Impact of Sociodemographic Variables and Clinical Parameters on Outcome of Pediatric Tetanus Patients: A Retrospective Study from an Infectious Disease Hospital in Bangladesh

Humayra Akter[1*] Mursheda Khanam[2] Farzin Akhter[3] Rumana Rashid[4]

Abstract

Background: Tetanus is a vaccine-preventable disease with high mortality. It is still a major cause of death in the pediatric age group particularly in developing countries. This study aimed to determine the demographic and clinical profile and their impact on the outcome of tetanus in children.

Materials and methods: This retrospective study was conducted at the Bangladesh Institute of Tropical and Infectious Diseases (BITID), Fouzderhat, Chattogram. The medical records of pediatric tetanus patients (age ≤ 17 years) admitted between January 2014 and December 2021 were retrieved. Data regarding the demographic and clinical profile and final outcome of the patients were noted. The statistical analysis was conducted using SPSS version 25.

Results: There were a total of 81 pediatric tetanus cases during the study period. Male to female ratio was 1.6:1. Most (69.1%) of the patients came from rural areas. Eighteen (22.2%) cases were neonates. The majority of the patients were between 6-10 years of age (28.4%). The median incubation period was 7 days (IQR: 5-10 d, range: 3-12 d). Median age at presentation was 10 days (IQR: 7-10.25 days) in neonate and 8 years (IQR: 5-11 years) in non-neonatal group. Lockjaw (85.2%) was the commonest presentation, followed by convulsion (80.2%) and then fever (44.4%). About one-fourth (25.9%) of the patients developed complications during the hospital stay. Nearly two-thirds (67%) of mothers of neonatal tetanus cases were not vaccinated against tetanus. Most of the non-neonatal tetanus cases (80.9%) were either partially immunized or unimmunized. Overall in-hospital mortality was 28% and mortality was high among neonates (44.4%). There was a significant increase in mortality among ethnic minority group ($p = 0.03$) and patients with complications ($p=0.02$). Recovered patients had a significantly longer duration of hospital stay (Median 19.5 days; IQR: 16–25 days) than those who died (Median 2 days, IQR 1-4 days) ($p<0.001$).

Conclusion: Higher tetanus rate among children older than 5 years and high mortality among unimmunized ethnic minority group implies the necessity of incorporating booster doses of tetanus toxoid into the Expanded Program on Immunization (EPI) schedule and strengthening routine immunization coverage targeting the rural and hill tract areas.

Key words: Immunization; Neonatal tetanus; Outcome of tetanus; Pediatric tetanus; Tetanus mortality.

Introduction

Tetanus is a vaccine-preventable rare infectious disease with a high case fatality rate. In developed nations, tetanus primarily affects the elderly due to a decline in protective antibodies, whereas in developing countries, tetanus is prevalent among the young due to a lack of an effective immunization program and proper treatment of injuries.[1] In 2019, the Global Burden of Disease study estimated more than 73,000 total tetanus cases, 49 percent of those younger than five years old, including more than 27,000 neonatal tetanus infections.[2] South Asia and sub-Saharan Africa accounted for 45 percent and 44 percent of all neonatal tetanus-related deaths, respectively.[3,4]

Tetanus is a neurological disordercausedby *Clostridium tetani*. The disease can be contracted through two methods: direct contact of a wound with dirt containing the bacteria, and mothers and newborns can acquire tetanus through birth-related wounds, known as Maternal/Neonatal Tetanus (MNT). Suppurative Otitis Media (SOM) and circumcision performed by traditional "surgeons" are significant entry points in some cases. Spores of Clostridium tetani enter the body through skin breaks and germinate in anaerobic

1. Assistant Professor of Neonatology
Chittagong Medical College, Chattogram.
2. Senior Consultant of Pediatrics
Chittagong 250 Bed General Hospital, Chattogram.
3. Junior Consultant of Medicine
Bangladesh Institute of Tropical and Infectious Diseases (BITID)
Fouzderhat, Chattogram.
4. Assistant Professor of Epidemiology and Community Medicine
Bangladesh Institute of Tropical and Infectious Diseases (BITID)
Fouzderhat, Chattogram.

***Correspondence: Dr. Humayra Akter**
Cell : 01716 23 53 21
E-mail: shakila_046@yahoo.com

Submitted on : 04.12.2023
Accepted on : 16.03.2024

environments.[1] Clinical features include muscle stiffness, lockjaws, risus sardonicus, abdominal stiffness and posterior dorsal stiffness, also known as the opisthotonos position, which causes serious problems with ventilator mechanics and can be fatal from the very first spasm. When an infant with normal sucking and crying abilities in the first two days of life presents with failure to suckle between 3 and 28 days of age, accompanied by rigidity or spasms, this is known as Neonatal tetanus.[5]

Admission to a dark and quiet room, control of muscle spasm and rigidity, control of autonomic dysfunction, ventilator support when necessary, neutralization of tetanus toxin, wound management, administration of antibiotics and prevention of recurrence with booster vaccination are core principles of tetanus management. Due to the high prevalence of the bacterium that causes tetanus, the disease cannot be eradicated.[5,6] There is no natural immunity to tetanus, not even recovery from tetanus confers immunity. But tetanus is a vaccine-preventable disease, as evidenced by the WHO's report of a reduction in mortality rates following vaccination. Vaccination against tetanus is effective at any age, and the duration of protection depends on the number and spacing of doses.[6] Tetanus in the newborn can be prevented by immunizing the mother, who passes on her immunity to her newborn.

Even though South Asia still has the highest incidence rate of tetanus, it has decreased 14-fold in just three decades, from nearly half a million cases in 1990 to 33,000 cases in 2017.[7] Recent estimates indicated an annual decline of 8.9% in tetanus-related mortality.[8] Globally, the percentage of newborns protected against tetanus increased from 74% in 2000 to 86% in 2020, and the rate of births assisted by a skilled birth attendant increased from 64% in 2000-2006 to 83% in 2014-2020. The number of reported cases of neonatal tetanus has decreased by 88 percent, from 17,935 in 2000 to 2,229 in 2020, and the number of estimated deaths has reduced by 92 percent, from 170,835 in 2000 to 14,500 in 2020.[3]

This decreasing trend in neonatal mortality is a result of the Maternal and Neonatal Tetanus Elimination (MNTE) program. The Tetanus Toxoid (TT) vaccine is a risk-free public health measure designed to reduce MNT deaths.[3,9] As a result of vaccination, neonatal tetanus now accounts for less than 1 percent of all neonatal deaths, a significant decrease from its 7 percent contribution in 2000. Even though the Government of Bangladesh has achieved MNT elimination status as of June 2008, tetanus remains a major health concern.[10] In addition, underreporting of cases has worsened the situation. Very few studies have been conducted on patients diagnosed with tetanus, with the majority focusing on adult tetanus patients, providing a glimpse of the current status of tetanus in the country.[11,12]

In this context, we conducted this eight-year retrospective analysis of all pediatric tetanus cases admitted to a hospital for infectious diseases in Chattogram. This study aimed to determine the demographic and clinical profile and their impact on the outcome of tetanus in children. This is one of the few attempts in Bangladesh to investigate the factors associated with the in-hospital mortality of pediatric tetanus patients.

Materials and methods

This was a retrospective hospital-based descriptive observational study. It was conducted at the Bangladesh Institute of Tropical and Infectious Diseases (BITID) Fouzderhat, Chattogram. This hospital has a specialized isolation unit for treating patients infected with tetanus, except for the provision of intensive care and assisted ventilation.

The medical records of pediatric tetanus patients admitted between January 2014 and December 2021 were retrieved from the hospital's medical records office. Prior to conducting the study, permission was taken from the authority of the Bangladesh Institute of Tropical and Infectious Diseases (BITID) for data collection and analysis. All data were analyzed anonymously and no information of study participants was disclosed.

The selection criteria for recruitment of patients was age ≤17 years with a clinically confirmed diagnosis of tetanus by physician. Patients with incomplete basic information, as well as those with a doubtful clinical diagnosis of tetanus in the presence of other differential diagnoses such as Hysterical Conversion Reaction (HCR) and drug-induced rigidity, were excluded from this study.

Details of demographic information (i.e. age, sex, religion, tribal/non-tribal status, and residence),

tetanus immunization history, suspected portal of entry, incubation time, clinical presentations, post-exposure prophylaxis, management, complications, length of hospital stay and final outcome were extracted from medical records and entered into a Clinical Record Form (CRF).

Tetanus was diagnosed based on the presence of one or more of the following: i) Rigidity of the neck and/or abdomen/neck stiffness ii) Lockjaw iii) Muscle spasm. Clinical diagnosis of neonatal tetanus was made using all three of the following WHO diagnostic criteria: i) A child who has been crying and feeding normally during the first two days of life ii) onset of illness between the third and 28th day of life iii) Inability to suckle, followed by generalized stiffness (Muscle rigidity) with or without muscle spasms. The incubation period was defined as the time between an injury and the onset of symptoms and, in neonates, as the time between birth and the onset of symptoms.[5]

The statistical analysis was conducted using version 25.0 of the Statistical Package for the Social Sciences (SPSS). For categorical variables, descriptive statistics were expressed as frequency (Proportion) and for continuous variables, as median (Interquartile range). The significance of the association was examined using the Chi-square test and Mann Whitney U test. The level of significance was considered as $p < 0.05$.

Results

A total of 81 cases of pediatric tetanus were enrolled for the analysis during the study period from 2014 to 2021, with a range of 6 to 18 cases per year and a mean of 10 cases per year. Year wise neonatal and non-neonatal tetanus case distribution is shown in Figure 1. From 2014 to 2021, there were a total of 48170 admissions in the hospital, of which 81 (0.17%) were due to pediatric tetanus and among them, mortality was 28.4%.

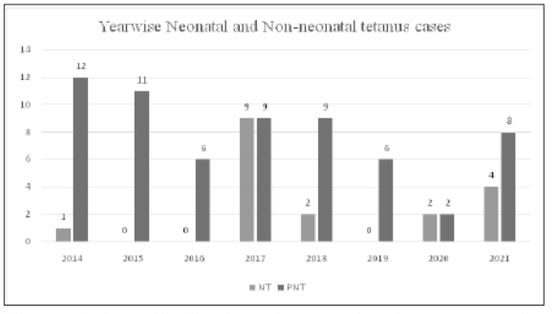

Figure 1 Case distribution of neonatal and non-neonatal tetanus by year

Table I presents the socio-demographic characteristics of the patients. Eighteen (22.2%) cases were neonates (Aged <28 d). The majority of the patients were between 6-10 years of age (28.4%) followed by 11-15 years of age (23.5%), then 1 to <5 years (19.8%) and only five (6.2%) patients were above 15 years. There was no patient in the infant age group. The median age at presentation in the neonatal age group was 10 days (IQR: 7-10.25 days) while in the non-neonatal age group, it was 8 years (IQR: 5-11 years).

Gender-wise distribution showed that 61.7% were male with a male-to-female ratio of 1.6:1. Epidemiological distribution shows that 56 (69.1%) of the patients were from rural areas and six (7.4%) patients were tribal. Among the study patients, 72 (88.9%) were Muslim and others were from different religions.

Among non-neonatal cases (n=63), the entry sites were surface wounds due to trauma in 39 (61.9%) cases and procedures in five (7.9%) cases. Five patients (7.9%) were infected following ear infection or ear pricking by traditional healer and the site of entry could not be established in 11 patients (17.5%).

Table I Demographic and Clinical characteristics of the pediatric tetanus cases (n = 81)

Characteristics		n (%)
Age distribution	<1 month	18 (22.2%)
	1 month-1 year	0
	1-5 year	16 (19.8%)
	6-10 year	23 (28.4%)
	11-15 year	19 (23.5%)
	16-18 year	5 (6.2%)
Gender	Male	50 (61.7%)
	Female	31 (38.3%)
Ethnicity	Tribal	6 (7.4%)
	Non-tribal	75 (92.6%)
Residence	Urban	25 (30.9%)
	Rural	56 (69.1%)
Cause of non-neonatal tetanus (n=63)	Trauma	40(63.5%)
	Otogenic	5 (7.9%)
	Procedure	5(7.9%)
	Unknown	13(20.6%)

The overall common signs and symptoms at admission were lockjaw (85.2%), followed by convulsion (80.2%), fever (44.4%), neck rigidity (38.3%), abdominal rigidity (38.3%) and then opisthotonus (29.6%). The median incubation

period was 7 days (IQR: 5-10 d, Range: 2-30 d). The median duration of symptom onset was 6 days (IQR: 4-7 d, Range: 1-7 d) among neonates and 7 days (IQR: 4-10 d, Range: 2-30 d) among non-neonatal cases. The median duration of illness before hospitalization was 3 days (IQR: 2-5 d, range 1-21 d) and the median length of hospital stay was 16 days (IQR: 3-23 d, Range 1-40 d).

Complications of tetanus were documented in 21 (25.9%) patients. Among them most common was respiratory complication (pneumonia, respiratory failure) in 10 cases (12.3%), followed by shock (7.4%), septicemia (4.9%), wound infection (2.4%), DIC (1.2%), hypoalbuminemia and hypocalcemia (1.2%).

Table II Clinical characteristics of the pediatric tetanus cases (n = 81)

Clinical presentation	Fever (Temp > 38 C)	36(44.4%)
	Lockjaw	69 (85.2%)
	Neck rigidity	31 (38.3%)
	Opisthotonus	24 (29.6%)
	Convulsion	65 (80.2%)
Incubation period, d (Range)		7 (2-30)
Interval between S/S and hospitalization, d (Range)		3 (1-21)
Length of hospitalization, d (Range)		16 (1-40)
Complications	Sepsis	4 (4.9%)
	Respiratory complications	10(12.3%)
	Shock	6 (7.4%)
	DIC	1 (1.2%)
	Hypoalbuminemia	1 (1.2%)
	Hypocalcemia	1 (1.2%)
	Wound infection	2 (2.4%)

In non-neonatal cases, only seven (11%) patients were fully immunized, while 20 (31.7%) were partially immunized and 31(49.2%) were unimmunized. Immunization status was unknown for 7.9% of cases [Figure 2]. The patients who came from the ethnic minority residing in hill tract areas were not immunized against tetanus.

In case of neonatal tetanus, overall, 12 (66.7%) neonates were born to mothers who did not receive a tetanus vaccination at all, two (11.1%) were born to mothers who were partially vaccinated and three (16.7.7%) mothers received two doses vaccine during pregnancy. Only one patient (5.6%) was born to a mother who was completely immunized with five doses of tetanus vaccine before pregnancy.

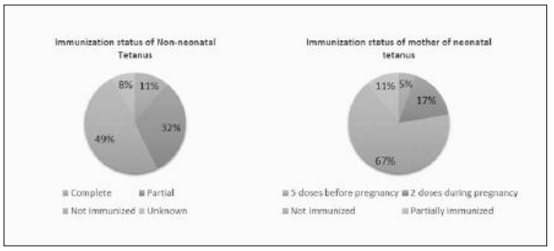

Figure 2 Immunization status of pediatric tetanus cases

Overall in-hospital mortality was 28%. A total of 51 patients (63%) were discharged from the hospital and 9% patients left against medical advice (Figure 3). In-hospital mortality among neonatal tetanus was 44.4% and non-neonatal tetanus was 23.8%.

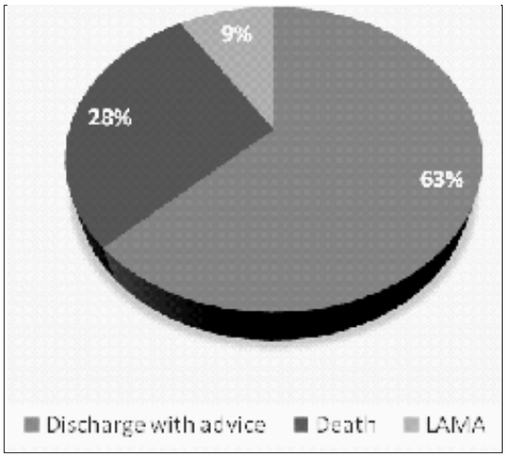

Figure 3 Outcome of the pediatric tetanus cases

Table III shows the comparison of demographic and clinical characteristics of the patients with outcome. No statistical significance was noted in the outcome with different variables like age, sex, residence or cause of tetanus. But, there was a significant increase in mortality among ethnic minority groups (p-value 0.03). Out of 81 patients, 21 (25.9%) developed at least one complication, and this was significantly related to mortality (p=0.02).

The median duration of hospitalization for non-survivors was 2 days (IQR: 1-4). Recovered patients had a significantly longer duration of stay (Median 19.5 days; IQR: 16–25 days) than those who died (p<0.001).

Table III Relationship of clinical characteristics with outcome

Characteristics		In-hospital mortality	Other outcome	p value
Diagnosis	Neonatal Tetanus	8	10	0.08
	Non-neonatal Tetanus	15	48	
Age distribution	<1 month	8	10	0.29
	1 -5 year	4	12	
	6-10 year	5	18	
	11-15 year	6	13	
	16-18 year	0	5	
Gender	Male	16	34	0.36
	Female	7	24	
Ethnicity	Tribal	4	2	0.03
	Non-tribal	19	56	
Residence	Rural	15	41	0.63
	Urban	8	17	
Cause of tetanus	Neonatal	8	10	0.28
	Trauma	10	30	
	Otogenic	0	5	
	Procedure	2	3	
	Unknown	3	10	
Interval between symptom onset and hospitalization		3 (2-4)	3.5 (2-6)	0.06
Incubation period	7 (5-8)	7 (5-11)	0.1	
Length of hospital stay	2 (1-4)	19 (16-25)	<0.001	
Complications during hospital stay	Yes	10	11	0.02
	No	13	47	

Statistical test: Chi-square test and Mann-Whitney U test.

Discussion

In our study, there was total 81 cases of pediatric tetanus of which 18 (22.2%) were neonatal tetanus and 63 (77.8%) were post-neonatal tetanus, giving a mean of 10 cases per year.

The prevalence of neonatal tetanus in this study was 22.2%, which is lower than reported by Chaudhari A. et al. in Gujarat (28.6%), but higher than reported in Nepal by Poudel et al. which was 20.8%.[13,14] So far, no study targeting only pediatric tetanus cases were found in Bangladesh. Among studies on all age group tetanus cases, Ehsan et al reported 7% neonatal tetanus in 2015 and Tauhid et al. reported 8.7% neonatal tetanus in 2021.[15,16] The high rate of neonatal tetanus may be explained by socio-demographic factors like poverty and ignorance, given that the majority of our patients are from rural communities (69%). Besides, their caregivers might not have appreciated the beneficial effect of tetanus immunization in women of childbearing age.

Regarding gender bias, male children were more affected than their female counterparts, with a ratio of 1.7:1. This observation is consistent with the findings of the previous studies from India, Pakistan and Nigeria.[17,18,19,20] The exact reason for the male preponderance is not known. This could be explained by the hyperactive nature of male children who engage in lots of risky physical activities and are more likely to walk and play barefoot, therefore making them more susceptible to injury and exposure to C. tetani which is ubiquitous in the soil. This observation also may be attributed to the perceived higher value placed on male children in certain Asian settings, leading to them receiving more health care compared to their female counterparts.

Notably, the majority of the patients were aged 6-10 years and above, with a median age of 8 years (IQR: 5-11 years). Similar research conducted in developing nations supports this finding.[14,18,19,21,22] The prevalence of patients beyond the preschool age range may be attributed to the decline in immunity against tetanus, which occurs five years after receiving triple tetanus toxoid immunization. This immunological trajectory underscores the importance of incorporating booster doses of tetanus toxoid into the Expanded Program on Immunization (EPI) schedule for children.

In this study, surface wounds resulting from trauma were identified as the most common entry sites (61.9%), a trend consistent with findings in other studies from this subcontinent.[13,18,21,22] This observation may be attributed to the increased likelihood of pediatric trauma going unnoticed and the inadequate provision of tetanus prophylaxis for healthcare-seeking patients.

The median incubation period in the current study was 7 days (Range 2-30 days) which is comparable to other studies, being 7.7 days as observed by Poudel et al. 6.2 days as seen by Mishra et al. and 9.4 days in the study conducted by Mondkar et al.[14,24,18] This study did not find a significant association between the incubation duration and in-hospital mortality (p=0.1), (p=0.1), which is in agreement of the study by Poudel et al.[14]

In our study, common signs and symptoms at admission were lockjaw (85.2%), followed by convulsion (80.2%) and fever (44.4%). This finding is similar to the clinical pattern reported by other studies.[13,14,19,25]

A majority of the mothers were either unvaccinated (67%) or partially vaccinated (11%). However, four babies from vaccinated mothers also developed neonatal tetanus (Three mothers received two doses during pregnancy and one mother completed five doses before pregnancy). Possible explanations for this occurrence could include concerns related to the quality of the vaccine, potential degradation during transportation and inadequate storage facilities. However, these findings should gravely concern us regarding the maintenance of the cold chain of tetanus vaccine, as well as the proper technique and timing for administering Tetanus Toxoid (TT). It is imperative to stress the importance of maintaining the appropriate cold chain for vaccines at all levels. In this study, 89% of cases of post-neonatal tetanus were either not immunized, partially immunized, or had unknown immunization status. Notably, none of the patients hailing from ethnic minority communities living in the hill tract areas received tetanus immunization in this study. In-hospital mortality in this group was significantly high (p=0.03). Our finding signifies the importance of strengthening the immunization program, especially in rural and hill tract regions.

In hospital mortality in our study was 28%, which closely aligns with rates reported by Poudel et al. in Nepal (29%), Mondkar et al. in India (32%) and Tadele et al. in Ethiopia (29.2%).[14,19,23] However, it notably differs from the rates documented by Chaudhary et al. in Gujarat (51%) and Conde et al. in Guinea (53.8%) which were substantially higher.[13,25] Furthermore, it exceeds the rates reported from Pakistan by Duggal et al. (21%).[20] This relatively lower rate of in-hospital mortality in our study and other similar studies from this subcontinent may be attributed to a higher rate of patients Leaving Against Medical Advice (LAMA).

In our study, the case fatality rate for neonatal tetanus was 44.4%, which is comparable to findings by Ehsan et al (50%) and Tauhid et al (53%) from Bangladesh.[16,17] Although the neonatal tetanus group had a twofold higher risk of mortality than the post-neonatal tetanus group, the difference was not statistically significant (p = 0.08).

Recovered patients had a significantly longer duration of hospital stay (median 19.5 days; IQR: 16–25 days) than those who died (Median 2 days, IQR 1-4 days) (p<0.001). This finding suggests that the risk of mortality is highest within the initial days of the illness. This trend implies that patients who can survive this critical early phase tend to have higher rates of survival and eventual hospital discharge. This observation agrees with the findings of previous studies from different countries.[14,19,20,25] Late presentation to the hospital might have contributed to early deaths in some of their patients, though in our study late presentation was not significantly associated with mortality (p= 0.06).

In the present study, the most common complication was respiratory complications like pneumonia and respiratory failure, followed by shock and septicemia. The finding is in agreement with Poudel et al from Nepal.[14] While the study by Chaudhary et al. reported Septicemia as the most common complication.[13] Complications from severe disease were significantly related to in-hospital mortality (p=0.02), which is in agreement with the above-mentioned studies.[13,14]

Limitations

The limitation of this study is its retrospective nature. Poor documentation and missing data are the limitations of this research. In particular, there was a substantial amount of missing data concerning immunization status due to inadequate documentation. Additionally, it was not possible to follow up the patients who were discharged against medical advice, which could have provided valuable insights into their outcomes and recovery.

Conclusion

We observed high mortality rates among neonates and children from ethnic minorities who had not been immunized. This signifies the importance of strengthening routine immunization coverage targeting the rural and hill tract areas. Also, a higher tetanus rate among children older than 5 years implies the necessity of incorporating booster doses of tetanus toxoid into the Expanded Program on Immunization (EPI) schedule.

Recommendation

Conducting large-scale studies to find out the real scenario of pediatric tetanus and also awareness should be created about the necessity of antenatal checkups. Vaccination after injury should be ensured and updated treatment should be practiced.

Acknowledgement

The authors would like to extend their sincere gratitude to the hospital authority for grantingthe necessary permission to conduct the study.

Contribution of authors

HA-Conception, design, acquisition of data, data analysis, manuscript drafting & final approval.
MK-Acquisition of data, critical revision & final approval.
FA-Analysis, critical revision & final approval.
RR-Conception, critical revision & final approval.

Disclosure

The authors declared no conflict of interest.

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