

Original article

A study on the clinical presentation and outcome of tetanus in adults with special reference to autonomic nervous system dysfunction

Apu Adhikary¹, Tuhin Santra², Smarajit Banik³, Debaroti Bhar⁴, ParthaSarathi Karmakar⁵, Alok Kumar Kole⁵

¹ RMO, Department of General Medicine, North Bengal Medical & Hospital, Thiknikata, West Bengal, India.

² RMO, Department of Medicine, Midnapore Medical College and Hospital, Paschim Medinipur, West Bengal, India.

³ Assistant Professor. Department of General Medicine, North Bengal Medical & Hospital, Thiknikata, West Bengal, India.

⁴ RMO cum Clinical Tutor Department of General Medicine, R.G. Kar Medical & Hospital, Kolkata, West Bengal, India.

⁵ Professor, Department of General Medicine, R.G. Kar Medical & Hospital, Kolkata, West Bengal, India.

Corresponding author: Dr. PS Karmakar

Abstract:

Aims: To evaluate the clinical profile and outcomes of the tetanus patients and to detect autonomic nervous system dysfunction in this group of patients and their outcomes.

Methodology: Descriptive cross-sectional study in a tertiary care center. All adults' patients diagnosed of tetanus as per WHO criteria were included in the study. Autonomic dysfunction was also noted in the study subjects. The autonomic nervous system (ANS) dysfunction was defined as presence of labile or persistent hypertension (>140/90 mmHg) or hypotension (<90/60 mmHg) and persistent sinus tachycardia (heart rate >100 bpm), tachyarrhythmia or bradycardia (heart rate <60 bpm) alternating with tachycardia on ECG. At least one criteria is to be present to define ANS dysfunction.

Results: Mean age of ANS patients was 40.63 years lower than without ANS patients of 41.51 years. Nine of 11 (81.8%) patients died in ANS group as compared to six of 31 (19.3%) in without ANS dysfunction. Corrected chi-square test value between death and ANS dysfunction and full recovery is statistically significant (< p = 0.05) but the outcomes regarding partial recovery with ANS dysfunction is not statistically significant. ANS dysfunction was noted in the tetanus patients in the form of resting tachycardia, persisted hypertension, BP fluctuation, and electrocardiogram (ECG) changes in RR ratio during deep inspiration, excessive sweating, and urinary retention.

Conclusion: The present study highlights the detection of ANS dysfunction in tetanus patients to be of utmost importance who showed a statistically significant increment in both complete recovery and mortality as well. Hence, careful early detection of ANS dysfunction is a must to reduce mortality and achieving full recovery.

Keywords: Tetanus, ANS dysfunction, clinical profile.

Medworld asia

Dedicated for quality research

Introduction:

Tetanus is a devastating neurological syndrome characterized by generalized rigidity, convulsive spasm of skeletal muscles and autonomic instability. It is caused by clostridium tetani which is an anaerobic, gram positive, spore-forming bacilli commonly found in soil and feces. Tetanus occurs sporadically and affects non-immunized, partially immunized, or even fully immunized persons who fail to maintain adequate immunity with booster doses of tetanus vaccine. Despite the availability of an effective active vaccination since 1924, tetanus remains a major health problem in the developing world and mortality being higher among neonates, pregnant women and elderly population and is still encountered in the developed world.^{1,2} The global incidence of tetanus is estimated to be one million cases annually, with case fatality rate ranging from 20-50%.^{3,4} Care of the preventable but potentially fatal disease has been revolutionized with advent of mechanical ventilation. . WHO definition of tetanus requires at least one of the followings signs: (i).trismus (Inability to open mouth) or (ii) Risussardonicus (sustained muscle spasm of the facial muscles); or (iii) Painful muscular contractions.⁵

However, still a significant minority, at least 10%, would die despite every effort.⁶ Respiratory arrest used to be a common problem during pre-ventilation era; but presently autonomic nervous system dysfunction has emerged as a major problem in these patients in post ventilator era.⁶ Autonomic disturbances develop a few days later in course. The pathogenesis of autonomic nervous system disturbances is unclear; however, several theories have been put forward, including damage to brain stem and hypothalamic nuclei⁷ and direct disturbances in autonomic nerve. Violent autonomic disturbances, severe hypertension and tachycardia alternating with hypotension and

bradycardia are reported in relation to severe tetanus. In addition to the cardiovascular system, other autonomic effects include profuse salivation, increased bronchial secretions, gastric stasis, diarrhea, urinary retention and high output renal failure may all be related to autonomic disturbance.⁸

The aim of this study is to review the clinical presentation, and outcome with special reference to autonomic nervous system dysfunction in tetanus patients. Detail history taking including immunization status, nature of injuries and thorough clinical examination and daily monitoring of pulse, blood pressure are done to evaluate the pattern of clinical presentations and possible complications, with particular emphasis on signs of autonomic insufficiency. This study highlights the importance of this previously not well-known aspect of tetanus.

Aims and Objectives:

To evaluate the clinical profile and outcomes of the tetanus patients admitted in our hospital and to detect autonomic nervous system dysfunction in this group of patients and their outcomes.

Materials and Methods:

Study Area:

This study was conducted at the Infectious Disease unit of North Bengal Medical College under the department of General Medicine. North Bengal medical college and hospital, is the tertiary referral care center in this six district of North Bengal region and nearby countries like Bhutan, Bangladesh and Nepal.

Study Design:

Descriptive cross sectional study about all adults' patients as per WHO criteria admitted with the diagnosis of tetanus.

Study Period:

May 2011 - April 2012.

Study Population:

All tetanus patients diagnosed as per WHO criteria admitted in Infectious Disease unit of North Bengal Medical College and hospital was considered as study population and study subject. This study included 42 consecutive tetanus patients above the age of 12 yrs. They were attending north Bengal medical college and hospital, a tertiary referral center, on an inpatient basis. As admitted patients of tetanus was not found regularly, so recruited sample size in my study became restricted to total number of 42.

Exclusion criteria:

The patients with preexisting malignancy, immunosuppression (AIDS/drugs), hypertension, diabetes, significant cardiac dysfunction and renal impairment and pediatric age group were excluded from the Study.

Tools for data collection were under the following points:

- A) Proforma of written informed consent.
- B) Proforma for data collection includes age, gender, profession, residence, date of admission, outcome - death /full recovery/partial recovery.
- C) Detail history taking regarding history of injuries, skin lesions, immunization status before injury, previous operation abortion, child birth or routine vaccination before delivery.
- D) Data were collected regarding presence of signs like trismus, muscle spasm, rigidity, and opisthotonus posture of all patients or major complaints – like back pain, neck pain , difficulty in opening of mouth, generalized muscle pain or rigidity, dysphagia .

F) Clinical parameters of autonomic nervous system dysfunctions

- I. Regular manual recording of pulse and BP twice daily and mean value filled in the data sheet.

II. Monitor other features of ANS dysfunction (excessive sweating, excessive oro-tracheal secretion, urinary retention)

III. ECG changes in deep breathing.

IV. Postural BP measurement (whenever the patient could be made in standing position for at least 3 minutes).

The autonomic dysfunction was defined as presence of labile or persistent hypertension (>140/90 mmHg) or hypotension (<90/60 mmHg) and persistent sinus tachycardia (heart rate >100 bpm), tachyarrhythmia or bradycardia (heart rate <60 bpm) alternating with tachycardia on ECG.³⁶ At least one criteria is to be present to define ANS dysfunction. These values were recorded at resting state, not during tetanic spasm. The values regarding BP and pulse were mostly recorded in sedated and relaxed position.

The values recorded during tetanic spasms were not included in the study. The heart rate and blood pressure of all tetanus patients were measured noninvasively at least twice a day during the period of hospitalization. The patients were treated as per standard protocol for the management of tetanus which included surgical toilet or debridement of wound, infusion of Diazepam, crystalline penicillin or metronidazole.⁷⁴ The poor outcome was defined as either death or partial recovery at the time of discharge from the hospital. Partial recovery was defined as neck pain, back pain, walking difficulty and abnormal gait at discharge, in various combinations. Complete recovery was defined as absence of all the symptoms and normal gait on examination at discharge.

Statistical Analysis of Data:

Results were tabulated in Microsoft office excel worksheet and statistical analysis were done with SPSS version 12.0 software with Chi – square test and Independent samples t test. Results were considered significant if the p value < 0.05.

Results:

The mean age of the patients was 41.29 years and distribution range 13 -74 years Most of them were more than 35 years. 16.7% patients belonged to the urban population whereas 83.3% belonged to rural population. Of the 42 patients who were included in the study, 31(73.8%) were male and 11 (26.2%) were female. In occupational distribution most of the patients were from agriculture farms 19 (45.2%) and next one was tea garden worker as this area has a significant number of tea garden.

The most common clinical features were trismus 42 (100%), generalized rigidity / muscle spasm 20 (47.6%), followed by dysphagia 13(30.9%), back and neck pain 8(19%), body ache 8 (19%) and opisthotonus posture 2 (4.8%). Two types of cases generalized (95.2%) and cephalic presentation (4.8%) was noted in those patients. Clinical symptoms consist of isolated or combined dysfunction of the cranial motor nerves, most frequently cranial nerve VII. This dysfunction may remain localized or progress to generalized tetanus. The mean incubation period was 8.48 days (ranging from 2-30 days). The Mean hospital stay 11.62 days, range 3-23 days. Identifiable risk factors were noted in all of the patients. Lower limb injuries 20 (47.6%) is more frequent than upper limbs 16(38%). Other type of injury 6 (14%) is illegal abortion, boil in back, ear injury and operative intervention of piles. The major identifiable injury site was lower limbs (47.6%)

followed by upper limbs (38%). Among the immunization status, only twelve (28.6%) vaccinated after injury and 73.8% didn't give proper h/o tetanus toxoid injection after injury. Autonomic instability was noted in eleven patients (26.2%) among the total tetanus patients.

In the outcome analysis during the study period, 42 clinically diagnosed tetanus, 15 patient expired during the hospital stay, 19 patients fully recovered and 8 patient partially recovered as per previous outcome criteria.

Table 2 demonstrates the characteristics comparison of autonomic nervous system dysfunction versus no autonomic dysfunction. Mean age of ANS patients 40.63 years lower than without ANS Patients of 41.51 years. Nine of 11 (81.8%) patients died in ANS group as compared to six of 31 (19.3%) in without ANS dysfunction. Corrected chi-square test value between death and ANS dysfunction and full recovery which is statistically significant ($p = 0.05$) but the outcomes regarding partial recovery with ANS dysfunction is not statistically significant. (Table 2) ANS dysfunction was noted in the tetanus patients in the form of resting tachycardia, persisted hypertension, BP fluctuation, and electrocardiogram (ECG) changes in RR ratio during deep inspiration, excessive sweating, and urinary retention.

Figure 3 demonstrates the spectrum of ANS dysfunction (%).

Table 1: Clinical Features in Subjects with Tetanus

| Clinical features | Number of patient (%) |
|------------------------------|-----------------------|
| Trismus (lockjaw) | 42 (100%) |
| Generalized rigidity / spasm | 20 (47.6%) |
| Dysphagia | 13 (30.9) |
| Back and neck pain | 8 (19%) |
| Bodyache | 8 (19%) |
| Opisthotonus posture | 2 (4.8%) |

Table 2: Comparison of autonomic nervous system dysfunction versus no autonomic dysfunction.

| variable | ANS patients (n=11) | Non ANS patients group(n=31) | p value |
|------------------|------------------------|---------------------------------|---------|
| Male : female | 8:3 | 24:7 | 0.9218 |
| Death | 9 | 6 | 0.0008 |
| Full recovery | 1 | 18 | 0.0142 |
| Partial recovery | 1 | 7 | 0.5947 |

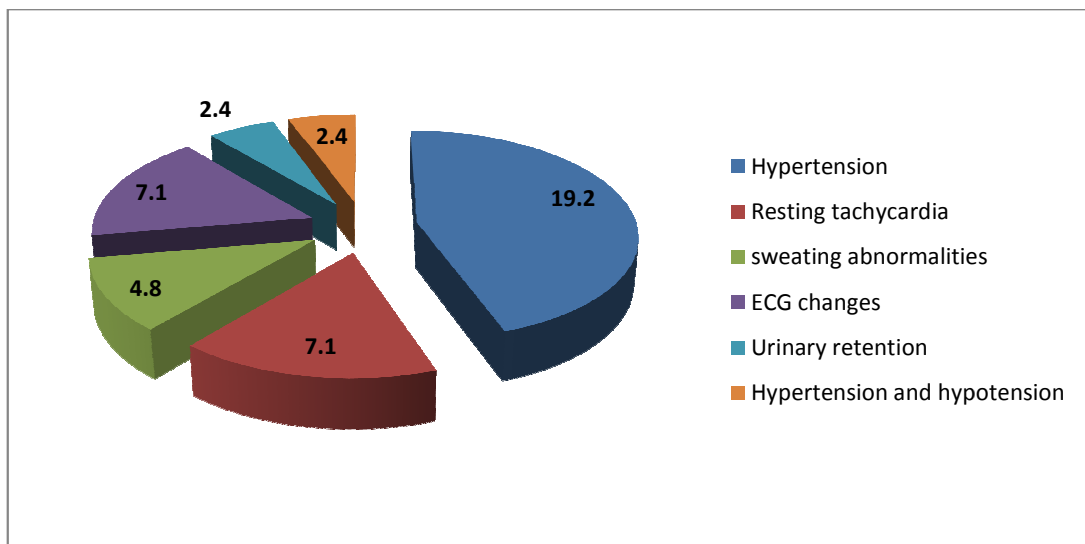
Figure 1: LMN type of facial nerve palsy (Right) in a patient with cephalic tetanus



Figure 2: Foot injury leading to tetanus in one of the patient



Figure 3: Spectrum of ANS Dysfunction



Discussion:

Tetanus is disease of antiquity. It was first described in Egypt 3000 years ago. Tetanus is still a major health problem in developing countries⁸ and associated with high morbidity and mortality rate. In this study we recruited a total 42 of patients during the study period and 32 male and 10 were female. So this was profoundly male predominant disease in my study as documented in other studies too. This could be explained by the fact that men tend to spend more time in outdoor activities and field jobs, they are more likely to be exposed to penetrating injuries and clostridium tetani is ubiquitous in soil in tropical and hot climate countries. And females at least get a dose of tetanus toxoid during pregnancy. In this study, agricultural farms are the main outdoor jobs where males are working predominantly.

The mean \pm SD age of the patients were ± 14.94 years which are quite similar to study conducted by Petermans et al⁹ and Lau et al.¹⁰ Most commonly affected age group was 35-45 years in my study population. In contrast to this my study the prevalence of tetanus in older age was more prevalent in a population based survey of immunity to tetanus in the United States. It showed that the prevalence of Americans with protective levels of tetanus antibody declined rapidly starting at the ages of 40 years and that most cases of tetanus occurred in persons of older age group.¹¹ In the UK and USA, Serological surveys have demonstrated an increasing proportion of patients with inadequate immunity as age increases: 49-66% of patients over 60 year had antibody levels below the protective level.¹² Serological testing for immunity has revealed a low level among elderly individuals in the United States. Approximately 50% of adults older than 50 years are non-immune because they never were vaccinated or do not receive appropriate booster doses. Prevalence of immunity to tetanus in

the United States is greater than 80% for those aged 6-39 years but only 28% for persons older than 70 years. This difference in age-ranges in peak incidence of tetanus in this study showing younger age group could be due to less and less involvement in outside activity of a farmer above the age of 45 years. In my study farmers formed the main bulk of patients. Identifiable injury is present in 100% patients in my study contrary to other study. Most of the study patients had identifiable acute injuries at the time of presentation and majority of injuries were inflicted on lower limbs (47.6%) an observation also reported by Lau et al¹⁰ and Komolafe et. al.¹³

The clinical presentation of the study patients were similar to the experience as is observed by other investigators and the most common presenting symptoms were trismus and rigidity. In my study trismus was present in 100% cases and reason may be patient came later to get admitted in-hospital facilities when they have already developed trismus. This suggests unawareness of this people about tetanus in pre-trismus stage. The other investigators had found body stiffness / spasm, trismus and dysphagia to be the most common presenting symptoms. As none of them were specific to tetanus, therefore, high index of suspicion for tetanus should be exercised whenever patients present with any of these symptoms as tetanus is an essentially a clinical diagnosis and laboratory results as well as cultures are of little value.

In the present study, nine of 42 patients (21.42%) had an incubation period of less than 7 days and mean 8.47 days with a range of 2-30 days and mortality of 40%. In the study by Peetermans et al,⁹ mean incubation period was 10.8 days with a range of 3-28 days, of which 5 patients had an incubation period of less than 7 days. Study by Pawar et al, showed 75% mortality in those patients with

incubation period of less than 7 days and a mortality of 94.15%.¹⁴

The prognosis of patients with tetanus has been reported variably. Overall mortality is approximately 10-50%, however in certain age groups e.g. neonates it is as high as 90-95%.

In this study, mortality rate was 37.5% which is quite consistent with the observation reported by Lau et al.¹⁰ But the mortality rate was significantly lower (11%) by Peetermans et al in their study.⁹ Due to paucity of ventilator in our medical college led many patients unprotected of respiratory complications and could be playing some role in increasing the mortality rate. Autonomic instability in tetanus is usually most prominent in the first week, peaking second week and then resolves. In eleven (26.2%) patients out of total 42 tetanus patients in the present study, autonomic signs were found to be present 3-5 days after the onset of body stiffness and gradually resolved by 7-14 days. Initially autonomic dysfunctions were considered to be sympathetic overactivity; however, later studies with hemodynamic monitoring showed that both sympathetic as well as parasympathetic systems are involved.⁴ The autonomic disturbances can be fatal. Though sudden cardiac arrest is most devastating complication, various tachyarrhythmia and bradyarrhythmias can be fatal. In the present

study, it was also noted that the autonomic system dysfunction was associated with higher mortality

Conclusion:

Tetanus is still not uncommon problem in developing countries like India and mortality is very high. Autonomic dysfunction is a commonly encountered problem in tetanus. Around one third of studied patients showed autonomic dysfunction. Presence of autonomic dysfunction definitely associated with higher mortality in tetanus and commonly manifests as hypertension, resting tachycardia, BP fluctuation and sweating abnormalities. The present study highlights the detection of ANS dysfunction in tetanus patients to be of utmost importance who showed a statistically significant increment in both complete recovery and mortality as well. Hence, careful early detection of ANS dysfunction is a must to reduce mortality and achieving full recovery.

Limitations of the study are as follows:

1. Sample size is small and it is single centre, a multicenter study involving a wider segment of population leading to a larger number of cases would have been better.
2. Comparative analysis of similar patients in an intensive care monitoring set up would have revealed more confirmatory results for planning and intervention than in a peripheral set up.

References:

1. Hodes RM, Teferedegne B: Tetanus in Ethiopia: analysis of 55 cases from Addis Ababa. *East Afr Med J* 1990; 67: 887-93.
2. Patel JC, Mehta BC. Tetanus: Study of 8697 cases. *Indian J Med Sci* 1999;53:393-401 1990; 67: 887-93.
3. Stanford JP. Tetanus-forgotten but not gone. *N Eng J Med* 1995; 332:812-813.
4. Udawadia FE, Lall A, Udawadia ZF, Sekhar M, Vora A: Tetanus and its complications: Intensive care and management experience in 150 Indian patients. *Epidemiol Infect* 1987; 99:675-84.
5. WHO technical note. Current recommendations for treatment of tetanus during humanitarian emergencies 2010;2:5.

6. Farrar JJ, Yen LM, Cook T, Fairweather N, Binh N, Parry J, Parry CM: Tetanus. *J Neurol Neurosurg Psychiatry* 2000; 69:292-301.
7. Cook TM, Protheroe RT, Handel JM: Tetanus: a review of the literature. *Br J Anaesth* 2001; 87: 477-87.
8. Ernst ME, Klepser ME, Fouts M et al. Tetanus: Pathophysiology and management. *Ann Pharmacother* 1997; 31:1507-13.
9. Peetermans WE, Schepens D. Tetanus still a topic of present interest: a case report of 27 cases from a Belgian referral hospital. *J Intern Med* 1996; 239:245-52.
10. Lau LG, Kong KO, Chew PH. A ten year retrospective study of tetanus at a general hospital in Malaysia. *Singapore Med J* 2001; 42:346-50.
11. 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. *N Engl J Med* 1995 ; 332: 761-68
12. Goulon M, Girard O, Glosbius S, et al. Les corps antitetaniques. *Nouv Presse Med* 1972; 1:3049-3050.
13. Komolafe MA, Komolafe EO, Ogundare AO. Pattern and outcome of adult tetanus in Ile-Ife, Nigeria. *Niger J Clin Prac* 2007;10(4):300-303.
14. Pawar .A.B. et al: Epidemiological study of tetanus cases admitted to a referral hospital in Solapur: *Indian Journal of Community Medicine* vol.XXIX, No3,2004(S)