



# Trauma-induced tetanus: case series and an up-to-date pharmacoeconomic overview in Nepal

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**Introduction and significance:** Tetanus is an acute, fatal, and vaccine-preventable infectious disease which is caused by anaerobic bacteria *Clostridium tetani*. This case series emphasizes on the importance of vaccine, and impact of financial status in the recovery of the patient and pharmacotherapeutic review of tetanus.

**Methods:** This case series was performed at the Department of Internal Medicine at a Tertiary Teaching Hospital. The authors here report two cases of rare and fatal tetanus that were diagnosed clinically, their treatment modality, and impact of socioeconomic status on the prognosis. The authors also review different pharmacotherapeutic modalities of tetanus.

**Discussion:** Tetanus is a fatal disease, which requires antitoxin measures, spasm control, and airway management. The treatment of this disease requires prolonged; intensive care unit stay which also increases the incidences of other comorbid fatal conditions like pneumonia. This case series presents cases of 39-years-old male and 41-years-old male who presented to the hospital after cut injury, however financial constraints of 41 years old male made him withdraw from ventilator support whereas 39-years-old male had good recovery due to his better financial status and immunoglobulin access in time.

**Conclusion:** In this study, we describe the clinical history of a rare and fatal but vaccine-preventable condition, tetanus associated with comorbidities, in an adult male who was successfully treated and another who chose to discontinue treatment due to financial constraints, resulting in death.

**Keywords:** benzodiazepines, dysarthria, spasm, tetanus

## Introduction

Tetanus is a rare acute, fatal disease caused by an exotoxin generated by the anaerobic bacteria *Clostridium tetani*. It is preventable with vaccination<sup>[1,2]</sup>. The method of entry into the human body is through wounds, which have a strong effect on the central nervous system and impede inhibitory neurotransmission, resulting in spastic paralysis<sup>[2]</sup>. Though it is uncommon in developed countries due to widespread vaccination against it, it remains a big problem in tropical and subtropical areas<sup>[1]</sup>. The symptoms include abdominal, neck, and jaw stiffness, which is followed by violent muscle spasms. Tetanus treatment consists of antitoxin measures, spasm control, and airway management.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2025) 87:1808–1813

Received 13 August 2024; Accepted 11 February 2025

Published online 27 March 2025

<http://dx.doi.org/10.1097/MS9.0000000000003084>

## HIGHLIGHTS

- The article highlights two contrasting cases of tetanus, demonstrating variability in clinical presentation, from progressive lower-limb stiffness to generalized spasms with autonomic dysregulation. It also emphasizes the profound impact of socioeconomic constraints on treatment outcomes, with one patient recovering due to comprehensive ICU care and the other succumbing to financial limitations.
- The detailed management strategies in both cases underline the importance of therapies like immunoglobulin, magnesium sulfate, benzodiazepines, and neuromuscular blockers. The discussion also explores the potential role of novel treatments like plasma exchange in severe tetanus, particularly its ability to reduce toxin burden and ICU stays, while highlighting its cost and feasibility challenges in resource-limited settings.
- The case series delves into the pharmacoeconomics of tetanus management, comparing the cost-effectiveness of preventative measures, such as vaccination and booster doses, with the high financial burden of prolonged ICU care for advanced tetanus. It calls for the integration of affordable and scalable treatment strategies to improve outcomes in low-income countries like Nepal.

## Methods

This case series was performed at the Department of Internal Medicine at our hospital. This case series is prospective and

consecutive where the patient was managed at our institution. The authors here report two cases of rare and fatal tetanus of 39 and 41-year-old males after puncture wounds that were diagnosed clinically, their treatment modality, and impact of socioeconomic status on the prognosis. Databases such as PubMed, Scopus, and Web of Science were searched using the keywords “tetanus,” “pharmacoeconomics,” and “case series.” Inclusion criteria encompassed peer-reviewed articles published in English, focusing on clinical management, pharmacoeconomics, and outcomes of tetanus in resource-limited settings. Our case series has been reported in line with PROCESS criteria<sup>[3]</sup>.

Case 1

A 39-year-old male arrived at the hospital 2 months back with the chief complaints of trismus, dysphagia, shortness of breath, and abnormal jerky movement. He had a cut injury (approximately 7 × 0.5 cm) on his left hand due to a sickle 2 months back which he had received tetanus toxoid after 2 days of cut injury and was well dressed and sutured. He had visited two different hospitals where he received Injection Human Tetanus Immunoglobulin 500 IU, Amoxicillin 500 mg + Clavulanic Acid 125 mg tablet, and Paracetamol 500 mg tablet, CPR and intubation. There was no history of fever, headache, chest pain, nausea, vomiting, loss of consciousness, loose stool or urinary continence. On examination, Glasgow Coma Scale scoring was E1 V1 M1 showing no eye-opening, verbal response unapplicable while intubated, and motor response (flaccid). The pupils were 3 mm, round, regular, and reactive. All vital signs were within

normal limits. Laboratory investigations revealed a leukocyte count of 7100/cmm (normal: 4000–11 000/cmm). Hemoglobin was recorded at 8.1 gm%, which is significantly below the normal range (normal: 12–18 gm%), indicating anemia. The platelet count was 252 000/cmm (normal: 150 000–450 000/cmm). The urea level was 20.7 mmol/L, and creatinine was elevated at 148 μmol/L (normal: 62–106 μmol/L for males, 44–80 μmol/L for females). Sodium levels were 135 mEq/L (normal: 135–145 mEq/L), at the lower limit of the normal range, while potassium was elevated at 6.5 mEq/L (normal: 3.5–5.0 mEq/L). Bicarbonate levels were within normal limits (normal: 22–28 mEq/L). Liver function test, erythrocyte sedimentation rate, and C reactive proteins were normal. These findings highlight abnormalities in hemoglobin and potassium levels, necessitating further clinical evaluation, although other parameters, including bicarbonate, remained within normal limits. Based on the clinical findings, tetanus was diagnosed. Blood culture was done to rule out systemic septicemia and was found to be sterile. The medical team planned on sedation, controlling spasms, managing autonomic dysregulation, and monitoring ventilatory and cardiovascular status, along with supportive care measures (Fig. 1). The patient was intubated with IV propofol which started at 50 mcg/kg/minute and IV midazolam at 25 mcg per hour. On the first day of admission, patients were having frequent spasms on light stimulation and sudden rise in BP and HR during spasms – autonomic dysregulation for which IV Labetalol was given. Flowchart showing treatment plan of Case 1. Then, magnesium sulfate (MgSO<sub>4</sub>) infusion started at 1 g/hour, IV Diazepam 20 mg every 12 hours, IV Ketamine 50 mcg/kg/hour.

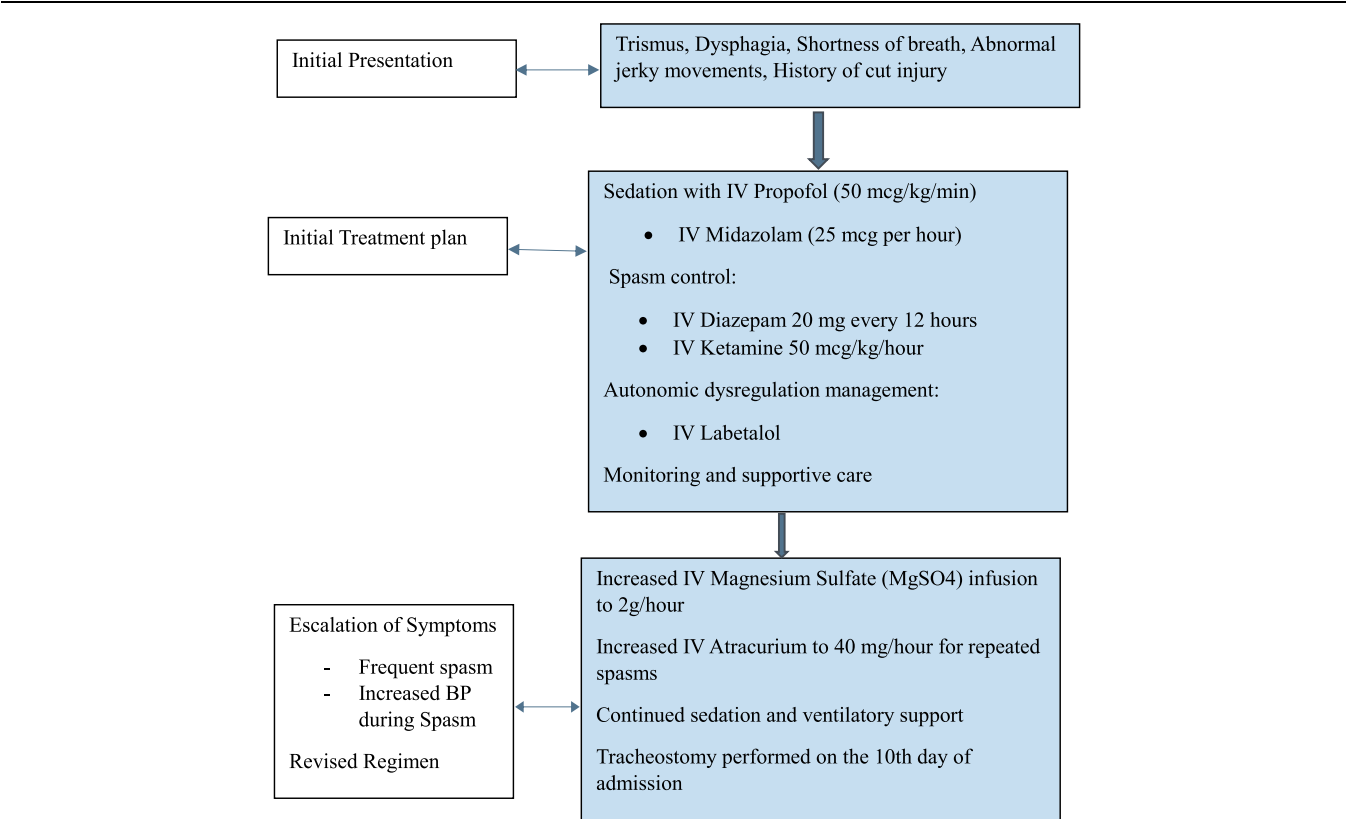


Figure 1. Flowchart showing treatment plan of Case 1.

IV Atracurium 30 mg/hour for repeated spasms that are not controlled by diazepam and ketamine. Patients have had multiple episodes with two to four episodes of spasm every night since admission. Subsequently,  $\text{MgSO}_4$  infusion was increased at 2 g/hour and injection atracurium to 40 mg per hour while sedation was tapered. Tracheostomy was done on the 10th day of admission and  $\text{MgSO}_4$  was stopped after the 13th day of admission. After the 36th day of admission, diazepam was also stopped. His hospital course was complicated with aspiration pneumonia for which he had given IV antibiotics. The condition was resolved, and the patient had not encountered spasm, shortness of breath, or generalized weakness of body.

## Case 2

A 41-year-old male, construction worker by occupation who had episodes of alcohol abuse and smoke, arrived at the hospital with chief complaints of weakness and stiffness in bilateral lower limbs for 1 month, as well as inability to open mouth, dysarthria, and dysphagia. One month ago, he had a prick injury to both hands from a corroded nail, which caused him pain at the site of injury for three days and cured on his own. After 5 days, he had discomfort, pain, and stiffness in his right lower limb, extending from the leg to the thigh.

On examination, the patient was afebrile, with a pulse of 94 bpm, a respiratory rate of 18 per minute, a blood pressure of 120/70 mm Hg, and a  $\text{SpO}_2$  of 92%. The cranial nerves were examined and confirmed to be normal. On motor examination, the lower leg was extended in attitude, and there was an increased tone in both lower limbs, with normal mass and no evident wasting or fasciculation. Neck stiffness was observed, and neck flexion and extension were limited. The power of shoulder abduction, adduction, flexion, and extension was measured as 4/5. A respiratory and cardiovascular system examination yielded a normal result. Upon investigation, the leukocyte count was elevated at 14 800/cmm (normal: 4000–11 000/cmm), suggesting leukocytosis. Hemoglobin was 12.4 gm% (normal: 12–18 gm%), which is within the normal range. The platelet count was 190 000/cmm (normal: 150 000–450 000/cmm), also within the normal range. The random glucose level was 7.8 mmol/L (normal: 3.9–11.0 mmol/L), indicating a normal range for a random glucose test. Urea was measured at 9.8 mmol/L (normal: 2.5–6.7 mmol/L), slightly elevated, and creatinine was significantly raised at 268  $\mu\text{mol/L}$  (normal: 62–106  $\mu\text{mol/L}$  for males, 44–80  $\mu\text{mol/L}$  for females), indicating renal dysfunction. Electrolyte levels showed sodium at 137 mEq/L (normal: 135–145 mEq/L), potassium at 4.4 mEq/L (normal: 3.5–5.0 mEq/L), and magnesium elevated at 3.6 mg/dl (normal: 1.7–2.2 mg/dl). Calcium was measured at 2.2 mmol/L (normal: 2.1–2.6 mmol/L), falling within the normal range. Albumin was critically low at 25 gm/dl (normal: 35–50 gm/dl), indicating hypoalbuminemia. Total bilirubin was markedly elevated at 83  $\mu\text{mol/L}$  (normal: 5–21  $\mu\text{mol/L}$ ), with direct bilirubin at 32  $\mu\text{mol/L}$  (normal: <7  $\mu\text{mol/L}$ ), suggesting significant hyperbilirubinemia. Liver function tests revealed an AST level of 71 U/L (normal: 8–40 U/L), which is elevated, and an ALT level of 34 U/L (normal: 7–56 U/L), which is within the normal range. Blood culture was done to rule out systemic septicemia and was found to be sterile. His C-reactive protein quantitative was also high, at 263.97 mg/L. Following admission to the intensive care unit (ICU) (Fig. 2), he started on IV Diazepam 10 mg,

IV Metronidazole 500 mg, IV  $\text{MgSO}_4$  2 gm, IV Paracetamol, and IV KCL. Following continuous monitoring and tachypnea, the patient was instructed to undergo intubation with Fentanyl 150 mcg and IV Ketamine 50 mg. Still, the patient had spasm, therefore the antibiotic was changed from IV Metronidazole to Tazobactam/Piperacillin 4.5 grams. After 24 hours, no spasms were detected, thus IV Midazolam was reduced to 25 mg/hour. IV Vecuronium 5 mg stat was used to alleviate spasms and rigidity. Due to financial constraints, the patient's party has opted to discontinue ventilator support after 2 months of hospitalization along with midazolam infusion, and request morphine at the last minute for the patient's comfort.

## Discussion

We report two cases of tetanus. Both patients had a history of puncture wounds (Case 1: sickle injury; Case 2: corroded nail), known to be associated with *C. tetani* infections. The diagnosis of both the conditions was made clinically. The usual tetanus signs of trismus, dysphagia, and muscular rigidity were present in both patients. But Case 1 also had autonomic dysregulation and aberrant jerky movements, whereas Case 2 mostly experienced lower limb weakness and stiffness. The clinical presentation of both cases was similar and presented with dysphagia, stiffness, and generalized weakness. Apart from clinical presentation, demographic status, age of presentation, and treatment modalities were different. The prognosis of the one who got immunoglobulin and tetanus toxoid was better than the one who hadn't got the immunoglobulin. To prevent spasms in both situations, deep anesthesia and muscular relaxation were necessary. IV propofol, midazolam, diazepam, ketamine, and atracurium were used to treat Case 1. IV ketamine, vecuronium, midazolam, diazepam, and finally morphine were used to treat Case 2. Due to financial constraint, one had withdrawn from ventilator support, midazolam infusion, and requested morphine at the last minute for the patient's comfort whereas another patient had recovered after 46 days of ICU admission. Studies indicate that the introduction of mechanical ventilation and advanced ICU care has led to a notable decrease in mortality rates among patients with severe tetanus. Different studies have reported that the availability of mechanical ventilators in ICU and prolonged ICU Stay has significantly reduced mortality rates in tetanus, as these facilities allow for effective management of muscle spasms and autonomic disturbances through high-dose sedatives and muscle relaxants<sup>[4–6]</sup>. Case 2 succumbed due to financial constraints that limited prolonged mechanical ventilation, a critical component in managing severe tetanus. These two examples highlight the serious consequences that can result from tetanus infections, especially in cases where prompt or inadequate initial care is provided. The two patients' glaringly different results highlight how important thorough, ongoing treatment is for tetanus management. Vaccination has significantly reduced the incidence of tetanus, making it one of the most successful interventions in history.

Tetanus treatment consists of three steps: antitoxin measures, spasm control, and airway management (Table 1). However, treatment for this disease is ineffective, leading to significant fatality rates in case series worldwide. Wound debridement, along with other pharmacological control methods, is a critical component of tetanus treatment<sup>[7]</sup>. In tetanus instances, surgical

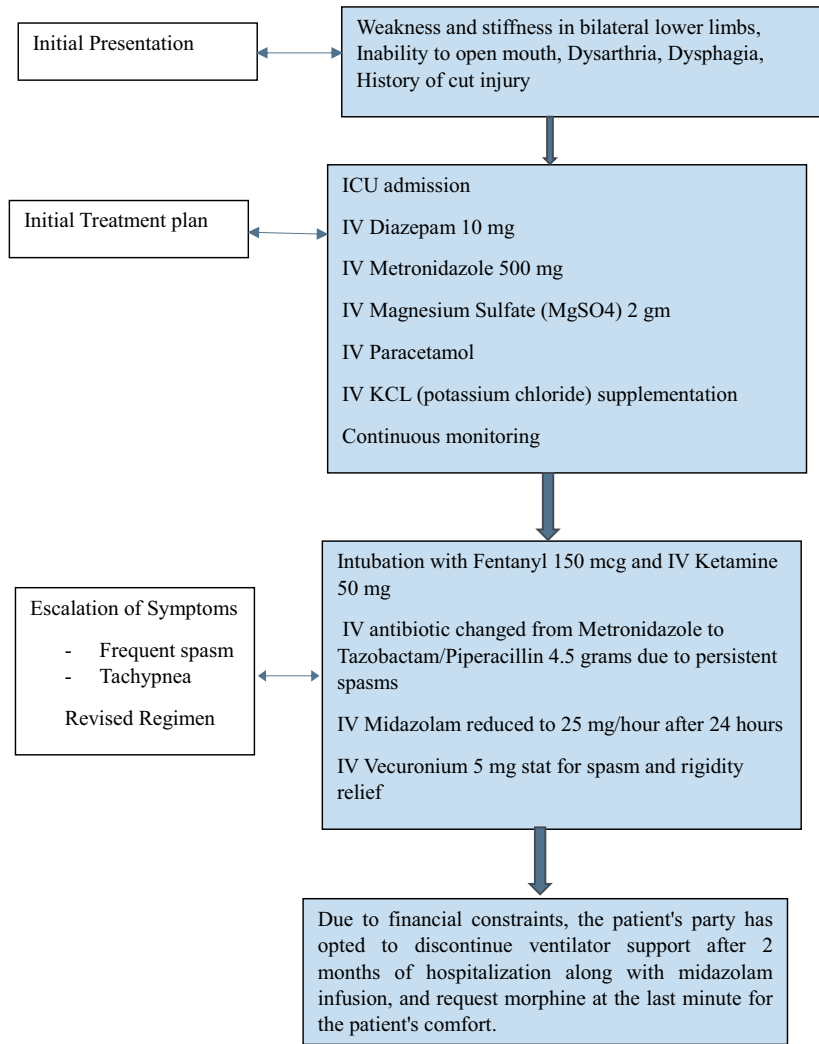


Figure 2. Flowchart showing treatment plan of Case 2.

debridement of diseased tissue is very crucial because it minimizes the quantity of bacterial spores and inhibits disease progression<sup>[8]</sup>. *C. tetani* isolates have exhibited susceptibility to different antibiotics, including chloramphenicol, metronidazole, penicillin, and tetracyclines<sup>[9]</sup>. In our first case as well, Metronidazole was started and then shifted to Tazobactam/Piperacillin. Adults with severe wounds should receive a booster dose of tetanus toxoid if it has been more than 10 years since their last vaccine<sup>[4]</sup>.

Tetanus, a potentially fatal infectious condition characterized by muscle spasms and respiratory distress, has historically been treated with sedation and muscle relaxants, which may require extended mechanical ventilation<sup>[10]</sup>. Recent study has investigated potential methods to manage spasms without the requirement for anesthesia and artificial ventilation. MgSO<sub>4</sub> has shown potential in tetanus treatment, particularly in resource-limited situations. Studies show that MgSO<sub>4</sub> can successfully decrease muscular spasms and rigidity, particularly in mild to moderate cases. MgSO<sub>4</sub> has shown potential in tetanus treatment, particularly in resource-limited situations. Studies show that MgSO<sub>4</sub> can successfully decrease muscular spasms and rigidity, particularly in mild to

moderate case<sup>[11]</sup>. When paired with diazepam, MgSO<sub>4</sub> may prevent the likelihood of autonomic instability, respiratory depression, and cardiac arrhythmias in severe situations<sup>[12]</sup>. While no mortality advantage has been reported, MgSO<sub>4</sub> therapy has been related with lower requirement for mechanical breathing and shorter hospital stays of 3–7 days<sup>[13]</sup>. Magnesium toxicity is believed to be extremely rare, with asymptomatic hypocalcemia being a typical and manageable side effect<sup>[11,13]</sup>. Benzodiazepines (diazepam, midazolam) are utilized for both their sedative and spasm-controlling effects. General anesthetics, such as propofol, can also be employed<sup>[14]</sup>. Neuromuscular blocking agents (NMBAs) are essential for treating severe tetanus, especially in patients with substance use problems. Among NMBAs, Rocuronium has shown good results in controlling spasm in tetanus and control achieved within 24–48 hours<sup>[15]</sup>. Vecuronium infusion has also been shown to decrease cardiovascular effects and allow speedy restoration of neuromuscular blockade<sup>[16]</sup>. Intrathecal baclofen has emerged as a viable treatment for severe tetanus, especially in resource-constrained environments. This GABAB receptor agonist immediately counteracts tetanus toxin's effects, lowering muscular stiffness and spasms<sup>[17]</sup>.

**Table 1**  
**Different modality of treatment of tetanus**

Treatment modality	Description	Advantages	Shortcomings
Non-pharmacological – Quiet environment – Minimal stimulation	Reducing external stimuli that can trigger muscle spasms and autonomic dysregulation.	Reduces frequency and severity of spasms; supports overall patient comfort and recovery.	Limited efficacy in extreme situations.
Tetanus immunoglobulin	Passive immunization given intramuscularly to neutralize circulating tetanus toxin.	When provided early, it is effective in lowering mortality and severity.	Ineffective once the toxin has bound to nerve tissue; requires early administration.
Antibiotics – Metronidazole – Beta lactams	Used to eradicate <i>Clostridium tetani</i> at the wound site.	Reduces bacterial load, preventing further toxin production.	Does not neutralize the already circulating toxin; antibiotic resistance can be a concern.
Wound debridement	Surgical removal of necrotic tissue at the site of the tetanus-prone injury to reduce bacterial load.	Reduces the bacterial burden, potentially lowering the production of tetanus toxin; promotes wound healing.	Invasive procedure; risk of further infection or injury.
Neuromuscular blockers – Vecuronium – Atracurium	Used for severe cases to provide muscle paralysis.	Effective in preventing muscle spasms, particularly in intubated patient.	Requires mechanical ventilation.
Magnesium sulfate (MgSO <sub>4</sub> )	Used for muscle relaxation and to control autonomic dysfunction.	Helps in controlling severe spasms; also has a stabilizing effect on the autonomic nervous system.	Risk of magnesium toxicity; requires careful monitoring of serum levels.

Airway care is critical because severe masseter and intercostal muscle spasms might impede airway access and ventilation. In resource-limited settings, general anesthetics like propofol and sevoflurane can ease tetany, allowing for airway control without intubation<sup>[18]</sup>. Early intubation or tracheostomy is advantageous in the overall care of individuals with widespread tetanus<sup>[19]</sup>. Despite lowering tetanus incidence rates, case fatality remains high in African care institutions. High tetanus case mortality rates suggest poor medical care in hospital settings. The most prevalent causes of mortality are complications from dysautonomia and respiratory arrest due to laryngospasm<sup>[19]</sup>. In resource-constrained environments, involvement of the respiratory system necessitates prolonged breathing and predicts mortality. In the context of Nepal, the state of tetanus prevention and management presents both significant progress and notable challenges. Nepal has achieved considerable success in immunization under the Expanded Program on Immunization (EPI), with over 85% of women of reproductive age receiving at least two doses of tetanus toxoid during pregnancy. However, adult booster doses (ADP-m) are not routinely administered, leaving older populations, particularly men, vulnerable to tetanus infections<sup>[20]</sup>. Limited vaccination access in remote and mountainous regions, combined with low awareness about the need for adult boosters, exacerbates the issue<sup>[21]</sup>. Expanding ADP-m coverage through government programs and awareness campaigns is critical to bridge this gap<sup>[22]</sup>. Financial barriers significantly impact tetanus treatment in Nepal, particularly for patients requiring intensive care. Prolonged ICU stays, mechanical ventilation, and medications like immunoglobulin and MgSO<sub>4</sub> contribute to high treatment costs, often exceeding NPR 500 000 for a single case. This cost is unaffordable for many families reliant on subsistence farming or informal employment<sup>[23]</sup>. While immunization services are provided free of charge, there are no comprehensive subsidies for tetanus treatment, leaving patients dependent on out-of-pocket expenditures or limited NGO support<sup>[24]</sup>. Introducing financial assistance or integrating tetanus care into Nepal's Social Health Security

Program could alleviate this burden<sup>[25]</sup>. Pharmacoeconomic analyses emphasize that preventative measures, such as routine adult booster doses, are significantly more cost-effective than managing advanced tetanus cases requiring ICU care. A single tetanus booster costs approximately NPR 200, a fraction of the costs associated with prolonged hospital stays<sup>[26]</sup>. Collaborating with pharmacoeconomics specialists to evaluate the cost-benefit of nationwide ADP-m implementation could provide evidence for policy shifts. Countries like Sri Lanka, which have integrated adult booster programs into public health systems, demonstrate the efficacy of such initiatives in reducing both tetanus incidence and healthcare costs<sup>[27]</sup>. The development of ventilator-associated pneumonia compounds this with multidrug gram-negative resistance pathogens due to insufficient infection control methods<sup>[14]</sup>. In our case series as well, one patient developed pneumonia as a complication. Due to a lack of financial resources, the first patient chose to withdraw ventilator support and passed away.

## Conclusion

This case series highlights the critical challenges in tetanus management, emphasizing the variability in clinical presentations and outcomes influenced by treatment and socioeconomic factors. Both cases involved hallmark tetanus symptoms, with Case 1 recovering after intensive care including immunoglobulin, MgSO<sub>4</sub>, benzodiazepines, and neuromuscular blockers, while Case 2 succumbed due to financial constraints limiting prolonged mechanical ventilation. Early interventions such as wound debridement and vaccination were pivotal in Case 1, underscoring the importance of prompt care. Socioeconomic barriers played a significant role in Case 2's unfavorable outcome, reflecting disparities in access to advanced care. Overall, the cases demonstrate that effective management with antitoxins, muscle relaxants, and supportive measures can improve outcomes, systemic challenges like financial limitations and delayed care significantly impact prognosis.

## Ethical approval

The Institutional Review Board of the Institute of Medicine, Nepal, does not mandate ethical approval for the writing or publication of case reports, and patient consent was obtained. Informed written consent was obtained from the patient before writing this case report.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Sources of funding

Not applicable.

## Author contribution

Conceptualization, data curation, formal analysis, methodology, project administration, original writing, review, editing, and visualization: B.S.; resources, supervision, validation, conceptualization, investigations, and data curation: P.S.; conceptualization, data curation, validation and investigation: G.A.; supervision, validation, and investigations: S.B.; supervision, validation, and investigations: S.K.; supervision, validation, and investigations: R.K.G.

## Conflicts of interest disclosure

Not applicable.

## Research registration unique identifying number (UIN)

Not applicable.

## Guarantor

Sudip Bastakoti and Bibek Shrestha.

## Provenance and peer review

Not commissioned, externally peer reviewed.

## Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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