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Clinical profile of adult tetanus patients and the impact of early tracheostomy on the outcome; a retrospective observational study

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Abstract

Back ground & Objective: Tetanus is a preventable disease that is still prevalent in the developing countries due to inadequate vaccination practices. It has a prolonged disease course and requires an extended intensive care unit (ICU) stay, as supportive care is the mainstay for a better outcome. This study examines the clinical profile of adult tetanus patients and the impact of early tracheostomy on the final outcome in patients admitted to our ICU.

Methodology: In this retrospective observational study, patients with age of 18 y or above, diagnosed as a case of tetanus on the basis of the presence of at least two of the clinical features; trismus with or without risus sardonicus, and the rigidity of the abdominal wall and reflex spasm, were included. Neonates, pregnant and epileptic patients were excluded. The study was conducted at the ICU of our institute after approval from the Ethical Review Committee (ERC No.000003/SMBBIT/Approval/2019–2020). Medical records from August 2017 to February 2021 were collected in a pre–defined questionnaire. The primary outcome was the impact of early tracheostomy on survival and secondary outcomes were the risk factors of mortality.

Results: 48 patients were included in the study with 44 (91.7%) males and 4 (8.3%) females. The median age of patients was 25.5 (22–35) y. Lower limb was the primary site in 32 (66.7%) of the patients. Neck rigidity (39.6%) and trismus (35.4%) were the main presenting symptoms. The median incubation period was 14 (10–16) days. The median length of stay in the ICU was 28 (25–30) days. The most common complication was ventilator–associated pneumonia (VAP) acquired by 16 (33.3%) patients. Almost all patients showed a significantly higher level of creatine phosphokinase (CPK) 3908.85 ± 2974.91 IU/L, which gradually decreased on discharge to 430.48 ± 360.7 IU/L. 43 patients underwent tracheostomy. Early tracheostomy (within 7 days) was associated with a lower incidence of VAP ($p = 0.000$) and lesser need of mechanical ventilation (MV) ($p = 0.000$) with better survival rate ($p = 0.000$). The overall survival rate was 81.3%.

Conclusion: We conclude that the patients who underwent early tracheostomy, had better survival and lower risk of being mechanically ventilated and development of ventilator associated pneumonia. Periodic estimation of CPK level can be used as a valuable prognostic tool and predictor of mortality in tetanus patients. Age, any comorbid, mechanical ventilation and complications were the probable risk factors. Over all we had a good rate of survival.

Abbreviations: ICU – Intensive care unit; VAP – Ventilator–associated pneumonia; CPK – Creatine phosphokinase; EPI – Expanded Program of Immunization; TT – Tetanus toxoid

Key words: Tetanus; Outcome; Survival; Intensive Care Unit; Tracheostomy; Ventilator–associated pneumonia; VAP

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1. Introduction

Tetanus is potentially a preventable infectious disease which has been significantly decreased in the developed countries worldwide. It was labeled as one of the 6 targeted diseases for the Expanded Program of Immunization (EPI) by the World Health Organization (WHO) in 1974.[1] Despite overall reduction in mortality rate, the frequency of tetanus is still higher in developing countries due to poor healthcare infrastructure and lack of awareness. Cases of tetanus from South Asia and Sub–Saharan Africa account for 82% of all tetanus cases in the world.[2]

Coverage of Tetanus Toxoid (TT) vaccination in Pakistan varies from 60% to 74% over the last decade.[3] Exact disease burden is unknown. Even though no population–based study is available from Pakistan, individual institutes have reported their cases in different time frames.[4,5] Tetanus outbreak was noted in 2005 during a major earthquake in the northern areas of Pakistan with 23 reported deaths.[4] Three years retrospective study was conducted in DHQ Hospital, Faisalabad that reported 198 patients with clinical signs and symptoms of tetanus.[5] Mortality from tetanus approaches close to fifty percent in low resource settings . Tetanus can affect people of all ages but newborns and young persons are mostly affected. Body stiffness, trismus and dysphagia are the three most common presenting features.[6]

The incidence of tetanus has greatly declined in the developed world, whereas it continues to pose a significant risk of mortality in the underdeveloped nations. Therefore, there is an appalling need for improvement in immunization program and to raise awareness in the general population.[7]

We studied the implications of early tracheostomy on tetanus patient survival along with its clinical manifestation and other associated complications observed during management.

2. Methodology

A retrospective observational study was conducted on clinically diagnosed adult tetanus patients who were admitted in Intensive Care Unit (ICU) of Shaheed Mohtarma Benazir Bhutto Institute of Trauma (SMBBIT), a tertiary care medical facility, after obtaining ethical approval (ERC No.000003/SMBBIT/Approval/ 2019–2020). Hospital records of patients admitted between August 2017 to Feb 2021, were reviewed. The hospital caters patients mainly from rural and urban Sindh and from neighboring provinces of Pakistan. All adult patients (aged 18 y or above) with one or more of the following clinical features were included; trismus, rigidity of the neck and or abdominal wall and reflex spasm.[8] Pregnant and epileptic patients were excluded. The institute ethical review committee waived the need for consent.

A non–randomized sampling technique was used to enroll participants in the study. The details of the demographic data, clinical presentation, management, complications and outcome were recorded.

Trismus was defined as reduced opening of the jaw caused by spasm of the muscles of mastication. Risus sardonicus was defined as an abnormal, sustained spasm of the facial muscles that appears to produce grinning. Opisthotonus was characterized by the spasm of the muscles causing backward arching of the head, neck, and spine.[9]

Additionally severity of tetanus was recorded at time of admission according to the Albett classification of tetanus. Patients were divided into four grades; Grade 1 (mild) patients had mild trismus, general spasticity, and no respiratory compromise; Grade 2 (moderate) had moderate trismus, rigidity, short spasm, moderate respiratory involvement with a respiratory rate of more than 30 breaths/minutes; Grade 3 (severe) had severe trismus, generalized rigidity, prolonged spasm, apneic spell, respiratory rate of more than 30 breaths/min, and pulse rate of more than 120/min, and Grade 4 (very severe) patients had all features of Grade 3 as well as autonomic dysfunction.[10]

All the patients were admitted in ICU from ER. Standard treatment was given that included tetanus toxoid (TT), immunoglobulin (IG) , magnesium sulfate ($MgSO_4$) and sedation primarily with diazepam, maintaining Ramsay sedation score 3 (Ramsay Score 0 = awake, 1 = anxious, 2 = awake cooperative, 3 = sleep cooperative, 4 = deep sedation, quick response to painful stimuli, 5= deep sedation, slow reaction to pain stimuli, 6 = deep sedation, no reaction to painful stimuli). For uncontrolled muscular spasm, intravenous propofol 0.1 to 0.15 mg/kg/min was added, if still not controlled, then we added atracurium in a dose of 0.005 to 0.01 mg/kg/min.

Table 1: Demographics of 48 tetanus patients.

Parameters		n (%)
Age (y) median[IQR]		25.5 [22–35]
Age groups (y)	18–25	24 (50)
	26–35	14 (29.2)
	36–45	3 (6.3)
	46–55	3 (6.3)
	> 55	4 (8.3)
Gender	Male	44 (91.7)
	Female	4 (8.3)
Residence	Urban	24 (50)
	Rural	24 (50)
Co–morbids	Hypertension	9 (18.8)
	Respiratory	7 (14.6)
	IHD	5 (10.4)
	Diabetes	3 (6.3)
		5 (10.4)
Occupation	Farmer	19 (39.6)
	Labor	9 (18.8)
	Mechanics	12 (25)
	Students	4 (8.3)
	Other	4 (8.3)
Type of Injury	Superficial	41 (85.4)
	Deep	7 (14.6)

Our institutional criteria for tracheostomy were airway compromise, uncontrolled spasm, or need of prolonged (more than 7 days) intubation and ventilation.[10] Tracheostomies were delayed (late tracheostomy) more than 7 days only if there were some issues like deranged laboratory results, the non-availability of operating room or the ENT surgeon, as the facility for bedside percutaneous tracheostomy was not available.

Statistical analysis: The statistical analysis was performed using SPSS, version 22.0. Continuous variables were compared using student t–test. The percentages and frequencies were calculated for the various parameters that were under study and the chi–square test was applied to test the significance. A $p \leq 0.05$ was considered statistically significant.

3. Results

The demographic data are presented in Table 1. Out of 48 patients, 7 (14.6%) patients were hypertensive and 5 (10.4%) were diabetic. Entry wounds were on lower limb 32 (66.7%) and were superficial 41 (85.4%) (Table 1). Main characteristics of disease are detailed in Table 2. Vaccination rate was 66.7%, out of which 12.5% received tetanus toxoid (TT) in the last 5 y. The median incubation period was 14 [IQR 10–16] days. On arrival

Table 2: Disease Characteristics

Parameters	n (%)
Vaccinated	32 (66.7)
Unvaccinated	5 (10.4)
Booster in last 5 years	6 (12.5)
Not known	5 (10.4)
Incubation period (days) median [IQR]	14[10–16]
Site of injury	
Upper Limb	10 (20.8)
Lower Limb	32 (66.7)
Cephalic	3 (6.3)
Not known	3 (6.3)
Presenting symptoms	
Neck rigidity	19 (39.6)
Trismus	16 (33.3)
Dysphagia	2 (4.2)
Abdominal rigidity	1 (2.1)
Opisthotonus	2 (4.2)
Spasms	2 (4.2)
Autonomic dysfunction	5 (10.4)
Risus Sardonicus	1 (2.1)
Grades Of Tetanus	
11	5 (10.4)
111	38 (79.2)
1V	5 (10.4)
CPK level (U/L) mean ± SD	
On Arrival	3908.85 ± 2974.91
On Discharge	430.48 ± 360.7

CPK level (creatinine phosphokinase) was 3908.85 ± 2974.91 µg/L (Normal value: 10 to 120 µg/L), which gradually tapered down and at discharge mean CPK level was 430.47 ± 360.7 µg/L (Table 2).

All the patients were managed with the tetanus toxoid (0.5ml I.M.), human tetanus immunoglobulin (5000 IU IM), and antibiotic therapy (metronidazole). Most of the patients 36 (75%) were intubated within 24 h of admission. Benzodiazepine (diazepam or midazolam) was infused in all patients and propofol infusion was needed in 12 (25%) with a muscle relaxant in 12 (25%) depending on the severity of rigidity and spasm. Intravenous magnesium (Mg) infusion was given to all patients with a median duration of 21[18–24] days tapered when rigidity subsided and spasm controlled. Around 43 (89.5%) patients underwent tracheostomy. Complications noted and the morbidity and mortality rate is given in Table 3.

Table 4 summarized the factors associated with tetanus mortality. 4 (44.4%) of 9 (18.8%) patients who were

Table 3:Management characteristics of Tetanus Patients

Parameters	n (%)
Immunoglobulin	48 (100)
Tetanus Toxoid	48 (100)
Benzodiazepine	48 (100)
Propofol	12 (25)
Relaxants	12 (25)
Wound debridement	7 (14.6)
Duration of magnesium therapy (days)median [IQR] (min–max)	21[18–24] (10–28)
Intubation	
≤ 24 h	36 (75)
> 24 h	10 (20.8)
Not intubated	2 (4.2)
Mechanical ventilation needed	32 (66.7)
Tracheostomy	
≤7 days (Early)	24 (50)
>7 days (Late)	19 (39.6)
Not done	5 (10.4)
Tracheostomy wound infection	17 (35.4)
Bed sores	16 (33.3)
LOS (days)median[IQR] (min–max)	28[25–30] (12–38)
Outcome	
Not survived	9 (18.8)
Survived	39 (81.3)

aged 40 years and above died compared to 5 (12.8%) out of 39 (81.3%) from the under forty years age group proving strong association of age with mortality (p = 0.028) . Patients with comorbid 9 (18.8%) had less survival rate (p = 0.007). Most common comorbidity was hypertension with 71.4% mortality (p = 0.001), while patents with ischemic heart disease and diabetes mellitus were associated with 100% mortality (p = 0.005 and 0.000 respectively). Complications developed during the stay in ICU, including VAP, AKI, ARDS were associated with poor outcome ($p \leq 0.05$). Those who underwent mechanical ventilation had lesser survival rate (p = 0.017). Gender and site of injury did not show any significant relationship with the outcome.

The impact of the timing of tracheostomy on the outcome of tetanus patients is summarized in Table 5. Patients who had tracheostomy within 7 days of admission had significantly lower rate 10 (34.5%) than 19 (65%) to be on MV as compared to late tracheostomy group (p = 0.000) .Moreover, they were less prone to develop VAP, none of the patients from the early tracheostomy group–developed VAP [p = 0.000, OR 9 (3.09–26.16)]. Patients in which tracheostomy was delayed, there were more incidences of tube blockage and dislodgement as a result 12 (70.6%) patients needed reinsertion of endotracheal tube. Survival was also better in patients who underwent tracheostomy earlier. However, length of stay was more in the early tracheostomy group ie 28.5 (21–32) days compared to late tracheostomy group i.e. 26 (12–38) consequently most of the patients 24 (66.7%) with early tracheostomy had ICU stay more than 20 days (p = 0.006).

4. Discussion

Our study has provided a better understanding of baseline characteristics of our patients with tetanus and their clinical outcomes. We found that most of the patients admitted to the intensive care unit of our hospital were predominantly young males, which is similar to numerous other studies, including Pakistan and India.[8,9 ,12] Young men spend more time working outdoors and hence are more prone to injuries and exposed to the causative organism *Clostridium tetani*, which is ever present in soil in a tropical country like Pakistan. Moreover, females have a chance to get boosters of tetanus vaccine during their antenatal periods that lead to partial protection in young females of fertile age.

Although persons who were vaccinated in early age–acquired tetanus due to decreasing immunity with increasing age. A serological study conducted in the USA reveals that decreasing titers of antibodies in old age make old persons more prone to acquire tetanus.[25] In our study sixteen 32 (66.7%) patients were vaccinated and 6 (12.5%) had received boosters in the last 5 years, which is unlike results of other studies conducted in neighboring countries in which vaccination coverage was very low.[8,9]

Hot and humid climate and cultivated soil rich in organic matter is the place where tetanus is found. In SMBB Institute of Trauma, we received a patient from both the city as well as near and far rural areas. Most of the patients who came from rural areas were farmers by profession; they worked in fields barefooted so and have a higher risk of exposure, which is in strong agreement with other studies from neighboring countries with warm and wet climate like Pakistan.[26]

The incubation period reported from other studies were similar to our study and same were with site and type of injury, which is mostly superficial 42 (85.4%) and in lower limb 32 (66.7%).[10,11] A study conducted in Pakistan by Moazzam et al. reported trismus as most common presenting symptom in 94 (47.5%) of patients,[5]

Table 4 : Risk factors for mortality

Parameter	Total (n=48)	Died (n=9)	Survived (n = 39)	p –value
Age (years)				
18–25	24 (50)	0 (0)	24 (100)	0.000
26–35	14 (29.2)	4 (28.6)	10 (71.4)	
36–45	3 (6.3)	1 (33.3)	2 (66.7)	
46–55	3 (6.3)	0 (0)	3 (100)	
>55	4 (8.3)	4 (100)	0 (0)	
Gender				
Male	44 (91.7)	9 (20.5)	35 (79.5)	.423
Female	4 (8.3)	0 (0)	4 (100)	
Co–morbids	9 (18.8)	5 (55.6)	4 (44.4)	.007
Hypertension	7 (14.6)	5 (71.4)	2 (28.6)	.001
Respiratory	5 (10.4)	1 (11.1)	4 (80)	.670
Ischemic heart disease	3 (6.3)	3 (100)	0 (0)	.005
Diabetes mellitus	5 (10.4)	5 (100)	0 (0)	.000
Site of injury				
Upper Limb	10 (20.8)	2 (20)	8 (80)	.772
Lower Limb	32 (66.7)	6 (18.8)	26 (81.3)	
Scalp	3 (6.3)	0 (0)	3 (100)	
Unspecified	3 (6.3)	1 (33.3)	2 (66.7)	
Tracheostomy				
Early	24 (55.8)	0 (0)	24 (100)	0.000
Late	19 (44.2)	9 (47.4)	10 (52.6)	
Mechanical ventilation	32 (66.7)	9 (28.1)	23 (71.9)	0.017
Complications				
VAP	16 (33.3)	6 (37.5)	10 (62.5)	0.019
CLABSI	6 (12.5)	0 (0)	6 (100)	0.208
AKI	1 ()	1 (11.1)	0 (0)	0.035
ARDS	11 (22.9)	9 (81.8)	2 (18.2)	0.000

Data presented as n (%); VAP-ventilator associated pneumonia; CLABSI-central line associated blood stream infection; AKI-acute kidney injury; ARDS-adult respiratory distress syndrome

Table 5: Comparison of outcomes between patients with early and late tracheostomy

Parameters	Total (n=43)	Early Tracheostomy (n=24)	Late Tracheostomy (n=19)	p–value
Mechanical Ventilation	29 (67.4)	10 (34.5)	19 (65.5)	0.000
VAP	16 (37.2)	0 (0)	16 (100)	0.000
Length of ICU stay (days) median (min–max)	28 (12–38)	28.5 (21–32)	26 (12–38)	0.001
≤ 20	7 (13.6)	0 (0)	7 (100)	
> 20	36 (83.7)	24 (66.7)	12 (33.3)	
Outcome				0.000
Not survived	9 (20.9)	0 (0)	9 (100)	
Survived	34 (79.1)	24 (70.6)	10 (29.4)	

Data presented as n (%) unless specified; VAP,= ventilator associated pneumonia

while we reported neck rigidity as most common presenting symptom in 19 (39.6%) of patients. Trismus was the second most common presenting feature 16 (33.3%).

On receiving most of the patients had generalized tetanus with raised level of CPK and over the period of 3 weeks when the patients were in recovery phase and spasm was subsided CPK level tapered down (Table 2).These findings are in agreement with the study published in IOSR journal of dental and medical sciences.[23] CPK can be used as a valuable tool to monitor the response to treatment in tetanus and a predictor of mortality, further analytical studies reach on definitive conclusion.

Mostly wounds that lead to tetanus are so trivial that they go unnoticed but if there is dirty and infected wound early debridement is recommended along with human tetanus immune globulin that binds the released toxins and shorten the course of illness.[15] In this study we had seven patients (14.6%) who underwent debridement due to infected wound. Immunoglobulin (IG) and Tetanus Toxoid (TT) were given on admission to all patients, and most patients (75%) were intubated within 24 h of admission and 50% patients underwent tracheostomy within 7 days. Most other studies reported the similar line of treatment.[11,13]

In our study, the main complication was VAP, 16 (33.3%) patients acquired it and most commonly isolated organism was *acinatobacter spp* and *klebsiella* from ETT culture, these results are similar to findings of a study conducted by Nilton et al. in brazil.[14,24]

The prolonged duration of hospital stay impacts hospital resources and on increased cost of health care, loss of productivity and reduced quality of life. In this study median duration of ICU stay and the duration of magnesium infusion was 28 (12–38) days and 21 (10–28) days, respectively. However, other studies reported comparatively shorter duration of ICU stay i.e. 11.8 ± 6.5 days and 12.3 ± 9 days in a Chinese[10] and Pakistani [6] study, respectively. Due to the long stay in ICU and immobility due to sedated most of time, patients tend to develop bed sores. We reported 16 (33.3%) of cases who developed bedsores in sacral area. There is fear of eliciting spasms or tracheostomy tube dislodgement, which compromise positioning of tetanus patients in ICU.

The mortality in our center was comparatively lower (18.8%) than those reported in the previous studies from other developing countries.[16,17,18,19] Risk factors for mortality were found to be age [p value 0.028, OR 5.4 (1.09–27.4)], comorbids [p value 0.007, OR 5.4 (1.8–16.2)], timings of tracheostomy (p–value 0.000), mechanical ventilation (p– value 0.017) , and VAP, which is in sound agreement with other studies.[26,27] In a study by Moazzaum et al., 40% of admitted tetanus patients were expired. [5] Altaf et al. revealed a mortality rate for tetanus to be 25.19%. [6] According to a South Asian study mortality was high reaching up to 45%.[12]

However, if we look into the data of the developed countries, their mortality rates are remarkably lower than ours. A multi–centered study conducted in French ICUs report only 16% mortality[28]. The reason for this difference be because in developing countries resources are limited and facilities of ICU care are sparse.

Proper timing to perform the tracheostomy in intubated patients remained controversial. Some international studies recommend the preferable timing of tracheostomy between 7 and 15 days postintubation.[30,31] many studies reported that early tracheostomy is associated with lower rates of VAP, shorter ICU stay and mortality. A study by Awan et al. and Saeed et al. reported the same in patients with tetanus.[20,21,22] An interesting finding of our study was that patients who had early tracheostomy within 7 days of admission did not develop VAP and none of them died in ICU but had longer ICU stay compared to those with late tracheostomy . The reason might be that those who had delayed tracheostomy were more severe and did not survive longer. Despite the advantages of early tracheostomy in ICU, there are some challenges related to tracheostomy itself. It needs proper wound care by trained staff. We reported a higher rate of tracheostomy wound site infection i.e. 35.4% compared to 7.69% in a study by Fasunla et al.[20, 21.] Our hospital is a public sector set up with high patient flow and high bed occupancy rates, there is relative shortage of ICU trained staff and consequently it compromises nursing care.

5. Conclusion

The results of our study conclude that early tracheostomy offers a better survival, and is associated with a lower risk of being mechanically ventilated and subsequently developing ventilator–associated pneumonia in tetanus patients. Periodic estimation of CPK level can be used as a valuable prognostic tool and predictor of mortality in tetanus patients. Age, comorbid, mechanical ventilation and complications were the probable risk factors of mortality.

6. Limitation

There is a shortage of skilled nursing staff in our setup resulting in high rates of bed sores, tracheal site infections and VAP. We did not assess the long–term survival of discharged patients due to lack of follow up.

7. Recommendation

We emphasize the need to improve healthcare systems and ICU facilities especially in the peripheral areas.
Media and healthcare workers should play a role to remove the misconceptions about immunization in our society.
We recommend early tracheostomy in patients with severe tetanus for better outcome.

8. Conflict of interest

None declared by the authors.

9. Authors' contribution

AN: Supervised, conceived and designed the study, data collection, manuscript writing, editing, analysis and interpretation of data
GR, SU, HI, VK, SK, SJ: Revising article critically for intellectual content
ZR: Final revision of manuscript, accountable for accuracy and integrity of article

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