Study of Tetanus in the Infectious Diseases Hospital, Dhaka, Bangladesh
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Abstract:

Background: Tetanus is a vaccine preventable serious disease that can affect people of all age group with a high mortality. Although tetanus incidence is significantly reduced due to nationwide vaccination coverage, it is not uncommon in our country.

Aims & Objectives: To determine of the socio-demographic profile, nature of injury, incubation period and outcome of the tetanus patients who were admitted in the Infectious Diseases Hospital, Dhaka during the study period.

Materials and Methods: This cross sectional observational study was done in the Infectious diseases hospital, Dhaka during the period of February 2017 to January 2018. The data, were collected, compiled and analyzed.

Results: Out of 149 patients, neonates were 13(8.7%) in number. Most of the cases were in middle aged group. Male-female ratio about 4.5:1. Majority of the patients (134, 89.9%) had no history of immunization but one patient was immunized within five years. Mean incubation period tetanus was 8.45 days with ±5.56 SD. Death occurs in 41(27.5%) patients and all of them had no history of immunization. Death rate of patients having early incubation period was significantly higher (p=0.003). Death rate in neonatal tetanus (53.84%) also significantly higher than that of non-neonatal tetanus (25%) (p= 0.026).

Conclusion: Tetanus is not uncommon in Bangladesh, especially in neonates and adult male and mortality rate is high. Short incubation period predicts were outcome.

Keywords: Tetanus, neonatal tetanus, immunization, incubation period, Tetanus mortality.

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Introduction.

Tetanus is a non-communicable infectious disease occurs due to exposure to the spores of the bacterium, Clostridium tetani, that exists worldwide and due to the ubiquity of the bacterium, the disease cannot be eradicated. People of all age can get tetanus but the disease is particularly common and serious in new born baby.\textsuperscript{1} Characteristic symptoms of tetanus are painful muscular contractions, primarily of the masseter and neck muscles and secondarily of trunk muscles. Trismus, or lockjaw, is a common sign of tetanus. Abdominal rigidity is also a common first sign suggestive of tetanus in older children and adult.\textsuperscript{2}

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Tetanus occurs sporadically and almost always affects non immunized, partially immunized, or fully immunized persons who fail to maintain adequate immunity with booster doses of vaccine.\textsuperscript{3} The case prevalence of tetanus is still high, probably due to lack of environmental hygiene, basic health education and inadequate vaccination.\textsuperscript{4} Tetanus is still one of the major killers of adults, children and neonates in developing countries.\textsuperscript{5} Neonatal (or umbilical) tetanus occurs whose mothers are not immunized. It presents as progressive difficulty in feeding (sucking and swallowing), associated hunger, and crying. Paralysis or diminished movement, stiffness and rigidity to the touch, and spasms, with or without opisthotonus, are characteristic.

Most non neonatal cases of tetanus are associated with a traumatic injury, often a penetrating wound inflicted by a dirty object such as a nail, splinter, fragment of glass, or unsterile injection.\textsuperscript{6} Worldwide, tetanus is estimated to cause over 200,000 deaths annually, mostly in neonates and young children, but the disease is so infrequently reported that all figures are only rough estimates.\textsuperscript{7} WHO estimates that in 2015, approximately 34 000 neonates died from neonatal tetanus. There are
no global estimates of tetanus deaths beyond 5 years of age, including for maternal tetanus.\textsuperscript{8} Data on tetanus incidence and mortality among men are limited.\textsuperscript{9} Case fatality rate of tetanus is about 20–50%.\textsuperscript{9} In developing countries, where the mortality rate can be nearly 100% in the newborn and around 40% in others.\textsuperscript{5} Mortality is highest at the extremes of age and in drug abusers.\textsuperscript{7} The incubation period is usually three to 21 days but ranges from one day to several months.\textsuperscript{10} The prognosis is poorer if the incubation period is short and symptoms progress rapidly or if treatment is delayed.\textsuperscript{3}

The aim of our study was focusing on the demographic profile, nature of injury, incubation period, length of hospital stay and outcome of tetanus patients in our hospital; thereby share our experience of managing tetanus patients.

Materials and method:
This cross-sectional observational study was done in the Infectious diseases hospital, Dhaka which is the central infectious diseases hospital in Bangladesh during the period of February 2017 to January 2018. This study included patents of all age group and gender who were admitted in the hospital during the study period with a diagnosis of tetanus. Patient consists of (1) any doubtful clinical diagnosis of tetanus or when other differential diagnosis was present or, (2) When patient or attendant was not interested to participate in the study was excluded from the study. Permission for the study was taken from the hospital authority and consents were taken from the patients/attendance after explanation. Tetanus case was defined by clinical illness characterized by acute onset of hypertonia and/or painful muscular contractions (usually the muscles of the jaw and neck), and generalized muscle spasms without other apparent medical cause and with or without history of injury.\textsuperscript{11} Neonatal tetanus was defined as “any neonate with normal ability to suck and cry during the first 2 days of life and who, between 3 and 28 days of age, cannot suck normally and becomes stiff or has spasms (i.e. jerking of the muscles)”.\textsuperscript{12} Tetanus diagnoses is strictly clinical.\textsuperscript{13} we diagnosed tetanus case clinically. Immunized was considered when at least three or more doses of a vaccine schedule was given.\textsuperscript{8} Early incubation period was considered less than 7 day.\textsuperscript{13} Treatment was started immediately after admission and diagnosis of tetanus according to govt.

protocol for the management of tetanus in Bangladesh\textsuperscript{14} Other disease manifestations and complications were managed accordingly. For control of muscle spasm, large doses of diazepam was required in severe cases and it can be up to 600 mg/day.\textsuperscript{13} Precaution were taken for any adverse reactions (e.g. apnea, hypotension) in acute seizure management when phenobarbital is given after benzodiazepines (e.g., diazepam).\textsuperscript{15}

Details of demographic data of the patients including tetanus immunization history, nature of injury, incubation period, management, length of hospitalization and outcome was obtained regularly and entered in a questionnaire. Tables were then made to summarize the various data of interest. The statistical analysis was performed using statistical package for social sciences (SPSS) version 25.0. The mean ± standard deviation (SD), were calculated for continuous variables. Test of significance was done in chi square test and Fisher exact test. $p$ value<0.05 was considered significant.

Result:
During the study period, a total of 149 patients were enrolled and analyzed for the study. Out of 149 patients, neonates were 13(8.7%) in number and up to five years above neonatal age were 5 (3.4%) in number. Most of the tetanus cases were middle aged group. 30-45 years of age group were 38 (25.5%) and 45-60 years of age group were 35 (23.5%). Mean age of the patients were 35.79 years. Highest age was 80 years and lowest age was 7 days (0.02 yrs) during admission. 81.9% patients were male and 18.1% patients were female giving a male-female ratio about 4.5:1. Out of 149 patients, 14 (9.4%) patients were from urban area and 135 (90.6%) patients were from rural area. Regarding the vaccination status, majority of the patients (134, 89.9%) had no history of immunization and 9 (6%) patients were partially immunized. Six (4%) patients were completely immunized (3 or more doses) among them 1 patients were immunized within five years (Table-I). The natures of injury in most cases were penetrating injury/foreign body (55, 36.91%) and cutting injury (47, 31.45%). History of home delivery or umbilical infection was present in 11 cases (7.38%) out of 13 neonatal cases. Other type of injury include skin/wound infection (7, 4.9%), ear infections/ COSM (4, 2.68%), RTA (4, 2.68%), blunt injury (3, 2.01%), lacerated injury (3, 2.01%), induced abortion (2, 1.34%), burn (2, 1.34%), crushed injury (1, 0.67%). Nine (6.62%)
patients had no definite history of injury (Table II). Mean incubation period tetanus was 8.45 days with ±5.56 SD. Incubation period less than 7 days were in 64(42.95%) patients, more than 7 days were 76 (51%) patients and nine (6.04%) patients were not known. (Table III). Out of 149 patients, 93(62.4%) patients improved and discharged without disability, 9 (6%) patients improved with mild disability and discharged and 6(4%) patients discharge on request before complete cure. Death occurs in 41(27.5%) patients. (Table- III). There was a significant relationship with immunization status, incubation period and age of onset to outcome (survival and death). All death (41) occurred among the patients (88) who had no history of immunization against tetanus and death rate among them was 30.56%. But those patient who were previously vaccinated either partially (9) or completely (6), death rate was zero. Regarding incubation period, 62 patients admitted with history of early incubation period and 26(41.94%) patients died. Seventy four (74) patients admitted with incubation period 7 days or more and 14(18.92%) patients died. Death rate of patients having early incubation period was significantly higher (p=0.003, Odd ratio (95% CI) 3.03(1.32-7.01). Among neonates 7 (53.84%) patients died out of 13 cases and among non-neonates 34(25%) patients died out of 136 cases. Death in neonatal tetanus is significantly higher than death in non-neonatal tetanus ( p= 0.026, Odd ratio (95% CI) 3.50(0.97-12.82). (Table- IV). Mean duration of hospital stay of those patients who survived was 24.05±13.04 (Mean ±SD) days and who did not survived was 3.93±4.96 (Mean ±SD) days.

| Table I |
| --- |
| **Demographic profile (n=149)** |

| Age       | Number of patients | Percentage |
|-----------|--------------------|------------|
| Neonates  | 13                 | 8.7        |
| >28days - 5 years | 5                | 3.4        |
| >5-18 years | 26                | 17.4       |
| >18-30 years | 18               | 12.1       |
| >30-45 years | 38               | 25.5       |
| >45-60 years | 35               | 23.5       |
| >60 years   | 14                 | 9.4        |
| Mean±SD (Years) | 4.95±21.84  | 35.79 ± 20.67 |
| Min-Max (years) | 0.02 - 80     |            |
| Sex        |                    |            |
| Male       | 122                | 81.9       |
| Female     | 27                 | 18.1       |
| Residence  |                    |            |
| Urban      | 14                 | 9.4        |
| Rural      | 135                | 90.6       |
| Immunization |                  |            |
| No history of immunization | 134     | 89.9       |
| Partially immunized (<3 doses) | 9        | 6.0        |
| Immunized (3 or more doses) |        |            |
| Within five years | 1       | 0.7        |
| Within five to ten years | 3       | 2.0        |
| More than ten years | 2       | 1.3        |
Table II

| Nature of injury                                      | Number of patients | Percentage |
|-------------------------------------------------------|--------------------|------------|
| Penetrating injury/Foreign body                       | 55                 | 36.91      |
| Cutting injury                                        | 47                 | 31.54      |
| Umbilical infection/unsafe delivery (neonates)        | 11                 | 7.38       |
| Skin/wound infection                                 | 7                  | 4.69       |
| Ear infection/CSOM                                    | 4                  | 2.68       |
| Road traffic injury (RTA)                             | 4                  | 2.68       |
| Fall from height/Blunt injury                         | 3                  | 2.01       |
| Lacerated injury                                      | 3                  | 2.01       |
| Induced Abortion                                      | 2                  | 1.35       |
| Burn                                                  | 2                  | 1.35       |
| Crushed injury                                        | 1                  | 0.67       |
| No definite history of injury                         | 9                  | 6.62       |
| **Total**                                             | 149                | 100        |

Table-III

| Outcome                                               | Number of patients | Percentage |
|-------------------------------------------------------|--------------------|------------|
| Improved & discharged without disability.             | 93                 | 62.4       |
| Improved & discharged with mild disability            | 9                  | 6.0        |
| Discharge on request (DOR)                            | 6                  | 4.0        |
| Death                                                  | 41                 | 27.5       |
| **Total**                                             | 149                | 100.0      |

Table-IV

| Predictors variable                                   | Death (n=41) (%)   | Alive (n=108) (%) | Total n (%) | Univariate analysis          |
|-------------------------------------------------------|--------------------|-------------------|-------------|------------------------------|
|                                                        | OR (95% CI)        | P value           |             |                              |
| Immunization                                          |                    |                   |             |                              |
| No history of Immunization                            | 41 (30.56)         | 93 (69.44)        | 134 (100)   | -                            |
| History of Immunation (partially or complete)         | 0 (0)              | 15 (100)          | 15 (100)    | * 0.006 s                    |
| Incubation period**                                   |                    |                   |             |                              |
| <7 days                                               | 26 (40.62)         | 38 (59.38)        | 64 (100)    | 3.03 (1.32-7.01) k 0.0037 s  |
| >7 days                                               | 14 (18.42)         | 62 (81.58)        | 76 (100)    |                              |
| Age of the patients                                   |                    |                   |             |                              |
| Neonates (up to 28 days)                              | 7 (53.84)          | 6 (46.16)         | 13 (100)    | 3.50 (0.97-12.82) k 0.026 s  |
| Non-neonates (>28 days)                               | 34 (25%)           | 102 (75%)         | 136 (100%)  |                              |

s =significant
*p value reached from Fisher exact test
** Incubation period of nine (9) patients were not known and excluded from analysis.
k p value reached from Chi-square test.
Discussion:
Tetanus is a rapidly progressing, painful disease with a high mortality rate, yet is inexpensive to prevent.9 High incidence of tetanus in developing countries is due to low levels of health facilities in terms of vaccination and availability of human and material resources.16, 17 In developing countries, tetanus is common among young age group but in developed countries, tetanus is common in older age group.18,19,20 This observation can be explained by the fact that in developing countries tetanus is common in the young due to lack of effective immunization program and inappropriate treatment of injuries.17, 21 whereas in developed countries tetanus occurs mainly in elderly due to decline in protective antibodies.22, 23 In our study tetanus is common in adult population especially 30-60 age group (49%) who are the main working force in our country. Neonatal tetanus are also 13(8.7%) cases in the study indicating the facts of still lacking of maternal immunization, safe delivery and umbilical cord care. Elimination of neonatal tetanus (NT) is a major public health burden. Elimination is defined as less than one NT case per 1000 live birth at district level per year. Higher coverage with tetanus toxoid among pregnant women and in high-risk areas among all childbearing aged women as well as improved access to clean delivery services are primary strategies for achieving this goal.12 Mean age of patient were 35.79 years which is similar (31.2yrs.) with the study of Kole et all.4 This is probably due to immunization program in early childhood but lack of booster doses of vaccine in adolescent age group in Bangladesh. Although both men and women are at risk of tetanus infection, There is an underlying burden of tetanus among adolescent and adult men who have been largely missed by vaccination programmes.9 In our study most of the patient were male (81.9%) as compared to other study,16,18,21,24 This could be explained as follows: First, low vaccination rates among males in the community as compared to females and children who get their vaccination during pregnancy and childhood respectively and Second, men spend more time in outdoor like farming activities and other types of field work and more prone to penetrating injuries. Tetanus can occur, rarely, in fully immunized individuals.25 In the study 134 (89.9%) tetanus patients had no history of vaccination. Remaining 15(10.1%) patient were either partially vaccinated or had at least three doses of vaccine. One important finding has shown in the study that; one of the patients (child) had completed the primary 3-dose TT series according to EPI protocol, but tetanus occurred within five years of age (at three years of age). It indicates the probability that primary 3 dose of TT series may not provide five year immunity against tetanus. WHO recommends 6 doses of TT vaccine for every child through routine immunization (3 primary doses should begin as early as 6 weeks of age plus 3 booster doses preferably be given during the second year of life with at least 4 years interval between booster doses and complete within adolescent age). These will provide protection throughout adolescent and adulthood.8 In the study, the most important risk factor for the diseases was acute injury (e.g., penetrating injury, cutting injury, lacerated injury) which is similar with the findings of Marualappa et al.20 Nine (6.62%) cases had no definite portal of entry. This reflecting that the injuries were very trivial for the patients to be recalled. 24, 26 The outcome of patients with tetanus reported variably. Overall, mortality reported approximately 10-50%.18 According to CDC, case fatality rate of tetanus in USA (2001-1008) is 13.2%.27 In our study overall mortality rate of tetanus patients were 27.5% which is comparable with the study of Kole et al4(21%) and the study of Ramachandra et al28(21.74%) but lower than the study (68.2%) of Khaskheli et al.18 Persistent high mortality from tetanus in developing countries is mainly due to delayed medical attention, limited access to an intensive care facility and associated co-morbidity .4 Tetanus is a life-threatening but preventable disease.26 If tetanus occur in a vaccinated person, illness is usually mild.25 No death occurred in the study among tetanus patients who were vaccinated (either partially or completely); It is probably due to less severity of diseases of previously vaccinated person. All of 41 (100%) death occurred among tetanus patients who were unvaccinated. It indicates that severity of the disease is more in unvaccinated cases which is life threatening. The incubation period of tetanus is usually between three and 21 days (median seven days)13 Mean incubation period of the study was 8.45±5.56 which is similar with the study in monipal hospital,india.28 Shorter incubation period are associated with higher mortality rate.8 Death rate of the patients having early incubation period in the study was significantly higher (p=0.003). Our study have shown neonatal age is an important risk factor for death in tetanus. In neonates, even if treated: death is about
80 to 90%.

In our study, mortality rate of neonatal tetanus (53.84%) was significantly higher than to non neonatal tetanus cases (p=< 0.026). Recovery period from tetanus is usually long. Duration of hospital stay of patients had ranged from 14-28 days.

The longer the duration of hospital stay, the more favorable the outcome. In the study of Aggarwal et al, mean duration of hospital stay in the survival group of tetanus was 19.2 ± 10.7 days. In our study, mean duration of hospital stay in the survival group was 24.05±13.04 and in group not survived was 3.93±4.96 which support the previous study. Long duration of hospital stay and expensive treatment cost make an economic burden on the patients and also for the hospital and for the country.

Conclusion:
In spite of nationwide vaccination program, tetanus including neonatal tetanus is not uncommon in our country and mortality rate is high especially among neonates. Middle aged male preponderance is also noticeable. Incidence and mortality of tetanus can be reduced by universal immunization program irrespective of age and sex, proper wound management and as well as intensive care management of all age group.

Conflict of interest:
The authors declare that they have no conflict of interest.

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