ORIGINAL ARTICLE 10.1111/j.1198-743X.2004.00767.x

Prognostic factors affecting deaths from adult tetanus

N. Saltoglu[1], Y. Tasova[1], D. Midikli[1], R. Burgut[2] and I. H. Dündar[1]

[1]Department of Infectious Diseases and Clinical Microbiology and [2]Department of Biostatistics, University of Çukurova, Faculty of Medicine, Adana, Turkey

ABSTRACT

The objective of this study was to determine prognostic factors related to death from adult tetanus. Fifty-three cases of tetanus, 25 females and 28 males, were treated in Çukurova University Hospital during 1994–2000. The mean age was 46.6 years. Forty-one (77.7%) patients came from rural areas. Most (64.1%) cases had minor trauma, but 19 (35.8%) had deep injuries. The mean incubation period was 11.5 days. Mortality was high (52.8%), caused by cardiac or respiratory failure or complications, and was related to the length of the incubation period. In cases with an incubation period ≤7 days, the mortality rate was 75% (p 0.07). Mortality was significantly associated with generalised tetanus ($p < 0.05$), fever of ≥40 °C, tachycardia of >120 beats/min ($p < 0.05$), post-operative tetanus (p 0.03), and the absence of post-traumatic tetanus vaccination (p 0.068). Patients who were given tetanus human immunoglobulin or tetanus antiserum ($p > 0.05$) had similar outcomes. Patients who were given penicillin had a mortality rate similar to patients who were given metronidazole (p 0.15). The mortality rate was higher (92%) in patients with severe tetanus than in patients with moderate disease (53%). By multivariate analysis, the time to mortality caused by tetanus, and also the mortality rate, were both related significantly to age and tachycardia.

Keywords Adult tetanus, prognostic factors, tetanus

Original Submission: 17 July 2002; **Revised Submission:** 5 February 2003; **Accepted:** 12 March 2003

Clin Microbiol Infect 2004; 10: 229–233

INTRODUCTION

Tetanus cases and deaths caused by tetanus have decreased to a great extent as a result of immunisation programmes [1,2]. However, although effective and inexpensive tetanus vaccines are available, the disease remains a continuing health problem, causing high mortality and morbidity in developing countries [3–5]. In developed countries, 59% of all reported tetanus cases and 85% of all reported deaths caused by tetanus occur among people aged ≥60 years [6,7]. The elderly are susceptible because many have not received primary immunisation or the recommended booster immunisation [2,6,8,9]. In contrast, most deaths from tetanus in developing countries are seen in neonates [10].

Corresponding author and reprint requests: N. Saltoglu, Department of Infectious Diseases and Clinical Microbiology, University of Çukurova, Faculty of Medicine, Balcalı, Adana, Turkey
E-mail: nsalt@mail.cu.edu.tr

Neonatal deaths caused by tetanus in Turkey have been reduced significantly as a result of tetanus immunisation programmes for pregnant women, but the mortality rate of neonatal tetanus in rural areas is *c*. 40% [10]. Expanded immunisation programmes have been recommended for elimination of neonatal tetanus in Turkey [11], but the study of Maral *et al.* [12] found that nearly 53% of pregnant women had not been vaccinated [12]. Moreover, considerably more rural women than urban women were vaccinated. One study conducted in Turkey found protective levels of tetanus antitoxin in 69% of the population, with a haemagglutination concentration of >0.125 haemagglutination U/mL being considered as protective [13]. However, tetanus remains an important health problem in Turkey because of the large number of traffic and work accidents, extensive agricultural activity, and abortion and/or delivery under non-hygienic conditions. Adult tetanus is seen in Turkey because injured people do not apply to heath institutions for prophylaxis.

In spite of modern medical care, the death rate among patients with generalised tetanus is still high (20%) [14–16]. Mortality can be influenced by a patient's age, the incubation time, type of injury, clinical signs, and delays in treatment or prophylaxis [17]. The aim of this study was to determine the important prognostic factors associated with deaths from adult tetanus in the eastern Mediterranean region of Turkey.

METHODS AND PATIENTS

In total, 53 tetanus patients admitted to the Infectious Diseases Department of Çukurova University Hospital (Adana, Turkey) between January 1994 and July 2000 were investigated retrospectively and were followed for 60 days if they survived. Çukurova University Hospital is a tertiary-care hospital with 860 beds and admits *c.* 28 000 patients annually for treatment. Tetanus patients were admitted to the hospital from other hospitals in the region. Patient data recorded were age, sex, disease localisation, type of injury, incubation time, onset of first symptoms, history of tetanus immunisation, post-trauma tetanus prophylaxis, clinical signs, mode of treatment, and complications. All patients were given benzodiazepine (diazepam 5 mg/kg) and, when needed, chlorpromazine and muscle relaxants for control of tonic–clonic contractions. Mechanical ventilation was used when generalised spasms were not controlled. Tracheostomy and/or mechanical ventilation were also used in patients who had respiratory problems. All patients received passive immunisation with human immunoglobulin (HIG) 4000–10 000 U, or tetanus antiserum 60 000–100 000 U, and active immunisation with tetanus toxoid. After admission, patients were followed for up to 2 months.

In addition to individual prognostic factors, the value of Wood's scoring scheme [17] prognosis was investigated, with one point being assigned for each of the following: incubation period <7 days; period of onset <2 days; acquired following burns, surgery, septic abortion, surgical wound or compound fracture; generalised tetanus; fever of >40 °C; tachycardia of >120 beats/min; and narcotic addiction.

Chi-squared tests or, when needed, Fisher's exact test were used to analyse the association between mortality and categorical variables such as gender, incubation period, tetanus type, etc. In evaluating the prognostic value of the scoring scheme of Wood [17], the trend test of Cochran and Armitage [18] was employed. In addition, the fatality rate among tetanus patients was examined by multivariate logistic regression models, which included variables of incubation period and symptoms simultaneously.

RESULTS

Of the 53 patients, 28 (52.8%) were male and 25 were female, with a mean age of 46.6 years (range: 20–75 years). Forty-one (77.3%) patients came from rural areas and 12 from urban areas, and no drug use among patients was reported. Most (64.1%) of the cases had minor trauma, but 19 (35.8%) had deep injuries. Nine (16.8%) patients developed tetanus after traffic accidents, two (3.8%) after an operation, one (1.9%) after a non-hygienic injection, two (3.8%) after compound fractures, two (3.8%) after septic abortion, two (3.8%) following non-hygienic delivery, and 35 (66%) after acute injury associated with foreign objects.

Thirteen (24.5%) patients had symptoms for >2 days before hospital admission, but only three patients had a period of <2 days between the first symptom and the first spasm. Most (79.2%) patients had generalised contractions, while 11 (20.7%) patients only had trismus on admission. However, six of these patients developed generalised contractions during the follow-up period.

The mean incubation period was 11.5 days (range: 2–40 days); 12 (22.6%) patients had an incubation period of ≤ 7 days, and 41 (77.3%) had an incubation period of >7 days. Eleven (20.7%) patients had head and neck injuries, 40 (75.5%) had injuries on extremities, and two (3.8%) had injuries on the torso. Before admission, 15 (28.3%) patients had received only one dose of tetanus vaccine, and 38 (71.7%) had not received primary tetanus vaccination. After trauma, tetanus immunisation was not administered to 32% of the patients. None received tetanus immunoglobulin at the time of trauma, but 43 (81.1%) received tetanus HIG (4000–10 000 U) on admission to hospital, while the remaining ten patients were given 60 000–100 000 U of anti-tetanus serum. Both groups of patients experienced similar mortality. During therapy, 22 (41.5%) patients had a tracheostomy, and seven (13.2%) were mechanically ventilated.

Among the total of 53 cases, 22.6% were mild, 52.8% were moderate, and 24.6% had severe clinical tetanus. Mild cases were given only sedation; moderate cases were given a tracheostomy plus sedation; and mechanical ventilation plus sedation was given to severe cases when generalised spasm was not controlled (7/13).

Nosocomial infection was seen in 14 (26.4%) patients. The fatality rate among all patients with tetanus was 52.8%. The causes of death were cardiac arrest in 16 patients, arrhythmia in two patients, respiratory failure in eight patients, and nosocomial infections in two patients. The relationship between mortality and prognostic factors for tetanus is shown in Table 1. Mortality was related to the length of the incubation period. The

Table 1. The relationship between mortality and prognostic factors for tetanus

		Fatality		
	Total (*n*)	***n***	**Rate (%)**	**p values**
Total number of patients	53	28	52.8	
Age (years)				
< 60	35	16	45.7	0.12
≥ 60	18	12	66.7	
Sex				
Male	28	17	60.7	0.17
Female	25	11	44	
Reasons for tetanus				
Post-traumatic	46	21	45.6	0.03
Post-surgery	7	7	100	
Place of wound				
Head or face	11	5	45.4	0.23
Extremities	40	21	52.5	
Trunk	2	2	100	
Incubation period				
≤ 7 day	12	9	75.6	0.07
> 7 day	41	19	46.3	
Patients who had received one dose of tetanus vaccine				
Yes	15	7	46.7	0.4
No	38	21	55.3	
Tetanus vaccine after trauma				
Yes	36	16	44.4	0.068
No	17	12	70.6	
Types of tetanus				
Generalised	48	28	58.3	0.00
Local	5	0	0	
Fever				
≥ 40 °C	26	19	73	0.006
< 40 °C	27	9	33.3	
Pulse				
≥ 120/min	31	22	71	0.002
< 120/min	22	6	27.3	
Nosocomial infection				
Yes	14	9	64.3	0.24
No	39	19	48.7	
Therapy				
Penicillin	40	19	47.5	0.14
Metronidazole	13	9	69.2	
Wood Prognostic Score				
0–1	12	1	8.3	0.000
2–3	28	15	53.6	Cochran –Armitage test
≥ 4	13	12	92.3	

fatality rate among cases with an incubation period of ≤7 days was higher (75%) than among the cases with an incubation period of >7 days (p 0.07). Mortality was significantly associated with generalised tetanus ($p < 0.05$), fever of ≥40 °C, tachycardia of >120 beats/min ($p < 0.05$), post-operative tetanus, post-injection tetanus, septic abortion (p 0.03), and the absence of post-trauma tetanus vaccination (p 0.068). Patients given tetanus HIG or tetanus antiserum showed similar outcomes ($p > 0.05$). Patients who were given penicillin had a fatality rate similar to that of patients who were given metronidazole (p 0.148). The fatality rate was higher among cases with severe tetanus (92%) than among moderate cases (53%). There was a trend in fatality rates as the Wood score increased; it was lower (8%) among patients with a score of 1, moderate (53%) among patients with a score of 2–3, and highest (92%) among patients with score of ≥4 ($p < 0.002$). The binary logistic model revealed that the existence of tachycardia and an age >60 years were simultaneously the most significant prognostic risk factors in relation to mortality among tetanus patients (Table 2).

DISCUSSION

The World Health Organisation has reported that tetanus is seen in one million people/year, and that >715 000/year die from tetanus or its complications [19]. Most cases of tetanus in developed countries occur among adults who were either not immunised or were immunised inadequately. Despite the higher rate of tetanus in men than in women in other studies [2,20,21], the patients in

Table 2. Results of binary logistic regression analysis, with fatality rate as a response variable

Variables	**Regression coefficient**	**Standard error**	**Significance (p)**	**Relative risk (RR)**	**95% CI for RR**	
					Lower	**Upper**
Age	1.707	0.840	0.042	5.513	1.062	28.629
Incubation period						
< 7 days	1.469	0.962	0.127	4.345	0.659	28.645
> 7 days (reference)				1.0		
Treatment with						
Metronidazole	1.371	0.815	0.092	3.939	0.798	19.440
Penicillin (reference)				1.0		
Tachycardia						
≥ 120/min	1.999	0.735	0.007	7.385	1.748	31.206
120/min (reference)				1.0		
Tetanus vaccine given after trauma						
No	1.015	0.761	0.183	2.759	0.621	12.267
Yes (reference)				1.0		
Constant	− 2.520	0.835	0.003	0.080		

CI, confidence interval.

the present study did not differ by gender, probably because most came from rural areas where women work as much as men in agricultural activities.

The incidence of tetanus depends on the social environment, season, climate and soil [22]. Tetanus can be seen in all seasons in the eastern Mediterranean region of Turkey, because of the sub-tropical climate and an agricultural society. The prognosis for tetanus depends on additional nosocomial infections, immunisation, other disease, disease severity, and delay in treatment [22]. Debridements and wound care after injury are also important for prevention of tetanus after injury, and this was not done properly for most of the cases in the present study. In other studies, the mortality rate ranges from 28% to 48% [21–23], but was 52.8% in the study reported here. Unlike other studies [2,7,21], no significant difference by gender was observed, and mortality rates did not differ significantly between those aged ≥60 years (67%) and those aged <60 years (46%; p 0.12), however, this might be a result of insufficient numbers of patients aged ≥60 years for comparison.

There is an important reported difference in the fatality rate among patients with an incubation period of <7 days compared to >7 days [21,24], and a similar observation was made in the present study (p 0.07). Mortality was high in patients with generalised tetanus, with high fever, or with tachycardia, and in patients who had developed tetanus after injection or surgery, with an incubation period of <7 days. Other studies have reported high mortality rates in patients with an incubation period of <7 days with generalised tetanus, as well as in those developing tetanus after abortion, post-injection, or with penetrating injuries [17,19,21]. Patients who were initially given tetanus antiserum or tetanus HIG did not show different mortality rates (p 0.2), which is similar to the findings of Patel and Mehtra [21]. It has also been reported that mortality is higher among patients given penicillin than among patients using metronidazole [25], but there was no difference in the present study.

The absence of primary immunisation is one of the most important risk factors in the development of tetanus. According to the Centers for Disease Control [2], 95% of affected patients have not completed primary immunisation, while the rest will have received no immunisation. When the immunity of the patients with tetanus in the present study was evaluated, absence of primary immunisation, or the administration of only one dose of vaccine, were among the most important mortality risk factors. In this study, there was no significant difference in mortality between those vaccinated with one dose and those never vaccinated (p 0.40), while 32% of the patients did not receive post-trauma tetanus vaccine because they did not attend a health centre after trauma had occurred. It has been shown in Turkey that 97.4% of patients who complete primary vaccination have antibodies 5 years after the last vaccine dose, compared with 53% of those with incomplete primary vaccination [26]. In another study, 20% of those aged >50 years were reported to have immunity against tetanus in Turkey [13]. In the present study, there was a trend towards increased mortality with an increasing Wood score, indicating a need to classify the severity and prognosis of disease on admission to hospital.

In conclusion, because of the high risk of death among patients, tetanus continues to be an important public health problem, even though it is preventable by vaccination. The Immunization Practices Advisory Committee of the Centers for Disease Control recommends a primary immunisation programme, with booster shots every 10 years [27]. The results of the present study suggest that there is insufficient adult immunisation and use of tetanus boosters in Turkey. As a result, it is essential that widespread campaigns of adult immunisation are started. In particular, those who live in rural areas should be well-informed and educated about the need to consult health service personnel after trauma because of the risk of developing tetanus.

REFERENCES

1. Weinstein L. Tetanus. *N Engl J Med* 1973; **289**: 1293–1296.
2. Richardson JP, Knight AL. The prevention of tetanus in the elderly. *Arch Intern Med* 1991; **151**: 1712–1716.
3. Wyszynski DF, Kechichian M. Outbreak of tetanus among elderly women treated with sheep cell therapy. *Clin Infect Dis* 1997; **24**: 738.
4. Gangrasso JG, Smith RK. Misuse of tetanus immunoprophylaxis in wound care. *Ann Emerg Med* 1985; **79**: 573–576.
5. Brand DA, Acampara D, Gottlieb LD. Adequacy of antitetanus prophylaxis in six hospital emergency rooms. *N Engl J Med* 1983; **309**: 636–640.

6. Sutter RW, Cochi SL, Brink EW, Sırotkin BI. *Am J Epidemiol* 1990; **131**: 132–141.
7. Jolliet P, Magnenat J-L, Kobel T, Chevrolet J-C. Aggressive intensive care treatment of very elderly patients with tetanus is justified. *Chest* 1990; **97**: 702–704.
8. Prevots R, Sutter RW, Sterbel PM, Cochi SL, Hadler S. Tetanus surveillance—United States, 1989–1990. *MMWR CDC Surveill Summ* 1992; **4**: 1–9.
9. Shroder JP, Kuhlmann WD. Tetanus immunity in man and women in the Federal Republic of Germany. *Immunol Infect* 1991; **19**: 14–17.
10. Gurkan F, Bosnak M, Dikici B *et al*. Neonatal tetanus: a continuing challenge in the southeast of Turkey: risk factors, clinical features and prognostic factors. *Eur J Epidemiol* 1999; **15**: 171–174.
11. Ozcebe H. The status of child health and child survival and development programs in Turkey. *Turk J Pediatr* 1998; **40**: 217–230.
12. Maral I, Baykan Z, Aksakal FN, Kayikcioglu F, Bumin MA. Tetanus immunization in pregnant women: evaluation of maternal tetanus vaccination status and factors affecting rate of vaccination coverage. *Public Health* 2001; **115**: 359–364.
13. Ural O, Fındık D. Investigation of tetanus antitoxin levels in some age groups with indirect hemagglutination. *Turk J Infect Dis Clin Microbiol* 1996; **1**: 31–35.
14. Crone NH, Reder AT. Severe tetanus in immunized patients with high anti-tetanus titers. *Neurology* 1992; **42**: 761–764.
15. Trujillo MH, Castillo A, Espana J, Guevara P, Eganez H. Tetanus in the adults: intensive care and management, experience with 233 cases. *Crit Care Med* 1980; **8**: 419–423.
16. Edmonston RS, Flowers MW. Intensive care in tetanus: management, complications, and mortality in 100 cases. *BMJ* 1979; **1**: 1401–1404.
17. Wood MJ. Toxin-mediated disorders: tetanus, botulism and diphtheria. In: Armstrong D, Cohen J, eds. *Infectious diseases*, 1st edn. London: Harcourt, 1999; 18.1–18.3.
18. Fleiss JL. *Statistical methods for rates and proportions*, 2nd edn. New York: Wiley, 1981.
19. Bleck TP. *Clostridium tetani* (tetanus). In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and practice of infectious diseases*, 5th edn. Philadelphia: Churchill Livingstone, 2000; 2537–2543.
20. Harding-Goldson HE, Hanna WJ. Tetanus: a recurring intensive care problem. *J Trop Med Hyg* 1995; **98**: 179–184.
21. Patel JC, Mehta BC. Tetanus: study of 8697 cases. *Indian J Med Sci* 1999; **53**: 393–401.
22. Sanders RK. The management of tetanus 1996. *Trop Doct* 1996; **26**: 107–115.
23. Sangalli M, Chierchini P, Aylward RB, Forastiere F. Tetanus: a rare but preventable cause of mortality among drug users and the elderly. *Eur J Epidemiol* 1996; **12**: 539–540.
24. Davies-Adetugbon AA, Torimiro SE, Ako-Nai KA. Prognostic factors in neonatal tetanus. *Trop Med Intern Health* 1998; **3**: 9–13.
25. Ahmadsyah I, Salim A. Treatment of tetanus: an open study to compare the efficacy of procaine penicillin and metronidazole. *BMJ* 1985; **291**: 648–650.
26. Atabey N, Gökoğlu M. The effect of period after tetanus vaccination on antitoxin levels. *Turk J Microbiol* 1992; **22**: 101–104.
27. Centers for Disease Control. Diphtheria, tetanus, pertussis: guidelines for vaccine prophylaxis and other preventive measures. *MMWR* 1985; **3**: 405–426.