Tetanus in adults: Clinical presentation, treatment and predictors of mortality in a tertiary hospital in Ethiopia

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ABSTRACT

Background: Tetanus remains a major health problem in the developing world. The aim of this study was to evaluate the clinical presentation, risk factors, complications, treatment, outcome and predictors of death in patients with tetanus.
Methods: Patients aged ≥13 years admitted to Tikur Anbessa Hospital from June 2001 to May 2009 with the diagnosis of tetanus were included in this retrospective study.
Results: Data from 68 patients were analyzed; majority (77.9%) were males, the mean age was 33.8 years. None of them was vaccinated for tetanus. The types were: generalized (91.2%), cephalic (7.4%), localized (1.5%), severe (72.1%), moderate (19.1%) and mild (8.8%). One or more complication(s) occurred in 75%; dysautonomia (58.8%), pneumonia (44.1%) and hypoxemia (41.2%). Tracheostomy and mechanical ventilation was used in 45.6% and 11.8%, respectively. Case-fatality was 35.3%. Predictors of mortality were age ≥40 years, duration of symptoms prior to presentation <4 days, severe tetanus, incubation period <7 days, period of onset <3 days and dysautonomia. The cause of death was early acute respiratory failure due to uncontrolled spasms in 87.5%.
Conclusions: Most tetanus patients were young males and there was high case fatality due to acute respiratory failure. Age ≥40 years and dysautonomia were independent predictors of mortality. Preventing tetanus by vaccination and treating patients in a well equipped ICU is recommended.

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1. Introduction

Though tetanus is an uncommon disease in the developed world due to effective vaccination coverage [1–6] it remains one of the major health problems in the developing world [7]. In the former tetanus occurs mainly in the older adults [5,6] while in the latter it occurs mainly in neonates and young adults because of inadequate vaccination coverage and preventive measures after sustaining an injury [7]. Most tetanus cases and deaths occur in Sub-Saharan Africa, and 40% of them are manifested as neonatal tetanus [7]. Lack of clean delivery is an important risk factor for neonatal tetanus. Tetanus is a severe disease associated with a high mortality which varies from 15% to 72.2% [3,4,8–24] depending on the available treatment facilities. Treating tetanus patients in intensive care unit (ICU) improves the survival rate [23]. Poor prognostic factors that have been observed in tetanus patients include: older age, short incubation period and period of onset, severe and generalized types, dysautonomia, pneumonia, sepsis, hypoxemia and renal failure.

There are limited studies done in adult tetanus patients in Ethiopia. Hadgu et al. [14] in 1975 studied tetanus patients admitted to three different hospitals in Addis Ababa and found case-fatality of 35.9% for patient's aged ≥11 years. Hodes and Teferedegn [15] in 1990 analyzed 55 cases from six different hospitals in the same city and found a mortality of 27%.

This study was designed to evaluate the clinical presentation, risk factors, complications, treatment, outcome and predictors of death in patients with tetanus who presented to Tikur Anbessa Hospital (TAH), the main teaching hospital of Addis Ababa University. TAH is a 626-bedded referral general hospital of the country which serves about 22,000 inpatients and 160,000 outpatients per year.

2. Methods

Patients aged ≥13 years admitted to TAH from June 2001 to May 2009 with the diagnosis of tetanus were included in this retrospective study. The study was started after getting ethical approval from the Faculty of Medicine Research and Publications Committee. Confidentiality was assured by assigning each patient record a unique number. Clinical records were searched manually and datasheet was used to collect the following data: age, gender, address, occupation, risk factor,

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type and duration of presenting symptoms, duration of hospital stay, physical findings, laboratory investigations, complication(s), treatment, outcome at hospital discharge and cause of death. Incubation period (time from injury to the appearance of symptom) and period of onset (interval between the first symptoms and the first spasm) was determined. Tetanus was classified into generalized, cephalic and localized types. The severity of tetanus was classified into mild, moderate and severe [25]. The diagnosis of dysautonomia was made when two or more of the following were fulfilled [22]. Labile blood pressure 2. High fever in the absence of infection 3. Tachycardia/dysrhythmia in the absence of fever 4. Sudden diaphoresis in the absence of fever. Hypoxemia was defined as arterial oxygen saturation (SaO_2) of <90% using pulse oximetry (arterial blood gas analysis was not available).

The data were analyzed using SPSS 13.0 for Windows (SPSS, Chicago IL, U.S.A). Logistic regression was used to assess each possible prognostic factor. Odds ratios and significance levels were calculated along with 95% confidence intervals. A p-value of less than 0.05 was considered significant. A multivariate logistic regression analysis was performed to determine which prognostic factors, when considered together, were the best predictors of hospital death. The independent sample t-test was used to compare continuous variables with normal distribution.

3. Results

Data from 68 patients with tetanus were analyzed. There were 53 male (77.9%) and 15 female (22.1%) patients. The mean age was 33.8 years (range 14–85). The majority of patients (88.2%) were ≤50 years old and the peak was in the age group 21–30 years (32.4%). The mean age of males and females was 30.5 and 45.4 years, respectively (p-value = 0.01). Forty-seven (69.1%) patients were from Addis Ababa. The incidence showed seasonal variations: Sep–Nov = 24 (35.3%), Jun–Aug = 19 (27.9%), Mar–May = 16 (23.5%) and Dec–Feb = 9 (13.2%). The June to November admissions were higher compared to the December to May admissions (OR = 2.96, 95% CI = 1.46–6.05). The occupation of patients was known in 56 (82.4%) and there were 24 (42.9%) daily laborer and 14 (25%) farmers. Forty-four (79.4%) patients were admitted to the medical ICU. The mean hospital stay for patients discharged cured was 30.3 days (range 9–71).

The initial symptom was: lockjaw (n = 57, 83.8%), neck pain/stiffness (n = 4), back pain (n = 3), abdominal pain (n = 2), rigidity of the extremities (n = 1) and dysphagia (n = 1). The mean and median duration of the initial symptom prior to presentation were 6.7 and 4 days, respectively. The range was 149.8 days (4 h–150 days) (one patient had duration of lockjaw of 5 months). Identifiable risk factors were present in 61 (89.7%) patients. Recent trauma was noted in 49 (72.1%) patients which consisted of: metallic injury (n = 19), fall down (n = 9), thorn (n = 8), stone (n = 5), others (n = 5) and unknown (n = 3). Other risk factors were ulcerated cancer (n = 4), recent surgery (n = 4), spontaneous skin ulceration (n = 3) and leprosy (n = 3). The body parts that were identified as portal of entry were: lower limb (n = 34), upper limb (n = 14), head and neck (n = 12) and male genitalia (n = 1). The majority (n = 39, 79.6%) of the 49 patients with recent trauma did not seek treatment. Treatment given to patients who sought treatment (n = 10, 20.4%) was wound care. Of these 10 patients 3 received oral antibiotics. None of them received tetanus antitoxin or toxoid. Some patients (n = 8) applied herbal and other traditional treatment to the wound. Vaccination status for tetanus of the 66 (97.1%) patients was known and none of them was vaccinated.

The clinical presentations were: lockjaw (100%), generalized rigidity (92.6%), generalized spasm (91.2%), dysphagia (82.4%), opisthotonos (64.7%), risus sardonicacus (55.9%), backpain (38.2%), urinary retention (29.4%), constipation (8.8%), localized rigidity (7.4%), palpitation (5.9%), altered mentation at presentation (4.4%) and localized spasm (2.9%). The clinical forms of tetanus identified were: generalized 62 (91.2%), cephalic 5 (7.4%) and localized 1 (1.5%). One patient with generalized

tetanus had chronic tetanus with duration of illness of 5 month prior to presentation who was discharged improved. One of the patients with cephalic tetanus developed generalized type. Cranial nerve palsy was detected in patients with cephalic tetanus: infranuclear facial nerve palsy (n = 3), and multiple cranial nerves (IX, X, XII) in another patient. Distribution of patients according to severity of tetanus was: severe 49 (72.1%), moderate 13 (19.1%) and mild 6 (8.8%). The incubation period could be determined in 59 (86.8%) and the mean was 12.2, the median 9 and the range 44 (1–45) days. The period of onset was possible to determine in 64 (94.1%) and the mean was 2.6 days and the range was 29.9 days (2 h–30 days). The clinical profiles of patients in relation to outcome are shown in Table 1.

One or more complications of tetanus were identified in 51 (75%) patients. The complications in relation to outcome are shown in Table 2.

Serum potassium level was determined in 55 patients and hypokalemia was detected in 13 (23.6%) cases. CSF analysis was done in 3 cases which was normal. Arterial oxygen saturation was determined by pulse oximetry in 53 (76.5%) and it was <90% in 28 (53.8%) cases.

The treatment given to tetanus patients was: diazepam (98.5%), chlorpromazine (98.5%), tetanus (equine) antitoxin (95.6%), crystalline penicillin (69.1%), wound care (48.5%), tracheostomy (45.6%), metronidazole (35.3%), heparin (33.8%), propranolol (32.4%), physiotherapy (16.2%), cimetidine/omeprazole (11.8%), mechanical ventilation (11.8%) and magnesium sulfate (5.9%). Two or more intravenous antibiotics (ceftriaxone, cloxacillin and gentamicin) were required in patients (n = 24, 35.3%) who developed hospital acquired infections. One patient was treated with phenobarbital because of temporary shortage of diazepam and chlorpromazine. Verapamil was given to two patients. The mean duration in days required to do tracheostomy after admission was 2.5 (range 1–7). The mean duration of stay of tracheostomy tube before removal was 14.2 days (range 2–45). For patients who were discharged cured the mean was 22.9 (range 10–45) while for deceased patients the mean was 4.9 (range 2–9) days.

The following comorbidities were identified: cancer (n = 4), leprosy (n = 3), chronic osteomyelitis (n = 3), HIV/AIDS (n = 2) and bronchial asthma (n = 1).

The treatment outcome at hospital discharge was cured 43 (63.2%), dead 24 (35.3%), and one patient deteriorated clinically and

Table 1
Clinical profiles of tetanus patients by outcome status, n = 68.

		Total (n = 68)	Dead (n = 24)	Alive (n = 44)
Sex	Male	53 (77.9%)	16 (30.2%)	37 (69.8%)
	Female	15 (22.1%)	8 (53.3%)	7 (46.7%)
Age	Mean [SD]	33.8 [15.1]	41.4 [16.9]	29.7 [12.4]
	Median	28	39.5	26
	Range	14–85	15–85	14–65
Duration of initial symptom prior to presentation (days)	<4	29 (42.6%)	16 (55.2%)	13 (44.8%)
	4–7	30 (44.1%)	8 (26.7%)	22 (73.3%)
	>7	9 (13.2%)	0	9 (100%)
Clinical type	Generalized	62 (91.2%)	22 (35.5%)	39 (62.9%)
	Cephalic	5 (7.4%)	2 (40%)	3 (60%)
	Localized	1 (1.5%)	0	1 (100%)
Severity	Mild	6 (8.8%)	0	6 (100%)
	Moderate	14 (20.6%)	1 (7.1%)	13 (92.9%)
	Severe	48 (70.6%)	23 (47.9%)	25 (52.1%)
Identifiable portal of entry	Lower limb	34 (50%)	13 (38.2%)	21 (61.8%)
	Upper limb	14 (20.6%)	6 (42.9%)	8 (57.1%)
	Head and neck	12 (17.6%)	3 (25%)	9 (75%)
	Male genitalia	1 (1.5%)	0	1 (100%)
Incubation period (days)	>10	26 (38.2%)	2 (7.7%)	24 (92.3%)
	7–10	12 (17.6%)	5 (41.7%)	7 (58.3%)
	<7	21 (30.9%)	13 (61.9%)	8 (38.1%)
Period of onset (days)	≥7	3 (4.4%)	0	3 (100%)
	3–6	17 (25%)	1 (5.9%)	16 (94.1%)
	<3	44 (64.7%)	23 (52.3%)	21 (47.7%)

Table 2

Complications of tetanus in relation to outcome in 68 patients.

Complication[a]	Dead (n = 24)	Alive (n = 44)
None (17)	0	17 (38.6%)
Dysautonomia (40)	22 (91.7%)	18 (40.9%)
Aspiration pneumonia (30)	12 (50%)	18 (40.9%)
Hypoxemia (SaO$_2$<90%)(28)	11 (45.8%)	17 (38.6%)
Generalized sepsis (17)	8 (33.3%)	9 (20.5%)
Bedsore (9)	0	9 (20.5%)
Infected tracheostomy site (9)	1 (4.2%)	8 (18.2%)
Thrombophlebitis (10)	0	10 (22.7%)
Urinary tract infection (7)	2 (8.3%)	5 (11.4%)
Over sedation (8)	3 (12.5%)	5 (11.4%)
Acute renal failure (3)	2 (8.3%)	1 (2.3%)
Rhabdomyolisis (2)	1 (4.2%)	1 (2.3%)
Deep venous thrombosis (2)	0	2 (4.5%)
Altered mentation at presentation (3)	3 (12.5%)	0
Septic shock (3)	2 (8.3%)	1 (2.3%)
Upper gastrointestinal bleeding (1)	0	1 (2.3%)
Subcutenous emphysema (1)	1 (4.2%)	0

[a] Note that more than one type of complication may occur in one patient.

Table 3

Risk factors for case-fatality: logistic regression analysis.

Factor		n	%	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Sex	Male	53	77.9	1.00	1.00
	Female	15	22.1	2.64	5.24
				(0.82–8.53)	(0.35–78.99)
Age (years)	<40	45	66.2	1.00	1.00
	≥40	23	33.8	3.00	7.55
				(1.05–8.59)	(1.06–53.78)
Duration of symptoms prior to presentation	≥4 days	39	57.4	1.00	1.00
	<4 days	29	42.6	4.77	3.12
				(1.64–13.87)	(0.32–30.93)
Portal of entry: head and neck	No	56	82.4	1.00	1.00
	Yes	12	17.6	0.56	0.93
				(0.14–2.29)	(0.04–21.48)
Cephalic tetanus	No	63	92.6	1.00	1.00
	Yes	5	7.4	1.24	3.04
				(0.19–8.00)	(0.01–938.18)
Severe tetanus	No	20	29.4	1.00	1.00
	Yes	48	70.6	17.48	8.84
				(2.16–141.20)	(0.17–455.25)
Incubation period <7 days	No	47	69.1	1.00	1.00
	Yes	21	30.9	5.32	3.68
				(1.75–16.13)	(0.47–28.66)
Period of onset <3 days	No	24	35.3	1.00	1.00
	Yes	44	64.7	25.19	7.22
				(3.12–203.19)	(0.54–96.26)
Dysautonomia	No	28	41.2	1.00	1.00
	Yes	40	58.8	15.89	29.85
				(3.31–76.17)	(1.01–881.76)
Hypoxemia (SaO$_2$<90%)	No	40	58.8	1.00	1.00
	Yes	28	41.2	1.34	2.45
				(0.49–3.68)	(0.25–23.51)
Aspiration pneumonia	No	38	55.9	1.00	1.00
	Yes	30	44.1	1.44	3.72
				(0.53–3.93)	(0.32–43.58)
Generalized sepsis	No	51	75	1.00	1.00
	Yes	17	25	1.94	2.24
				(0.63–1.97)	(0.32–15.53)

discharged against medical advice for no obvious reason. The mean hospital stay for deceased patients was 5.9 days (range 2–14). The mean age of dead and alive patients was 41.4 and 29.7 years, respectively (p-value = 0.005). There was no significant difference in mortality between crystalline penicillin and metronidazole treated patients (p-value = 0.44). The mortality in tracheostomy and mechanical ventilation treated patients was (15/31, 48.4%) and (4/8, 50%), respectively. Of the dead patients 6 (25%) died in the first 3 days, 14 (58.3%) died within the first 5 days and 22 (91.7%) died within the first 10 days. The causes of death were respiratory failure (n = 21, 87.5%) due to uncontrolled spasms and cardiac arrest due to dysautonomia (n = 3, 12.5%). Univariate logistic regression analysis (Table 3) of potential predictors of death at discharge showed six variables significantly related to case fatality: age ≥ 40 years, duration of symptoms prior to presentation < 4 days, severe tetanus, incubation period < 7 days, period of onset < 3 days and dysautonomia. In multivariate analysis (Table 3) only age ≥ 40 years and dysautonomia were associated with significant mortality with odds ratio of 7.6 (95%CI = 1.06–53.78) and 29.9 (95% CI = 1.01–881.76), respectively. Of the patients who were discharged cured only 22 (50%) received tetanus toxoid.

4. Discussion

The objectives of our study were to assess the clinical presentations, risk factors, complications, treatment, outcome and predictors of death in tetanus patients who presented to the largest referral hospital in Ethiopia. Majority of patients were males (77.9%) in keeping with most other studies [2,3,10,12,13,21]. The mean age was 33.8 years similar to studies done in other developing countries [15,21] but in contrary to older adult dominance in high-income countries [2,3]. Women were older than men in this study. This could be due to immunization of younger women during pregnancy. Majority of cases (63.2%) occurred from June through November which is consistent with other studies [2,26]. This might be due to increased agricultural activities during this period in our area. The commonest clinical manifestations were: lockjaw (100%), generalized rigidity (92.6%) and spasm (91.2%) and dysphagia (82.4%) which is similar to other studies [10,12,16,17,19,22,24]. None of the patients had primary immunization and of the patients with recent trauma (n = 49, 72.1%) only 10 (20.4%) sought medical care and none of these received tetanus (equine) antitoxin (human tetanus immune globulin was not available). This is in contrast to a study [3] done in the United States where 37% of patients with recent trauma sought medical care and of these 63% received tetanus toxoid. To prevent development of tetanus after an injury improvement in wound care and administration of tetanus vaccine should be encouraged in this setup.

The hospital should implement a better system for ensuring that patients cured of tetanus leave the hospital fully vaccinated. The percentage of patients with no clinically identifiable portal of entry, which was 10.3% in our cases, varied from as low as 4.7%–18.2% [8,12,14–17] and as high as 36.6%–49% in other studies [9,24].

Most patients had generalized tetanus (91%) in keeping with other studies [9,14,15,19] and 72.1% had severe tetanus which is higher compared to 53.4% in another study [14] in Addis Ababa and lower compared to 86.6% in a study done in Caracas [23]. Most patients (75%) had one or more complication(s) identified and the common complications include: dysautonomia (58.8%), aspiration pneumonia (44.1%), hypoxemia (41.2%) and generalized sepsis (25%). Dysautonomia was more frequent in our cases compared to other studies [22,24] which was 29% and 32%, respectively. Hypokalemia which required potassium chloride replacement therapy was identified in 13 of 55 cases with potassium level determination (23.6%). This might be explained by the fact that sympathetic hyperactivity may cause transient hypokalemia [27]. The case-fatality in hypokalemic patients was 31% [OR = 1.4, CI (95%) = 0.4–5.6]. Tracheostomy was done in 45.6% of cases which is lower compared to other studies [16,22] which was 74% and 100%, respectively. Mechanical ventilation was utilized in 11.8% of our cases while it was used in other studies [16,22] in 45% and 86.4% cases, respectively.

The case-fatality in our study was 35.3% which is consistent with other studies [4,8,11,14,19,22] and the findings of which vary from 32% to 39%. In contrast to our finding, both lower (15% to 27%) [3,12,15,16,18,23,24] and higher (55% to 72.7%) [9,10,13,17,21] case-fatalities were observed. The case-fatality of tetanus observed in previous studies from Addis Ababa [14,15] was 35.9% and 27%, respectively. This shows that the mortality did not show improvement.

This might be due to the higher proportion of patients with severe tetanus in our study (72.1% vs 53.4%). These previous studies [14,15] were done in 3 and 6 different hospitals, respectively. The chance of including more mild/moderate cases was probably high in the previous studies and due to referral from other hospitals to our tertiary hospital the chance of admitting more severe cases might have been high. The fact that 97% of our patients were not vaccinated for tetanus (partially or fully) might also indicate that there was a bias in case-selection towards patients with severe tetanus. While patients treated conservatively (tracheostomy, non-paralyzing muscle relaxant and sedation) die as a consequence of early acute respiratory failure, the main cause of death in ICU treated patients (ventilatory support, sedatives and relaxant) is unexpected cardiac arrest, probably due to dysautonomia [23]. In our study 91.7% of deceased patients died within the first 10 days, the cause of death was respiratory failure due to uncontrolled spasms in 87.5% and only 11.8% of our patients were treated with mechanical ventilation. These show that our patients did not receive adequate ventilatory support.

Even though age≥40 years, duration of symptoms prior to presentation <4 days, severe tetanus, incubation period<7 days, period of onset<3 days and dysautonomia were significantly related to case-fatality in the univariate analysis, only age≥40 years and dysautonomia were significant in the multivariate analysis. The notable increase in the adjusted OR for female sex could be partly explained by gender bias in the utilization of health services in the study area that might cause delay in diagnosis and treatment [28].

There were some limitations to this study. The retrospective nature of the study might have caused unrecoverable missing data in some cases. TAH is a tertiary hospital which receives referral from all over the country and the chance of admitting selectively patients with severe tetanus is high. The relatively small sample size is reflected in wide confidence intervals around some of the variables. A larger sample would have detected more prognostic factors.

Tetanus is entirely preventable by vaccination. Universal primary immunization with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters (every 10 years) is necessary to protect all age groups. To improve treatment outcome of tetanus patients, they should be admitted to well equipped ICU where they can be monitored and observed continuously.

In conclusion, tetanus in adults in TAH affected mainly young males and it was associated with high case fatality as in most other studies. Most deaths occurred early due to acute respiratory failure due to uncontrolled spasms. Age≥40 years and dysautonomia were independent predictors of mortality. Prevention remains the best therapy. Tetanus is a devastating disease of muscle spasm and dysautonomia with a high mortality that requires well equipped ICU.

Conflict of interest

All authors report no conflict of interest.

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