



Characteristics and outcome of tetanus in adolescent and adult patients admitted to the Lagos University Teaching Hospital between 2000 and 2009

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ABSTRACT

This study was a case record review of adult patients with tetanus admitted into Lagos University Teaching Hospital between 2000 and 2009. Of 78,009 adults admitted, 190 had tetanus, constituting 0.25% of admission. Mean age was 30.4 ± 13.8 years. Male to female ratio was 3:1. The commonest occupation was commercial motorcyclists. 96% of the patients were unimmunized and 4% that had partial immunization had localized tetanus. Commonest presentation was trismus (83%). Twenty three patients had complications, 30% had autonomic dysfunction. Mean incubation period was 11.4 ± 4.8 days, and mean duration of onset was 72 ± 45.6 h. 31 patients died, case fatality rate was 16.3%. Twelve percent of those with long period of onset died while 43% with short period of onset died ($P = 0.002$). Patients with complications (78%) died of tetanus while only 8% of those without complication died ($P < 0.0001$).

Case fatality rate is still unacceptably high for a vaccine preventable disease. Attention to primary prevention of people at risk and active surveillance to prevent complications will further reduce mortality.

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1. Introduction

Tetanus is caused by tetanospasmin, a neurotoxin secreted by *Clostridium tetani*, which is a spore forming gram-positive, obligate anaerobic rod-shaped motile bacillus. The organism is ubiquitously distributed in the environment, and can be found in the intestinal flora of domestic animals and humans. The spore form is resilient and can survive in soil for months to years [1]. Following wound contamination and spore germination, tetanospasmin is produced. Inside the motor neurons, tetanus toxin is transported to the central nervous system by a specific retrograde axonal transport system. At the level of the spinal cord and brainstem, the toxin diffuses across synaptic spaces to enter the inhibitory interneurons.

Inside the inhibitory interneurons, the disulfide bond connecting the heavy and light chains of the toxin is broken. The freed light chain is a zinc-endopeptidase that cleaves synaptobrevin protein in synaptic vesicle membrane. Synaptobrevin is essential for the fusion of the synaptic vesicles to the presynaptic nerve membrane; when this process is disrupted, synaptic vesicles accumulate at the nerve ending and are unable to release neurotransmitter into adjacent synaptic space. The action of inhibitory neuron is thereby impeded, leaving α motor neuron excitation unopposed, resulting muscle

rigidity and longstanding painful spasms which are characteristic of tetanus.

The incubation period is usually 3–21 days [2] and tetanus is characterized by painful muscle spasm, increased muscle tone (rigidity) and in severe cases, cardiovascular instability caused by autonomic dysfunction.

The specific objectives of tetanus treatment are to stop the production of toxin at the site of infection by eliminating the organism through wound debridement and appropriate antibiotics e.g. metronidazole; to neutralize circulating toxin with human or equine tetanus immunoglobulin; and to provide effective management of muscle spasms with diazepam and treatment of autonomic dysfunction and other complications that arise during the course of illness.

Tetanus, a vaccine preventable disease (by active immunization of children, women of child bearing age and adults at risk) is an important cause of hospital admission and death in developing countries [3]. Despite the availability of passive immunization since 1893 and effective active immunization since 1923, tetanus still accounts for 1 million hospital admissions every year and about 400,000 deaths worldwide [4,5]; 80% of these deaths occur in Africa and Southeast Asia [6]. In Nigeria, mortality from adult tetanus ranges between 30% and 70% [3,7]. Previous studies in this center reported the case fatality to be between 30 and 48% [3,8].

The aim of this present study was to review the characteristics, complications and case fatality of tetanus among adolescents and adults admitted to Lagos University Teaching Hospital (LUTH) between 2000 and 2009.

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2. Materials and methods

2.1. Study type

This study was a retrospective descriptive study (case record review) of tetanus cases seen from January 2000 to December 2009.

2.2. Patients

Lagos University Teaching Hospital is a referral tertiary center for all the hospitals in Lagos and its environs. All adult tetanus cases with diagnosis of tetanus between January 2000 and December 2009 were included in the study.

2.3. Inclusion criteria

1. Adults ≥ 12 years with tetanus
2. Hospitalization dates from January 2000 to December 2009
3. Case records available for review

Records of all patients admitted to LUTH via accident and emergency (A&E) and intensive care unit with diagnosis of tetanus were included. Data were extracted from multiple sources including case records, ward and emergency room records and death certificates.

2.4. Diagnostic criteria

1. Trismus
2. Muscular rigidity
3. Spasms
4. With or without autonomic involvement

Tetanus was then classified into localized and generalized tetanus depending on extent of rigidity or/and spasm from the limb bearing the wound.

2.5. Data extraction

Demographic and clinical parameters including name, age, occupation, sex, presenting complaint, incubation period, period of onset, duration of hospitalization, immunization status and primary outcome at the time of discharge (dead or survived) were extracted from records using a structured questionnaire.

Mean period of onset was classified into long and short periods of onset. Short period of onset was defined as patient with period of onset of 24 h or less, while long period was more than 24 h.

3. Data analysis

Data were analyzed using SPSS 17.0 for Windows®. Continuous variables were compared by Student's *t* test. Proportions were analyzed with chi-square test, Fisher's exact test and a *P*-value of 0.05 or less was considered statistically significant. Multiple logistic regression analysis was used to explore relationships among tetanus variables.

4. Results

A total of 197 adolescent and adult patients (age range 12–78 years) were hospitalized with tetanus from January 2000 to December 2009. The total number of hospital admissions over the same period was 78,009. Tetanus accounted for 0.25% of the hospital admissions.

Of the 197 patients admitted with diagnosis of tetanus, 7 (3.6%) were excluded because of insufficient data, leaving 190 records for analysis.

One hundred and eighty three (96.3%) patients were admitted in a specialized tetanus bay in male medical ward of the hospital, while only seven (3.7%) were admitted in the ICU.

4.1. Gender

Of the 190 tetanus patients, there were 46 (24.2%) females and 144 (75.8%) males, giving a male:female ratio of 3:1.

4.2. Age

The mean age of patients with tetanus was 30.4 ± 13.8 years (range 12–78). The mean age for male was 31.5 ± 13.4 years (range 12–78) and for female (range 12–78) was 27.2 ± 14.6 years ($P=0.07$). See Table 1 for age distribution.

4.3. Occupation

One hundred and thirty seven of 190 (72.1%) patients had their form of occupation documented. Commercial motorcyclists constituted about 29.9% (41) of the reported cases. Others were students 13.9% ($n=19$), traders 11.9% ($n=17$), farmers 11.9% ($n=16$), unemployed 9.5% ($n=13$) and others 22.6% ($n=31$). There was no documentation for 53 patients.

4.4. Portal of entry

History of injury was reported in 179 (94.2%) patients while 11 (5.8%) patients had no history of injury. Of those with history of injury, the portal of entry were wounds in lower limbs in 124 (69.3%) cases, others (29.1%) involved wounds on the hands and heads, 2 (1%) of cases were postabortal and one (0.6%) case from chronic otitis media.

4.5. Type of tetanus

One hundred and eighty four (96.8%) had generalized tetanus, while 6 (3.2%) patients had localized tetanus, of which one was of cephalic type.

4.6. Mode of presentation

The commonest presentation was trismus which accounted for about 83% of presenting symptoms. Other symptoms were neck pain (67%), muscle spasm (43%), body stiffness (19%) and dysphagia (7%).

4.7. Incubation/period of onset

Only 179 patients had documentation on incubation period. The mean incubation period was 11.4 ± 4.8 days (range 3–24); while the mean period of onset was 72 ± 45.6 h (range 24–288).

4.8. Immunization status

One hundred and seventy five of 190 (92.1%) patients had their immunization status documented in the case note. Only 11 (4%) had

Table 1
Age distribution of tetanus patients.

Variables	n (N = 190)	%
Age groups (years)		
10–19	40	21.0
20–29	69	36.3
30–39	42	22.1
40–49	20	10.5
50–59	6	3.2
≥ 60	13	6.8
Total	190	100

at least one dose of tetanus toxoid in the past and 164 (96%) had no immunization in their lifetime.

4.9. Complications

Complications were documented in 23 (12.1%) patients. The commonest complications were autonomic dysfunctions and laryngeal spasm. Thirty percent had autonomic dysfunction, 26% had laryngeal spasm, 13% had deep venous thrombosis, 9% had Wernicke's encephalopathy and another 9% had sepsis. Table 2 shows the pattern of complications.

4.10. Case fatality rate (CFR)

Of the 190 patients admitted and managed for tetanus, 31 patients died of tetanus. Thus, the overall case fatality rate of tetanus for the period under review was 16.3%. Table 3 summarizes CFR by different age groups.

4.11. Determinants of outcome in tetanus

The determinants of outcome in this review were short period of onset (P = 0.02) and presence of complications (P < 0.001) (Table 4). Multivariate analysis was performed using outcome (death or discharged) as the dependent variable and age (≥40 years), gender (male, female), presence of complications, period of onset (≤24 h) and incubation period (≤7 days) as possible determinants of outcome. Presence of complications (P < 0.001) and period of onset (P = 0.04) were the independent predictors of outcome (Table 5).

5. Discussion

This 10-year review of tetanus admissions provides important data on outcome of tetanus in our center. One hundred and ninety patients were admitted and managed for tetanus in the last decade from our center giving 0.25% of total hospital admissions.

Most of the patients admitted for tetanus in this review were below forty years old; more than three quarters of the tetanus patients were less than 40 years of age. This finding is consistent with previous studies from Nigeria. Ojini et al. [9] and Onwuchekwa et al. [10] reported 75% of the patients with tetanus being less than 40 years old. Also study from Ethiopia by Ramos et al. [11] reported more cases of tetanus in the young adults. This is in contrast to findings from developed countries like Europe and North America, where the incidence of tetanus was higher among the elderly people, who had waning immunity [12]. The high occurrence of tetanus in the younger age group may reflect poor tetanus immunization program and non utilization among these people in developing countries, who are at risk of tetanus.

This review showed a male predominance resulting in a mean ratio of 3:1 regarding male to female incidence. The gender distribution in our review is consistent with other studies. Ojini et al. [9] from this center reported 66% in males and Arogundade et al. [13] reported 75% males in Ife. This is partly due to increased exposure by men to activities which have greater risk to injury than females. Other

Table 2
Complications of tetanus cases seen in LUTH.

Complications	No. of cases	%
Autonomic dysfunction	7	30.4
Laryngeal spasm	6	26.1
Deep venous thrombosis	3	13.0
Wernicke's encephalopathy	2	8.7
Sepsis	2	8.7
Others	3	13
Total	23	100

Table 3
Case fatality rates (CFRs) of tetanus in different age groups.

Age groups	No. in age group	No. of deaths	CFR (%)
10–19	40	5	12.5
20–29	69	14	20.9
30–39	42	7	16.7
40–49	20	3	15
50–59	6	0	0
≥60	13	2	15.4

possible reason is that females are likely to have been immunized against tetanus during pregnancy. Some authors have also suggested that there may be biological factors; males may be more sensitive to tetanus toxin than are females [14], but this is not likely.

Only 7 (4%) of the patients under review had at least one dose of immunization in their lifetime. Out of which six had local tetanus. It is of interest to note that 6 out of the 7 who had partial immunization were females. This could be attributed to better immunization program for women during antenatal care. The reason for low immunization coverage could be attributed to unawareness of the vaccine availability and utilization by the people at risk. There is need for mass education of the populace especially the people at risk of tetanus.

Interestingly, we also observed that motorcycling was the commonest form of occupation in our patients admitted for tetanus in this center over the last 10 years, which is not in agreement with previous studies from our center and other centers in Nigeria. Afonja et al. [7] and Bandele et al. [8] reported tetanus to be most frequent among students, while Arogundade et al. [13] reported farming as the commonest occupation in Ife. This could be attributed to the metropolitan nature of the city where most young people are engaged in commercial motor cycling as an occupation rather than farming. The importance of this finding is that compulsory immunization could be enforced on this group of people by policy makers to augment immunization program for children and mothers.

The most common presentation of tetanus in this review was trismus which is similar to most other studies [9,13]. Other forms of presentations include dysphagia, neck stiffness and muscle spasms.

With regard to complications, autonomic dysfunction, laryngospasm and deep vein thrombosis (DVT) were the most common complications. Previous studies have documented autonomic dysfunction and laryngospasm as major complications [9,10] in tetanus patients but only few studies reported DVT as a complication of tetanus. To improve mortality in our center we anticipate those patients that will develop laryngospasm and do tracheostomy, manage autonomic

Table 4
Determinants of outcome in tetanus.

Variables	Total (N = 190)	Dead (n = 31)	%	P
Gender				
Male	144	24	16.7	0.82
Female	46	7	15.2	
Age				
<40 years	151	26	17.2	0.51
>40 years	39	5	12.8	
Type of tetanus				
Generalized	184	30	16.3	0.05
Localized	6	1	16.7	
Incubation period*				
Short (≤7 days)	103	19	18.4	0.20
Long (>7 days)	76	12	15.8	
Period of onset**				
Long (>24 h)	156	19	12.2	0.02
Short (≤24 h)	14	6	42.9	
Complications				
No complication	167	13	7.8	0.000
Complications	23	18	78.3	

* N = 179.
** N = 170, n = 25.

Table 5
Multivariate logistic regression analysis to explore determinants of outcome in tetanus.

Parameters	Odds ratio	95% confidence interval		P values
		Lower	Upper	
Age (≥ 40 years)	0.66	0.14	3.01	0.60
Gender	1.52	0.50	4.65	0.46
Incubation period (≥ 7 days)	2.11	0.12	24.97	0.70
Period of onset (≤ 24 h)	0.27	0.08	0.94	0.04
Presence of complications	0.02	0.00	0.07	0.00

Dependent variable – outcome.

dysfunction aggressively and provide DVT prophylaxis in patients with additional risk factors for DVT. About 9% of our patients developed gait ataxia and confusion (Wernicke's encephalopathy) during recovery phase of the illness, after a long period of intravenous glucose infusion while on nil per oral (NPO). These symptoms resolved completely after administration of parenteral thiamine. Bandele et al. [8] reported similar complications in 15% of patients. The possible explanation for this manifestation could be thiamine deficiency precipitated by prolonged glucose infusion in people with borderline thiamine, and since most of these patients were in low socio-economic class. We now routinely add thiamine to glucose infusion for all our tetanus patients while on NPO; since commencement of this, no such complication has occurred.

The current mortality figure of 16.3% found in this review is lower than 33% reported by Ojini et al. [9] from 1990 to 1999 and 48% reported by Bandele [8] in this center between 1974 and 1984.

Moreover, the CFR in our center is also lower than other centers in Nigeria. Ajose et al. [3] reported a CFR of 70% from Lagos State University Teaching hospital in a recent review. Arogundade et al. [13] from Ife reported a CFR of 53.5% and Onwuchekwa et al. [10] reported CFR of 42.9% from Port Harcourt. The reason for lower mortality rate in our center was that the Neurology unit adopted a protocol driven management based on patho-physiology of tetanus designed to anticipate complications, and to provide prevention and early treatment of such complications.

Factors that influenced outcome of tetanus in this study were period of onset and presence of complications. The shorter the period of onset, the worse the outcome and this is similar to previous studies [8,15].

Presence of complications was also associated with poor outcome in our study, most (78%) patients with complications died of tetanus.

This is consistent with previous studies [3,15]. Therefore, prevention and early treatment of complications will reduce mortality.

In conclusion, this review showed that CFR of tetanus has reduced in our center; attention to primary prevention via increased public awareness on immunization especially among the motorcyclists should be desired. Presence of complications was associated with higher mortality; hence, prevention and early treatment of complications will further reduce mortality associated with tetanus.

Conflict of interest statement

The author and the co-authors have no conflict of interest to declare.

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