

Predictors of mortality among adult tetanus patients in Northwestern Nigeria

¹LF Owolabi, ²AG Habib, ³M Nagoda

¹Neurology unit and ²Infectious disease unit, Department of Medicine, Aminu Kano Teaching Hospital, Bayero University Kano; ³Department of Medicine, Murtala Muhammad Specialist Hospital Kano, Nigeria

Abstract

Background & Objective: Tetanus remains an important health problem in Kano, Northwestern Nigeria. It is associated with a high mortality rate, it is therefore necessary to identify predictors of mortality with the view to reducing the mortality rate. **Methods:** Demographic and clinical data of all adult tetanus patients managed at Aminu Kano Teaching Hospital and Murtala Muhammad Specialist Hospital between Jan 2004 to Dec 2009 were collected and analyzed. **Results:** A total of 146 patients were identified during the study period, out of which complete information was obtained in 126 patients. All the patients had generalized tetanus. There were 93 (73.8%) males and 33 (26.2%) females. Their age ranged between 17 and 62 with mean age of 35.2. Two fifth (39%) of the patients were in the age group of 21 – 30 years. The risk factors of high mortality were: age >40 years, incubation period <48 hours, onset <48 hours, absence of previous tetanus immunization, evidence of autonomic dysfunction, and severity. Mortality was not related to fever and gender. Binary logistic model revealed that severity of tetanus at presentation was the most significant ($p= 0.029$) prognostic factor to mortality. **Conclusion:** The mortality rate of adult tetanus in Northwestern Nigeria is high. Several risk factors for high mortality have been identified.

INTRODUCTION

The World Health Organization has reported that tetanus is seen in one million people per year, and that more than 715,000 per year die from tetanus or its complications.¹ While incidence of tetanus and mortality from tetanus in the developed countries is on the downward trend^{2,3}, it remains a major cause of mortality in developing countries like Nigeria^{4,5}, in spite of the availability of cheap and effective vaccines. Tetanus remains an important health problem in Nigeria possibly because of the large number of traffic and work accidents, extensive agricultural activity, and abortion and / or delivery under non-hygienic conditions in addition to low vaccination rate. Moreover, adult tetanus is not uncommon in Nigeria because injured adults do not usually go to health facilities for tetanus prophylaxis. Published data reports of mortality, mostly from the health facilities in the Southern and Eastern part of Nigeria, ranged between 26% and 60%.^{4,5}

The facilities available to manage severe tetanus have a major impact on the therapeutic options and mortality. In the United Kingdom intensive care costs USD1,500–2,500/patient/

day⁶; such costs are clearly beyond the means of average patients in most of the regions of the world where tetanus is a major problem. Without facilities to artificially ventilate patients, airways obstruction, respiratory failure, and renal failure are the major contributory factors to poor outcome. Availability of artificial ventilation should prevent most deaths caused directly by acute respiratory failure even in very severe cases.⁶

Tetanus is still common among residents of Kano; it is the sixth most common cause of neurologic admissions at Aminu Kano Teaching Hospital (AKTH)⁷ and one of the most common cause of medical admission in Murtala Muhammad Specialist Hospital (MMSH). MMSH and AKTH are the two tertiary centres in Kano which is the most populous state in Nigeria.⁸ The two centres have a wide coverage area including the neighboring states in the Northwestern Nigeria.

In addition to limited availability of intensive care facilities, mortality from tetanus can be influenced by a patient's age, the incubation time, type of injury, clinical signs, and delays in treatment or prophylaxis.^{4,9,10} It is against this background that this study was designed to determine common predictive factors of deaths

from tetanus among adults in Northwestern Nigeria.

METHODS

Adults tetanus patients admitted into medical wards of AKTH and MMSH, (these two facilities have a wide coverage of states in the Northwestern Nigeria), from January 2004 to December 2009 were included in this 6-year analytical study. The study had retrospective (2004-2006) and prospective (2007-2009) arms. Diagnosis of tetanus was based on the presence of two or more of (i) trismus (ii) rigidity of the neck or abdominal muscle and (iii) spontaneous or reflex spasm. Patients with other apparent medical causes of these symptoms were excluded from the study. Pulse rate of < 60 or >100 per minute and Blood pressure of < 90/60 or >140/90 mmHg (in patients not previously hypertensive) were defined as abnormal. Details about age, sex, site and nature of wound, incubation period, period of onset, history of tetanus immunization, post-trauma tetanus prophylaxis, clinical signs, mode of treatment, complications, hospital stay, and outcome were entered in structured questionnaires. Ablett Severity Score was used for grading severity of tetanus.¹¹ Analysis was done using SPSS version 16. Categorical variables were compared using Chi square, scores on severity scale were compared using Chi-square for trend. Multivariate logistic regression models was also used to further identify predictive factors.

RESULTS

During the study period, a total of 146 patients were admitted in the two facilities, out of which

complete information was obtained in 126 patients, which was included in this study. All the patients had generalized tetanus, trismus and muscular rigidity. There were 93 (73.8%) males and 33 (26.2%) females. The age ranged between 17 and 62 years with mean age of 35.2 years (s.d = 1.3 years). About two fifths (39%) of the patients were between 21 and 30 years old. The majority (73.8%) of the patients was between the ages of 20 and 50 years. The largest occupation group was farmer 64 (50.8%), followed by artisan 32 (25.4%), housewife 8 (6.3%), unemployed 9 (7.1%), civil servant 6 (4.3%), student 4 (3.2%), and trader 3 (2.4%). Portal of entry was not identifiable in 37 (29.4%) patients. The most common portal of entry was leg wound (cuts, lacerations, ulcers, punctures) and most of the injuries were farm work related. Sixty two (49%) patients historically had tetanus vaccination, significantly more (81%) were below 40 years of age (p=0.001). Incubation period was less than 48 hours in 46 (51.7%) of the 89 patients with identifiable portal of entry. The onset was less than 48 hours in 64 (50.8%) patients. Drugs used in the treatment of tetanus included metronidazole, antitetanus serum, diazepam and chlorpromazine. Only 55 (43.7%) patients had diazepam regularly. Only 3 (2.4%) patients were managed in Intensive Care Unit. Sixty eight (54%) patients survived and overall mortality rate was 46%. Table 1 showed significantly worse outcome for those with more severe disease (chi-square for trend, p<0.001). The hospital stay was between 1 - 6 days for all the patients who died. The majority (97%) of those who survived stayed in hospital for more than 8 days.

Table 1: Distribution of outcome of the patients by severity of tetanus at presentation

Grade*	Total	Outcome		Case fatality rate
		Survived	Died	
Mild	57	54	3	5.3
Moderate	17	8	9	52.9
Severe	39	5	34	87.2
Very severe	13	1	12	92.3
Total	126	68	58	

X² for linear trend = 71.303; p value = 0.001

*Grade by Ablett Severity Score

The relationship between mortality and prognostic indicators for tetanus is shown in Table 2. Higher mortality rate is significantly associated with age >40 years, incubation period <48 hours, period of onset <48 hours, absence of previous tetanus immunization, autonomic dysfunction with abnormal pulse or blood pressure, and more severe disease according to Ablett Severity Score. There was no significant

association of increased mortality with fever and gender. The mortality rate increased from mild tetanus (5.3%), moderate (53%), severe (87.2%) to very severe tetanus at 92.3% (Table 1). The binary logistic model including all the identified risk factors as covariates revealed that the severity of tetanus at presentation was the most significant (p= 0.029) prognostic risk factor in mortality.

Table 2: The relationship between mortality and prognostic indicators for tetanus

Factors	Proportion of patients who died		P value
	Proportion	%	
Age			
<40	22/74	29.7	p=0.009
>40	36/52	69.2	
Sex			
Male	39/87	44.8	NS
Female	19/39	48.7	
Incubation period*			
<48 hrs	41/46	89.1	p=0.001
>48 hrs	4/43	9.3	
Period of onset*			
<48 hrs	54/64	84.4	p=0.001
>48 hrs	4/62	6.5	
Previous tetanus immunization			
Yes	26/62	41.9	p=0.037
No	32/38	84.2	
Presence of autonomic dysfunction			
-Pulse			
Abnormal	49/57	86.0	p=0.009
Normal	9/69	13.0	
-Blood pressure			
Abnormal	22/29	75.9	p=0.036
Normal	36/97	37.1	
Fever			
Yes	38/73	52.1	NS
No	20/53	37.7	
Patient had diazepam**			
Yes	4/54	7.4	p=0.001
No	30/34	88.2	
Presence of co-morbidities			
Yes	17/19	89.5	NS
No	41/66	62.1	
Severity***			X ² for trend=76.25; p = 0.001

Notes: NS: Statistically not significant

*Incubation period is period from injury to first symptom. Period of onset is the duration of time between first symptom and occurrence of spasm, it does not reflect delay in seeking medical care.

** Regularly or adequately

*** See Table 1

DISCUSSION

Despite the availability of passive immunization since 1893 and an effective active vaccination since 1923, tetanus remains a major health problem in the developing countries. The mortality rate of tetanus in our series was 46%. This figure is higher than that obtained in some studies outside Africa.^{12,13} 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 this study is comparable with that obtained in other studies in Nigeria and Africa. Earlier study in the Southwestern Nigeria reported mortality rate of 44%^{14,15}, 42.9% in the middle belt of Nigeria⁴, and 36.96 in Lagos.¹⁶ In Ghana, mortality rate of 72.7% was reported by Hesse *et al*¹⁷, and 72.72% in Dare Es Salaam, Tanzania by Mabula and Victor.¹⁸

In this study, frequency of tetanus was higher among the males. A similar finding had been reported in studies from elsewhere.^{4,15,17} This may reflect the low vaccination rates among males in the community compared to their female counterparts who often get vaccinated during pregnancy. In addition, men tend to attend hospital more than the women in the studied community as wives often require the consents of their husbands to go to hospital. Moreover, involvement of males in jobs like farming with greater vulnerability to injury may also partly account for male preponderance in this study.

The majority (73.8%) of the patients in the present study was between the ages of 20 and 50 years. This age group constitutes the working force of the society. This trend, which has also been reported elsewhere¹⁸, has a great socioeconomic implication on the society. In this study, farmers accounted for 50.8% of the patients. Farming is the major occupation in Northwestern Nigeria. 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. This finding is similar to those of earlier studies in other parts of Nigeria.^{4,15,16} However, study from Port Harcourt (Nigeria's oil industry hub), where majority of the work force is engaged in the oil industry where safety measures are accorded high priority, have reported the predominance of students and civil servants among their tetanus patients.⁴

In our study, only about half (49%) of the

patients historically had tetanus vaccination. Among those vaccinated, only 19% were 40 years and above. We have also shown that the mortality rate is much higher in those above 40 yrs of age. The low rate of tetanus immunization may partly account for the higher mortality among those age 40 years and above. 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.¹⁹ Diminished levels of circulating antibodies to tetanus may be another factor for higher mortality in the older age group among our patients.

Significantly higher mortality rate was recorded in our patients with incubation period < 2 days, and onset of less than 2 days. Some studies have noted the differential mortality rate noticeable at 7 days of incubation period.^{4,20-22} Increased mortality among those with onset of less than 2 days has also been noted in other studies.^{22,23}

Mortality was also significantly higher in patients with autonomic dysfunction. The autonomic dysfunction noted in these studies included sinus tachycardia, bradycardia and diaphoresis. It is worth noting that our study is limited by paucity of hemodynamic and autonomic monitoring. Although autonomic instability has been recognized as a major complication in the post ventilator era, this phenomenon has been known since 1960s²⁴ and reported to occur in about a third of the patients.²⁵ An electrocardiographic study from India showed the incidence of sinus tachycardia as high as 85%.²⁶ Pathogenesis of autonomic disturbances is not well understood. Several theories have been put forward, including damage to brain stem and hypothalamic nuclei²⁷ and direct disturbances in autonomic nerves.^{27,28} Careful hemodynamic monitoring and cautious and judicious use of fluids and drugs like beta blockers, atropine may improve outcome in these patients.²⁹

Inadequacy or irregularity of diazepam use was another factor associated with high mortality in this study. Fever was not found to significantly affect the outcome, this finding corroborate some of the earlier studies.⁴ However, there were studies that reported fever as a prognostic factor in tetanus.^{22,23}

Other studies have reported high mortality rates in patients with generalized tetanus, as well as in those developing tetanus after abortion, post-injection, or with penetrating injuries.^{22,23}

It has also been reported that mortality is

higher among patients given penicillin than among patients using metronidazole.^{30,31} In this study, all the patients had metronidazole. In the present study, the most significant prognostic factors for high mortality was severity of disease. Saltoglu *et al* reported age > 60 yrs and severity of disease as the most significant risk factors in tetanus in Turkey.²² Hopefully identification of risk factors for high mortality may guide physicians to improve the care of the patients, and thus reduce the mortality.

In conclusion, the overall mortality rate of adult tetanus in Northwestern Nigeria is high. Older age, short incubation period, short period of onset, lack of tetanus immunization, presence of autonomic complications, and most importantly severity of tetanus on admission are factors associated with high mortality identified in this study.

REFERENCES

- Bleck TP. Clostridium tetani (tetanus). In: Mandell GL Bennett JE, Dolin R, eds: Principles and practice of infectious diseases, 5th ed. Philadelphia: Churchill Livingstone, 2000; 2537-43.
- 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; 332:761-6.
- Sanford JP. Tetanus - Forgotten but not gone. *N Engl J Med* 1995; 332:812-3.
- Onwuchekwa AC, Asekomeh EG. A 10-year review of outcome of management of tetanus in adults at a Nigerian tertiary hospital. *Annals of African Med* 2009; 8:168-72.
- Bandele EO, Akinyanju OO, Bojuwoye BJ. An analysis of tetanus deaths in Lagos. *J Natl Med Assoc* 1991; 83(1):55-8.
- Bennett D, Bion J. Organisation of intensive care. *BMJ* 1999; 318:1468-70.
- Owolabi L.F, Shehu M.Y, Shehu M.N, Fadare J. Pattern of neurological admissions in the tropics: Experience at Kano, Northwestern Nigeria. *Annals of Indian Academy of Neurology* 2010; 13(3):167-70.
- National Population Commission. List of Nigerian State by Population. Federal republic of Nigeria Census 2006 Census. 2006
- Farrar J.J, Yen L.M, Cook T, *et al*. Tetanus. *J Neurol Neurosurg Psychiatry* 2000; 69: 292-301.
- Ogunrin OA, Unuigbo EI. Tetanus: an analysis of the prognosticating factors of cases seen in a tertiary hospital in a developing African country between 1990 and 2000. *Trop Doct* 2004; 34(4):240-1.
- Ablett JLL, Analysis and main experiences in 82 patients treated in the Leeds Tetanus Unit: Symposium on tetanus in the Leeds Tetanus in Great Britain, Boston Spa, UK National Lending Library (1967).
- Lau LG, Kong KO, Chew PH. A ten year retrospective study of tetanus at a General Hospital in Malaysia. *Singapore Med J*. 2001; 42(8):346-50.
- Harding-Goldson HE, Hanna WJ. Tetanus: a recurring intensive care problem. *J Trop Med Hyg* 1995; 98:179-84.
- Oladiran I, Meier DE, Ojelade AA, OlaOlorun DA, Adeniran A, Tarpley JL. Tetanus: continuing problem in the developing world. *World J Surg* 2002; 26(10):1282-5.
- Arogundade FA, Bello IS, Kuteyi EA, Akinsola A. Patterns of presentation and mortality in tetanus: a 10-year retrospective review. *Niger Postgrad Med J* 2004; 11(1):58-63.
- Ojini FI, Danesi MA. Mortality of tetanus at the Lagos University Teaching Hospital, Nigeria. *Trop Doct* 2005; 35(3):178-81.
- Hesse IF, Mensah A, Asante DK, Lartey M, Neequaye A. Adult tetanus in Accra, why the high mortality? An audit of clinical management of tetanus. *West Afr J Med* 2005; 24(2):157-61.
- Mabula DM, Victor M. Tetanus and its treatment in Dar Es Sallam: Need for male vaccination. *East Afr J Publ Health* 2005; 2(2): 22-3.
- Gergen PJ, McQuillan G, 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; 332:761-6.
- Richardson JP, Knight AL. The prevention of tetanus in the elderly. *Arch Intern Med* 1991; 151:1712-6.
- Jolliet P, Magnenat JL, Kobel T, Chevolet JC. Aggressive intensive care treatment of very elderly patients with tetanus is justified. *Chest* 1990; 97:702-4.
- Saltoglu N, Tasova Y, Midikli D, Burgut R, Dundar IH. Prognostic factors affecting deaths from adult tetanus. *Clin Microbiol Infect* 2004; 10:229-33.
- Patel JC, Mehta BC. Tetanus: study of 8697 cases. *Indian J Med Sci* 1999; 53:393-401.
- Kerr JH, Corbett JL, Prys-Roberts C, Smith AC, Spalding JMK. Involvement of the sympathetic nervous system in tetanus. *Lancet* 1968; 2:236-41.
- Ablett JLL. Analysis and main experience in 82 patients treated in the Leeds tetanus unit. In: Ellis M, ed: *Symposium on tetanus in Great Britain*. Boston Spa, UK: National Lending Library; 1967:1-10.
- Mitra RC, Gupta RD, Sack RB. Electrocardiographic changes in tetanus: a serial study. *J Indian Med Assoc* 1991; 89:164-7.
- Cook TM, Protheroe RT, Handel JM. Tetanus: a review of the literature. *Br J Anaesth* 2001; 87:477-87.
- Udwadia FE, Sunavala JD, Jain MC, *et al*. Haemodynamic studies during the management of severe tetanus. *Q J Med* 1992; 83:449-60.
- Mohammad W, Bhojo A K, Naasha T, Rohmah S, Nadir A S, Naseem S. Autonomic nervous system dysfunction predicts poor prognosis in patients with mild to moderate tetanus. *BMC Neurology* 2005; 5:2.
- Wood MJ. Toxin-mediated disorders: tetanus, botulism and diphtheria. In: Armstrong D, Cohen J, eds. *Infectious diseases*, 1st ed. London: Harcourt, 1999; 18.1-18.3.
- Ahmadasyah I, Salim A. Treatment of tetanus: an open study to compare the efficacy of procaine penicillin and metronidazole. *BMJ* 1985; 291:648-50.