and hypotension. Mortality was also significantly higher in patients with autonomic dysfunction.<sup>12</sup> Trismus (92.78%), spasms (84.02%), dysphagia (80.93%) and rigidity (68.04%) were the prominent clinical manifestations agreeing with other studies.<sup>7,8,10,11</sup> Thus, a high index of suspicion for tetanus is of paramount whenever patients present with any of these symptoms as tetanus is essentially a clinical diagnosis and laboratory results as well as cultures are of little diagnostic value.<sup>7</sup>

The goal of therapy to tetanus cases is to eliminate the source of toxin, neutralize unbound toxin, active immunization, prevention and control of muscle spasm and rigidity and control of autonomic dysfunction.<sup>5</sup> The treatment of tetanus patients requires also a well-established intensive care facility with a medical and nursing staff experienced in treating artificially ventilated and hemodynamically unstable patients.<sup>7</sup> Among admitted tetanus patients, only 25 (12.89%) were admitted in the intensive care unit. ICU mortality rate (11.76%) was lower compared to ward mortality (14.67%) in the study. Nonetheless, ICU admission in this study did not significantly improve the prognosis of these patients in terms of mortality which is in congruent to one study.<sup>7</sup> All patients received metronidazole at a dose of 500 mg intravenously every six to eight hours which is the same to one study done in Nigeria.<sup>12</sup> Two studies concluded that there was no significant difference in mortality between crystalline penicillin and metronidazole treated patients.<sup>8,9</sup> For the control of muscle spasm and rigidity, majority (81.44%) of tetanus patients received benzodiazepine in the form of diazepam and clonazepam. Benzodiazepines are still the cornerstone for sedation and spasm control while magnesium sulfate is also currently recommended.<sup>1,2,3,5,18</sup> Inadequacy or irregularity of diazepam use was another factor associated with high mortality.<sup>12</sup> Three patients were able to receive magnesium sulfate due to uncontrolled autonomic dysfunction. Though no observe association between magnesium use and outcome.<sup>9</sup> Tetanus immunoglobulin were given to six (3.09%) patients. TIG is not readily available in Cagayan Valley and majority of the patients were farmer and financially incapable, hence, were not able to procure the vaccine. A study done in France concluded that there was no difference in outcome between the patients who received HTIg treatment and those who did not.<sup>9</sup> In contrast to TIG, majority of patients received tetanus toxoid (62.89%) and anti-tetanus serum (75.77%). Both vaccines were more

readily available and cheaper compared to tetanus immunoglobulin. Wound debridement is essential to hasten the eradication of the bacteria.<sup>9</sup> Among 45 patients with unhealed and infected wound, only 36 patients underwent debridement. Though majority (55.56%) of patients who underwent wound cleaning and debridement was higher in the "survived" group, debridement was not an independent factor for survival. The finding is consistent with the study done in China.<sup>13</sup> To alleviate laryngeal spasm and to enable tracheal suction of secretions, tracheostomy was performed in 14 (7.22%) patients. This contrasts with one study done in India<sup>10</sup> where no patient underwent tracheostomy while as high as 40% of tracheostomy were documented in another study.<sup>11</sup> The low rate of tracheostomy in our study may be responsible for high mortality rate among tetanus patients.

One or more complications were seen in 125 (64.43%) patients, with airway obstruction being seen in 63 (32.47%) patients, followed by dysautonomia (25.77%) and hypokalemia (23.20%). Hypokalemia might be explained by the fact that sympathetic hyperactivity may cause transient hypokalemia.<sup>8</sup> The autonomic dysfunction noted in these studies included fever, labile blood pressure, sinus tachycardia, bradycardia and diaphoresis. The presence of complications had a statistical significance with respect to the outcome of the patient which is similar to other studies.<sup>6,10,12</sup> This contrast to one study concluding that the presence of complication did not significantly affect the outcome of tetanus patients.<sup>16</sup> The duration of the hospital stays for patients who were discharged alive, was between two to 65 days, with a mean of 10.89 days. Majority (75%) of those who died had a hospital day of less than five. This can be explained by the fact that majority of the patients who were transferred to this institution were already in very severe form.

In the present study, respiratory failure (40.91%) was the principal immediate cause of death, agreeing with other studies.<sup>6,8,15</sup> This is followed by dysautonomia (20.45%) and sepsis (20.45%). The poor prognostic factors determined by univariate analysis were age more than 40 years (OR=2.24,  $p$ -value=0.0160), incubation period less than seven days (OR=2.65,  $p$ -value= 0.0027), period of onset less than three days (OR=2.52,  $p$ -value=0.0150), severity of disease upon admission (OR=17.35,  $p$ -value=<0.0001), need for ventilatory support (OR=22.20,  $p$ -value=<0.0001) and presence of complications (OR=2.96,  $p$ -value= 0.0013). However, only need for ventilatory support is associated with significant mortality (OR=31.57,  $p$ -value=0.000) in multivariate analysis which is congruent to one study.<sup>7</sup>

#### Limitations and recommendations

The main limitation of the study is lack of more detailed clinical information such as presenting symptoms and identified complications which may have contributed some bias into our findings. We encouraged follow-up of patients who transferred to other institution to determine the actual

outcome of the management done. In the present study, worst case scenario was used which significantly increased our mortality rate. We also recommend to future researcher that a prospective study be pursued to allow them to communicate, assess and monitor the clinical progress of patients. This is also to lessen potential source of bias and confounding factors.

#### Conflict of interest

We declare no conflict of interest.

## Conclusion

Though tetanus is a vaccine preventable disease, its prevalence is still high and is associated with high mortality rate. In the study, majority of patients were above 40 years old, rural dwellers, farmers, males and with unknown tetanus vaccination history. The mortality rate is 38.66%. Most deaths occurred early due to respiratory failure. Only need for ventilatory support is considered an independent factor for mortality.

Though the admission pattern in the study did not significantly affect the outcome, we still highly recommend establishing an ICU facility with adequate and readily available mechanical ventilators. Health education programs are highly encouraged to create awareness among people, especially those who live in rural or far flung areas, about basic wound management and importance of immunization.

## References

1. **Kasper D. Fauci A. Hauser S.** Harrison's Principles of Internal Medicine. New York: The McGraw-Hill Companies, Inc, 2019.
2. **Hamborsky J. Kroger A. Wolfe S.** Centers for Disease Control and Prevention. [2015]. Epidemiology and Prevention of Vaccine-Preventable Diseases, (13th ed), [online]. Communication and Education Branch, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Available: <http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/tetanus.pdf> [2015].
3. **Reddy P. Bleck T. Mandell,** Douglas and Bennett's Principle and Practice of Infectious Disease. Philadelphia: Elsevier, 2010.
4. **Global burden of disease Study. [2015].** Tetanus. Available: <http://global-disease-burden.healthgrove.com/1/8466/Tetanus-in-Philippines>
5. **Chua ML. Ambas CD. Quiambao, BP.** Management Protocols of Infectious and Typical Diseases. Philippines: Research of Tropical Medicine Vol. II, 2013.
6. **Derbie A. Amdu A. Alamneh A. Tadege A.** Clinical Profile of tetanus patients attended at Felege Hiwot Referral Hospital, Northwest Ethiopia: A Retrospective Cross-Sectional Study. Springerplus. 5(1): 892, 2016 June.
7. **Chalya PL. Mabula JB. Dass RM. Mbelenge N. Mshana SE. Gilyoma JM.** Ten-year experiences with Tetanus at a Tertiary hospital in Northwestern Tanzania: A Retrospective Review of 102 case. World Journal of Emergency Surgery. 6(1):20, 2011 July.
8. **Amare A. Melkamu Y. Mekonnen D.** Tetanus in adults: Clinical presentation, treatment and predictors of mortality in a tertiary hospital in Ethiopia. Journal of the Neurological Sciences. 317(1-2): 62-65, 2012 March.
9. **Mahieu R. Reydel T. Lerolle N.** Admission of tetanus patients to the ICU: A Retrospective Multicentre Study. Annals of Intensive Care. 7:112, 2017 November.
10. **Marulappa V. Majunath R. Mahesh K.** A Ten-Year Retrospective Study on Adult Tetanus at the Epidemic Disease (ED) Hospital, Mysore in Southern India: A Review of 512 Cases. Journal of Clinical and Diagnostic Research. 6(8): 1377-1380, 2012 October.
11. **Anuradha S.** Tetanus in Adults- A continuing problem: An Analysis of 217 patients over 3 years from Delhi, India, with special emphasis on predictors of mortality. Medical Journal Malaysia. 61(1): 7-14, 2006 March.
12. **Owolabi LF. Habib AG. Nagoda M.** Predictors of Mortality among adult tetanus patients in Northwestern Nigeria. Neurology Asia. 16(3):199-203, 2011 September.
13. **Sun C. Zhao H. Lu Y. Wang Z. Xue W. Lu S. Shen H. Wang Y. Peng Q. Huang L.** Prognostic factors for generalized tetanus in adults: A retrospective study in a Chinese hospital. The American Journal of Emergency. 37(2):254-259, 2018 February.
14. **Oladiran I. Meier DE. Ojelade AA. OlaOlorun DA. Adeniran A. Tarpley JL.** Tetanus: Continuing Problem in the Developing World. World Journal of Surgery. 26(10): 1282-1285, 2002 October.
15. **Chukwubike OA. God'spower AE.** A 10-year Review of Outcome of Management of Tetanus in Adults at a Nigerian tertiary hospital. Annals of African Medicine. 8(3): 168-172, 2009 July-September.
16. **Kyu H. Mumford JE. Stanaway J. Barber R. Hancock J. Vos T. Murray JL. Naghavi M.** Mortality from tetanus between 1990 and 2015: Findings from the Global Burden of Disease Study 2015. BMC Public Health. 17:179, 2017 February.
17. **Gergen PJ. McQuillan GM. Kiely M. Ezzati Rice TM. Sutter RW. Virella G.** A Population-based serologic survey of immunity to tetanus in the United States. New England Journal of Medicine. 332:761-66, 1995 March.
18. **World Health Organization [2015].** Vaccines and Diseases, Tetanus, [online]. Available: <http://www.who.int/biologicals/vaccines/tetanus/en/> [2015].

APPENDIX I  
Data Extraction Form

Code		Age	Sex
Service	( ) 1. Charity ( ) 2. Pay		
Room	( ) 1. Ward ( ) 2. ICU		
Residential address			
Date admitted	Date discharged	Length of Hospital Stay	
Pre-existing co-morbidities	( ) 1. Hypertension ( ) 2. Diabetes ( ) 3. Coronary artery disease ( ) 4. Chronic kidney disease ( ) 5. Cerebrovascular disease ( ) 6. Others, pls. specify _____		
Tetanus vaccination history	( ) 1. Vaccinated ( ) 2. Unvaccinated ( ) 3. Unknown		
Antecedent injury	( ) 1. Trauma wound ( ) laceration ( ) puncture ( ) abrasions ( ) avulsion ( ) Not identified ( ) 2. Burn wound ( ) 3. Infected mass ( ) 4. Surgical site infection ( ) 5. Diabetic extremity infection ( ) 6. Dental carries ( ) 7. Animal bite ( ) 8. Others, pls. specify _____		
Wound character	( ) 1. Healed ( ) 2. Wound		
Tetanus Anti-toxin prophylaxis	( ) 1. Yes ( ) 2. No ( ) 3. Unknown		
Clinical manifestation	( ) 1. Trismus ( ) 7. Fever ( ) 2. Rigidity ( ) 8. Dyspnea ( ) 3. Dysphagia ( ) 9. Sweating ( ) 4. Spasms ( ) 10. Tachycardia ( ) 5. Ophisthotonos ( ) 11. Elevated blood pressure ( ) 6. Back Pain ( ) 12. Others, pls. specify _____		
Clinical form	( ) 1. Local ( ) 2. Cephalic ( ) 3. Generalized		
Incubation period	Number of days: _____ ( ) 1. < 7 days ( ) 2. ≥ 7 days		
Period of onset	Number of days: _____ ( ) 1. < 3 days ( ) 2. ≥ 3 days		
Severity	( ) 1. Mild ( ) 2. Moderate ( ) 3. Severe ( ) 4. Very severe		
Management given	( ) 1. Antibiotic ____ 1a. Metronidazole Dose, Route and Frequency _____ ____ 1b. Pen G Dose, Route and Frequency _____ ____ 1c. Others, pls. specify _____ Dose, Route and Frequency _____ ( ) 2. Control of muscle spasm and rigidity ____ 2a. Diazepam Dose, Route and Frequency _____ ____ 2b. Midazolam Dose, Route and Frequency _____ ____ 2c. Magnesium sulfate Dose, Route and Frequency _____ ( ) 3. Neutralization of circulating toxin (TIG) Dose and Route _____ ( ) 4. Active immunization (Tetanus toxoid) Dose and Route _____ ( ) 5. Wound debridement ( ) 6. Airway protection ____ 6a. Endotracheal intubation ____ 6b. Tracheostomy ( ) 7. Others, pls. specify _____		
Complications	( ) 1. Aspiration pneumonia ( ) 8. Bowel ileus ( ) 2. Pneumothorax ( ) 9. UTI ( ) 3. Arrhythmia ( ) 10. Dysautonomia ( ) 4. Decubitus ulcer ( ) 11. Airway obstruction ( ) 5. Sepsis ( ) 12. Gastrointestinal bleed ( ) 6. Acute renal failure ( ) 13. Others, pls. specify _____ ( ) 7. Fracture		
Treatment outcome	( ) 1. Survived ( ) 2. Died ( ) 3. DAMA ( ) 4. THOC		
Cause of death	( ) 1. Respiratory failure ( ) 2. Sepsis ( ) 3. Multiorgan failure ( ) 4. Fatal arrhythmia ( ) 5. Others, pls. specify _____		

## APPENDIX II

### Sample Size Computation

Variable	Rate in the Exposed	Rate in the unexposed	Ratio Unexposed:Exposed	Sample Size alpha 0.05, power 80%
Age <sup>1</sup>	48.3	25.5	0.4	181
Complications <sup>1</sup>	94.5	0.4	1	10
Rural Residence <sup>2</sup>	77	50	0.67	102
Severity <sup>2</sup>	54.5	10.9	1	38
Dysautonomia <sup>3</sup>	55	7	0.5	38
Occupation (Farmer) <sup>4</sup>	67	36	0.33	107

The sample size formula for the method described in Kelsey is:

$$n_1 = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 \bar{p}q(r+1)}{r(p_1 - p_2)^2}$$

and

$$n_2 = r n_1$$

where

$n_1$  = number of exposed

$n_2$  = number of unexposed

$Z_{\alpha/2}$  = standard normal deviate for two-tailed test based on alpha level (relates to the confidence interval level)

$Z_{1-\beta}$  = standard normal deviate for one-tailed test based on beta level (relates to the power level)

$r$  = ratio of unexposed to exposed

$p_1$  = proportion of exposed with disease and  $q_1 = 1-p_1$

$p_2$  = proportion of unexposed with disease and  $q_2 = 1-p_2$

$$\bar{p} = \frac{p_1 + p_2}{r+1} \quad \text{and} \quad q = 1 - \bar{p}$$

<sup>1</sup> Marulappa V. Majunath R. Mahesh K. A Ten-Year Retrospective Study on Adult Tetanus at the Epidemic Disease (ED) Hospital, Mysore in Southern India: A Review of 512 Cases. *Journal of Clinical and Diagnostic Research*. 6(8): 1377-1380, 2012 October.

<sup>2</sup> Derbie A. Amdu A. Alamneh A. Tadege A. Clinical Profile of tetanus patients attended at Felege Hiwot Referral Hospital, Northwest Ethiopia: A Retrospective Cross-Sectional Study. *Springerplus*. 5(1): 892, 2016 June.

<sup>3</sup> Amare A. Melkamu Y. Mekonnen D. Tetanus in adults: Clinical presentation, treatment and predictors of mortality in a tertiary hospital in Ethiopia. *Journal of the Neurological Sciences*. 317(1-2): 62-65, 2012 March.

<sup>4</sup> Oladiran I. Meier DE. Ojelade AA. OlaOlorun DA. Adeniran A. Tarpley JL. Tetanus: Continuing Problem in the Developing World. *World Journal of Surgery*. 26(10): 1282-1285, 2002 October.

## APPENDIX III

The following tables show the frequency and percentage of the demography, clinical profile and treatment outcome of adult tetanus patient admitted in Cagayan Valley Medical Center over a six-year period.

Table I. Demographic data of adult tetanus patients (N=194)			
Variables	Frequency	Percentage	
Sex			
Male	178	91.75	
Female	16	8.25	
Age			
<20	1	0.52	
20-39	60	30.93	
40-59	96	49.48	
≥60	37	19.07	
Place of residence			
Urban	22	11.34	
Rural	172	88.66	
Co-morbidities			
Hypertension	13	6.70	
Diabetes mellitus	7	3.61	
Coronary artery disease	4	2.06	
Chronic kidney disease	1	0.52	
Cerebrovascular disease	2	1.03	
Antecedent injury			
Trauma wounds	164	84.53	
Laceration	17	8.76	
Puncture	123	63.40	
Abrasion	13	6.70	
Avulsion	2	1.03	

Table I. Demographic data of adult tetanus patients (N=194)			
Variables	Frequency	Percentage	
Not identified	9	4.64	
Dental carries	11	5.67	
Not identified	9	4.64	
Foreign body	3	1.55	
Chronic otitis media	2	1.03	
Burn wound	1	0.52	
Infected mass	1	0.52	
Diabetic extremity infection	1	0.52	
Animal bite	1	0.52	
Infected wound	1	0.52	
Tetanus vaccination history			
Vaccinated	6	3.09	
Unvaccinated	52	27.83	
Unknown	136	70.10	



**Table II. Clinical data of adult tetanus patients (N=194)**

Variable	Frequency	Percentage
Tetanus anti-toxin post-exposure prophylaxis		
Yes	18	9.28
No	176	90.72
Type of wound		
Healed	149	76.80
Unhealed	45	23.20
Incubation period		
< 7 days	56	28.87
≥ 7 days	138	71.13
Period of onset		
< 3 days	35	18.04
≥ 3 days	159	81.96
Clinical form		
Generalize	194	100.00
Severity		
Mild	8	4.12
Moderate	133	68.56
Severe	38	19.59
Very severe	15	7.73
Clinical manifestation		
Trismus	180	92.78
Spasms	163	84.02
Dysphagia	157	80.93
Rigidity	132	68.04
Elevated blood pressure	97	50.00
Back pain	83	42.78
Fever	72	37.11
Dyspnea	67	34.54
Tachycardia	56	28.87
Sweating	27	13.92
Ophisthotonus	22	11.34

**Table III. Management given to adult tetanus patients (N=194)**

Management	Frequency	Percentage
Antibiotic		
metronidazole	194	100
Control of muscle spasm and rigidity		
benzodiazepines	158	81.44
magnesium sulfate	3	1.55
both	33	17.01
Tetanus immunoglobulin	6	3.09
Tetanus toxoid	122	62.89
Anti-tetanus serum	147	75.77
Wound debridement (N=45)	36	18.56
Ventilatory support (N=63)		
Endotracheal intubation	42	21.65
Tracheostomy	14	7.22
Refused	7	3.61

**Table IV. Complications of adult tetanus patients (N=194)**

Complications	Frequency	Percentage
Respiratory	112	57.73
Pneumonia	49	25.26
Airway obstruction	63	32.47
Cardiovascular		
Arrhythmia	2	1.03
Gastrointestinal	35	18.04
Gastrointestinal bleed	18	9.28
Bowel ileus	16	8.25
Acute liver failure	1	0.52
Genitourinary	56	28.87
Acute renal failure	8	4.12
Hypokalemia	45	23.20
UTI	3	1.55
Neuromuscular	54	27.83
Dysautonomia	50	25.77
Hypoxic ischemic encephalopathy	4	2.06
Infectious		
Sepsis	9	4.64
Pneumonia	5	2.58
CAUTI	2	1.03
Infected wound	2	1.03
Musculoskeletal		
Pressure ulcer	3	1.55

**Table V. Length of hospital stay of adult tetanus patients**

Hospital Stay	Survived (n=119)		Died (n=44)	
	Frequency	Percentage	Frequency	Percentage
< 5	28	23.53	33	75
5-9	39	32.77	6	13.64
10-14	21	17.65	2	4.55
15-19	17	14.29	1	2.27
>20	14	11.76	2	4.55

**Table VI. Causes of death of adult tetanus patients (N=44)**

Causes	Frequency	Percentage
Respiratory failure	18	40.91
Sepsis	9	20.45
Dysautonomia	9	20.45
Arrhythmia	6	13.64
Multiorgan failure	2	4.55