

Pediatric and neonatal tetanus: a hospital based study at eastern Nepal

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ABSTRACT

A prospective hospital based study of childhood (<15 yrs) and neonatal tetanus cases from July 2004 – May 2006 was done to study the demography, clinical features and outcome of pediatric and neonatal tetanus cases at BPKIHS. During the study, 24 cases of tetanus were admitted from 9 districts including 5 neonatal tetanus. Among children with tetanus, 31.5% received 3 doses of DPT and 10.5% received TT vaccine as tetanus prophylaxis. In 16.0% children there was no recognizable injury preceding the disease. Otitis media preceded tetanus in 16.0%. All neonatal tetanus cases occurred following umbilical sepsis. Despite their mothers receiving 2 doses of TT during pregnancy, 2 neonates developed tetanus. A neonate delivered in hospital also developed neonatal tetanus. Average incubation period was 7.7 days and average onset time was 16.9 hours. Short onset time predicted the favorable outcome ($p= 0.005$). Generalized tetanus cases were 75.0%, neonatal tetanus 21.0% and cephalic tetanus 4.0%. Generalized spasm was present in all cases. Common autonomic dysfunctions were fever, tachycardia and hypotension. Respiratory failure, aspiration pneumonia, rhabdomyolysis and seizure were common complications. Only one case received Intensive Care Unit (ICU) care. Survival rate was 21.1% for childhood tetanus and 40.0% for neonatal tetanus. Respiratory failure was the cause of death in majority. Study finds tetanus as an important disease in eastern Nepal, with substantial morbidity and mortality, primarily affecting the unvaccinated and inadequately vaccinated individuals. Despite lack of adequate resources, we can still manage tetanus cases with comparable outcome to other case series reported in the literatures.

Keywords: Tetanus, neonatal tetanus, demography, clinical features, outcome.

INTRODUCTION

Tetanus, also called lockjaw or *Dhanushtankar* (In Nepal) is an acute disease induced by the exotoxin of *Clostridium tetani*. The global incidence of tetanus is about 18 cases per 100,000 population per year, with case fatality rate ranging between 20.0 to 50.0%.¹ It remains endemic in the developing world.² In places like USA, the incidence of this disease has dramatically reduced, whereas in developing countries it is still observed frequently.¹ At least 40.0%-50.0% of deaths occur in neonates especially due to unhygienic conditions during birth and social practices like smearing cow dung or ghee on umbilical stump.^{1,3,4} BP Koirala Institute of Health Sciences (BPKIHS) is a tertiary care centre at eastern Nepal where 282 cases were treated for tetanus with case mortality rate of 34.8% between 1993 and 2003.⁵ Eliminating neonatal tetanus (NT) was the target to be achieved by 2005 as per Expanded Programme on Immunization of Nepal.⁶ But we are still not able to achieve the target. Of the current global burden of NT, 75.0% lies in the following countries-Bangladesh, China, India, Indonesia, Nigeria and Pakistan.⁴ Tetanus is clinically characterized by triad of rigidity, muscle spasm and, if severe, autonomic dysfunction.² There are four clinical forms of this disease.¹ They are generalized, cephalic, localized and

neonatal tetanus.² Several grading systems for severity are reported.^{2,7} The involvement of sympathetic nervous system in tetanus is established, and it predicts poor outcome.^{2,8,9}

The diagnosis of tetanus is primarily clinical.¹⁰ Symptomatic management, early recognition of complications, careful monitoring for dysautonomia and respiratory assistance are the anchors for successful outcome. Immune globulin is given for neutralization of unbound toxin. Diazepam is the mainstay of treatment.² Trujilo and colleagues reported a reduction in mortality from 44.0% to 15.0% after the introduction of intensive care treatment.^{2,11} In developing countries, death from severe tetanus exceeds 50.0% with airway obstruction, respiratory failure and renal failure as prominent causes.² Tetanus is preventable through immunization. Advisory Committee on Immunization Practices (ACIP) has laid guidelines for tetanus prophylaxis in routine wound management.¹² Maternal and neonatal tetanus can be prevented by hygienic practices during childbirth, maternal immunization during pregnancy and supplemental immunization to women of child bearing age.

The aim of the study was to study the epidemiological and clinical profile as well as outcome of tetanus cases

at BPKIHS. By studying the epidemiological profile of tetanus in our set up with limited resources, we can find out the lacunae at prevention level, predict the problems related to tetanus; so that early and effective measures can be taken for prevention as well as management. By studying the outcome, it will be helpful as feedback to a clinician managing a case of tetanus, which will also point out what can be done to improve outcome of tetanus in our set up. By comparing outcome at our hospital with outcomes at various other parts of world, we can review our quality of care to tetanus cases in BPKIHS.

MATERIALS AND METHODS

Study was conducted at BPKIHS, Department of Pediatrics and Adolescent Medicine, from 2004 July to 2006 May. It was a prospective, single centre, hospital based study. All children \leq 15 yrs old, including neonates with diagnosis of tetanus, irrespective of type of tetanus were included in the study. Case of tetanus was defined with following 3 criteria. (a) Any case presenting with localized or generalized spasm suggestive of tetanus. (b) Other causes of spasm (eg. meningoencephalitis, hypocalcemia) ruled out with appropriate investigations when there was diagnostic dilemma. (c) Diagnosis confirmed with independent evaluation by at least two pediatricians. Who fulfilled the inclusion criteria and case definition criteria were enrolled in the study. Detailed history was taken from parents and from closest relatives when parents were not available. Detailed examination was done every day. History, examination findings, progress, complications and outcome were recorded. Investigations were done only when appropriate. Those who left against medical advice and those who died were collectively counted as non survivors. The data collected were analyzed using SPSS statistical software and Ms-Excel. Student t test was applied to calculate P value for the comparison of mean. For comparison of proportion, Fisher Exact test was applied. P value <0.05 was taken as statistically significant.

RESULTS

During the study, 24 cases of tetanus were treated. Of them, 5 cases were neonatal tetanus (NT). Majority of cases (62.5%) were between 6 to 14 years. Mean age of presentation was 7.2 days for NT and 9.1 years for childhood tetanus. Female to male ratio was 1:1. We got cases from 9 districts. NT reported from 4 districts.

Table-1: Comparison of mean incubation period and onset time among survivors and non survivors

Mean Incubation period		
Among survivors (n=5)	Among non survivors (n=16)	p
8.80 \pm 2.95 days	7.31 \pm 3.82 days	0.735
Mean Onset time		
Among survivors (n=5)	Among non survivors (n=13)	p
27.80 \pm 30.80 hours	12.76 \pm 13.54 hours	0.005

Majority of cases were from Jhapa and Udayapur districts- 21.0% cases from each. Among NT cases, only 40.0% mothers visited antenatal clinic during pregnancy and 75.0% mothers did not have any visits. In 80.0% of NT cases, new razor blade was used for cutting the umbilical cord. In all the cases, nothing like oil or mud was applied on cord stump. Among children with tetanus, only 31.6% children received 3 Doses of DPT vaccine whereas 36.8% never received DPT and immunization status was unknown in 31.6%. Tetanus Toxoid (TT) prophylaxis was received by 10.5% children for current injury, however, they developed tetanus. Among mothers of neonatal tetanus cases, 60.0% were unimmunized and 40.0% received recommended 2 doses of TT during pregnancy. Majority (87.5%) of unimmunized cases had lack of knowledge regarding importance of immunization. In one case each, unavailability and familial tradition was cause of non immunization respectively.

Majority (32.0%) of tetanus cases resulted from lacerated wound, 16.0% cases each were due to otitis media and unnoticed minor injury. All neonatal tetanus cases resulted from umbilical sepsis. Average incubation period was 7.7 days with range of 2-17 days. Average onset time was 16.9 hours with range of 2-72 hours. Incubation period was not significantly different but onset time was significantly different among survivors and non survivors, being longer in survivors (Table-1).

Generalized tetanus accounted for 75.0% of cases and 20.8% were NT. No cases of localized tetanus

Table-2: Autonomic dysfunction among tetanus cases

Dysfunction	n	%
Fever (T>100 OF)	20	83.3
Tachycardia	19	79.2
Hypotension/poor perfusion	11	45.8
Hypertension	6	25.0
Cardiac Arrhythmia	1	4.2
Diaphoresis	1	4.2

Table-3: Complications of tetanus

Complications	Total (n)	%
Respiratory failure	11	45.8
Aspiration pneumonia	9	37.5
Rhabdomyolysis / myoglobinuria	9	37.5
Hypoxic encephalopathy	6	25.0
Seizure	5	20.8
Acute renal impairment	5	20.8
Upper gastrointestinal bleeding	3	12.5
Anemia	2	8.3
Apnoea	1	4.2
Disseminated intravascular coagulation	1	4.2
Pulmonary hemorrhage	1	4.2
Tongue bite	1	4.2
Hypoglycemia	1	4.2

encountered. A child initially presented as cephalic tetanus, later progressed to generalized tetanus. Generalized spasm was presenting feature in 94.7% children and 60.0% neonates. Seizure was presenting feature in 5.3% children and 20.0% neonates. At presentation, all neonates had poor sucking, whereas 21.0% children and 20.0% neonates had fever. Generalized spasm appeared during the illness in all children and neonates. Ophisthotonus appeared in 100.0% children and 80.0% neonates. Touch spasm and trismus appeared in all children. Risus sardonicus occurred in 79.0% children and 20.0% neonates. Altered sensorium was present in 31.5% children. Autonomic dysfunction occurred in 96.0% cases. The most common autonomic dysfunction was fever (83.3%), followed by tachycardia (79.2%), hypotension (45.8%), hypertension (25.0 %), cardiac arrhythmia (4.2%) and profuse sweating (4.2%) (Table-2).

The most common complication was respiratory failure (45.8%) followed by aspiration pneumonia (37.5%), myoglobinuria due to rhabdomyolysis (37.5%), hypoxic encephalopathy (25.0%), acute renal impairment (20.8%), seizure (20.8%) and upper GI bleeding (12.5%) (Table-3). Most of the cases were treated in ward. Only 1 case was treated in ICU with mechanical ventilation. Tracheostomy was done in 1 (4.2%) case and 10 (41.7%) cases required endotracheal intubation. Vasopressor drugs were required in 45.0% cases. Diazepam was used to control muscle spasm and 29.2% cases

required chlorpromazine in addition. Seizure was controlled with Phenytoin in children and Phenobarbitone for neonates. Antibiotic used was either Crystalline Penicillin or Metronidazole. Broad spectrum antibiotics were added to treat infections like pneumonia and neonatal sepsis. All improved cases were discharged on oral Diazepam. Meticulous wound care was done. Those who survived, required lower dose of Diazepam to control spasm as compared to those who did not survive, but dose requirement was not significantly different statistically between the two groups (p=0.158). Only few cases were investigated wherever appropriate. Cerebrospinal fluid (CSF) analysis was done in 5 cases, all of them had normal CSF findings. Leukocytosis was present in 25.0% cases, elevated urea level in

20.8% cases, 8.3% cases had elevated serum creatinine, 4.2% cases each had hyponatremia and hypokalemia, 12.5% cases had hypernatremia and 8.3% cases had hyperkalemia.

Survival rate among NT was 40.0% and childhood tetanus 21.1%. Hospital death occurred in 40.0% neonates and 26.0% children (Table-4). A total of 45.8% cases left against medical advice because of financial reasons and clinical deterioration despite adequate treatment. Commonest cause of death was respiratory failure (57.1%). Shock, acute renal failure and cardiac arrest were causes of death in one case each (Table-5).

DISCUSSION

Despite all preventive efforts, tetanus and neonatal tetanus remain endemic problem in developing world. In Asian conditions, where there is no effective surveillance system for vaccine preventable diseases in general, the best assessment of the magnitude of problem may be achieved by community based tetanus and neonatal tetanus surveys. However, such surveys are expensive, lengthy, difficult to perform and cannot be

Table-4: Outcome of neonatal and childhood tetanus

Outcome	Neonatal Tetanus		Childhood Tetanus	
	n	%	n	%
Improved	2	40.0	4	21.1
Death	2	40.0	5	26.3
LAMA*	1	20.0	10	52.6
Total	5	100.0	19	100.0

LAMA* = Left against medical advice.

repeated routinely in small areas to assess the current situation. Results of hospital based studies on tetanus and NT were found to be useful in collecting information on clinical and epidemiological pattern of the disease and in assessing the impact of immunization programme.¹³ The magnitude of NT and tetanus in Nepal is not known with certainty.

In our study, we got 5 cases of neonatal tetanus and 19 cases of childhood tetanus in 23 months of study. Incidence in developed world is quite low, 43 cases per annum in USA with only 1 case of neonatal tetanus in 2 years period (1998-2000).¹² Poland reported only 30 cases of tetanus in 2003.¹⁴ Lau et al reported only 22 cases of tetanus in Sarawak General Hospital in Malaysia between 1990-1998, not even a single case of neonatal tetanus.¹⁵ Situation in developing countries is grave. Single hospital in Uganda reported 284 cases of pediatric tetanus during 5 years (1985-1989) with 32 cases of neonatal tetanus in the year 1989.¹³ More than 100,000 deaths were estimated in India because of neonatal tetanus in 1994.¹⁶ Quddus et al found 38.0% of all the neonatal deaths and 18.0% of the infant deaths in Lorali District Pakistan, because of neonatal tetanus in 1997.¹⁷

Among districts of eastern Nepal, we got cases from only 9 Districts. Probably cases from other districts did not come to BPKIHS, and not because tetanus incidence is low in those districts. Tetanus incidence is higher in children of parents of low education status, as such, parents do not give attention to preventive aspects because of lack of knowledge. In our study most parents were illiterate or just literate. Our and different others studies show that NT is common among home deliveries, particularly when mothers are unimmunized, do not attend antenatal care, deliveries conducted by untrained persons and with unsterile technique.¹⁷⁻¹⁹ Results from the same studies also show that immunization is more important than improvement in delivery practices in preventing neonatal tetanus, though combination of both methods has resulted in elimination of neonatal tetanus in developed world. Training traditional birth attendants in simple practices of hygiene and management of delivery should be emphasized in developing countries like ours. In our study, 1 hospital delivered baby and 2

babies from vaccinated mother also developed neonatal tetanus. But it is just a co-incident finding and limitation of small sample size. However, this finding should seriously make us think about the lacunae at hygiene of delivery practices even at hospital, and maintenance of cold chain of TT vaccine and proper technique as well as timing of giving TT. Maintaining sterility and good hygiene in hospital delivery and maintaining appropriate cold chain of vaccine at all levels should be emphasized. Our study shows 70.0% cases of tetanus were either not immunized or had unknown immunization status and only 10.0% cases received TT prophylaxis as a part of wound management. Study by Lau et al in Malaysia and Eman et al in Saudi Arabia also showed incidence of tetanus exclusively among unimmunized persons.^{15,20}

During the fiscal year 2002/2003, in Nepal, coverage of DPT3 and TT2 vaccine was 90.3% and 42.3% respectively at national level and 94.0% and 45.8% respectively in Eastern Development Region.⁶ With such a high degree of DPT3 coverage, tetanus should be a rare disease in children. However, getting so many cases of tetanus and NT within a short period in a single hospital is not reflecting the impact of given data of immunization coverage. The possible causes for this could be poor effectiveness of vaccine due to improper maintenance of cold chain, improper technique of vaccination or inaccuracy in data collection regarding immunization coverage. This should be seriously investigated.

Long incubation period and period of onset are associated with higher probability of survival.^{1,2,21} In our study, though incubation period was not significantly different (P=0.735), period of onset was significantly longer in survivors (P=0.005). But Arogundade et al in their study did not find any correlation between survival and incubation period and period of onset.²² But one study in 8697 tetanus cases concluded that mortality is inversely related to the length of incubation period.²³

All cases in our study were generalized tetanus. All cases of NT were because of sepsis of umbilical cord stump. Majority of cases were the result of unclean lacerated or cut wounds. Almost 16.0% patients had the otitis media as focus for multiplication of *C. tetani*. Patel et al also found 21.9% of their tetanus cases were because of otitis media.²³ Trismus and generalized rigidity were common presenting features which is similar to other studies.^{15,22} Seizure was quite common presenting feature (20.0%) in our study. Trismus, generalized spasm

Table-5: Causes of death among tetanus cases

Cause of death	n	%
Respiratory failure	4	57.1
Shock	1	14.3
Acute renal failure	1	14.3
Cardiac arrest	1	14.3
Total	7	100.0

and ophisthotonus were the commonest clinical features. In their study by Wasay *et al*, trismus was present in 89.0% cases and generalized spasm in 70.0% cases.⁹ In study by Lau *et al*, body stiffness, trismus and dysphagia were the three commonest clinical features.¹⁵ In our study, trismus, ophisthotonus and generalized spasm were present in all cases. Risus sardonicus, typical of tetanus was present only in 79.0% cases in our study. Altered consciousness is not a feature of tetanus, but in our study, 25.0% cases had altered sensorium. This can be explained with multiple hypoxic insults to brain leading to hypoxic encephalopathy. Wherever the doubt existed regarding the cause of altered sensorium, we did lumbar puncture to analyze CSF to rule out primary brain conditions, (eg.-meningitis) and in all such cases, CSF was found to be normal. In our study, clinical features of NT were almost similar to non neonatal tetanus. We found risus sardonicus as a less common feature of neonatal tetanus and poor sucking as one of the commonest feature.

Autonomic dysfunctions are significant problems in patients with tetanus.¹ Autonomic dysfunctions in our cases were fever, hypertension, hypotension, tachycardia, cardiac arrhythmia and diaphoresis. Different other studies show similar patterns of dysautonomia.^{9,21,23,24} We found fever and tachycardia as the commonest dysautonomia. Though included in autonomic dysfunction, fever could not be accounted for autonomic dysfunction alone. Many cases had concurrent aspiration pneumonia and wound infection, which might have caused fever rather than dysautonomia. Similarly fever could be the cause of tachycardia in those cases. In study by Saltoglu *et al*, fever was present in 49.0% cases, and in 73.0% cases by Patel *et al*.^{21,23} Hypertension in our study was present in 25.0% cases, comparable to study by Wasay *et al* (23.0%).⁹ In our study, hypotension was a common dysautonomia (45.8%), unlike most other studies.^{9,24} Moreover, autonomic dysfunction was present in most of the cases of our study. Since most of the studies for autonomic dysfunction were conducted including all age groups, our statistical result is slightly different from those studies because we studied in pediatric age group only. Another reason could be inclusion of fever and tachycardia as autonomic dysfunction, the cause of which might be infection rather than dysautonomia. But still, autonomic dysfunctions might be more common in pediatric population as we found in our study. This needs confirmation by more studies in larger number of pediatric cases. The most common complication, we encountered was respiratory failure, in 45.8% cases. In study by Eman *et al*, 80.0% cases had respiratory failure, and Patel *et al* reported respiratory failure in 21.7% cases.^{20,23}

Tetanus cases usually require ICU care and mechanical ventilation, which were the primary modes of treatment in most of the studies.^{15, 20, 25} Treatment methods in our study were largely different from most of other published studies in that we had to treat poor patients with limited hospital resources, so that we could not provide ICU care and mechanical ventilation, the key steps of management, to our patients, except for one patient. But mechanical ventilation is probably not the sole factor determining appropriateness of care, as Saltoglu *et al* managed 53 tetanus cases with good outcome (Survival rate = 47.8%) and they used mechanical ventilation in only 13.2% cases.²¹ Diazepam requirement for control of spasm in our study ranged from 20 to 120 mg/kg/day. Doses as high as 100 mg per hour has been reported in adults.^{2,26} Arogundade *et al*, in their study correlated the degree of sedation with poor outcome.²² We also tried to correlate the fact but there was no significant difference between diazepam requirement among survivors and non survivors in our study ($p= 0.158$). Most studies report benefit of use of magnesium sulfate in the management of tetanus.^{9,20,25} In our study we did not use magnesium sulfate in any of the cases as we had little experience about its use and our patients were treated in ward where side effects of this drug could not be monitored accurately, which requires ICU settings. As endotracheal tube seems to be strong stimulus for spasms, tracheostomy is said to be better in tetanus cases for control of airway.²⁵ Still we used ET intubation as the predominant mode of airway control (41.7%) against tracheostomy (4.2%). This needs modification in future.

The outcome of tetanus cases in our study was not satisfactory, as only 21.1% non neonatal cases survived and overall survival (neonatal + non neonatal) was 25.0%. In small series of NT studies, survival ranges from 100.0% in USA to 22.3% in Uganda.^{12,13} We were able to save 40.0% of NT cases in the settings of limited resources. Mortality is lower in children as compared to adults.¹² Many of the studies for non neonatal tetanus survival, were conducted including all age groups and survival rate varies- 84.6% (USA), 47.8% (Adana, Turkey), 44.7% (Osun, Nigeria), 78.0% (Bombay, India).^{12, 21, 22, 24} Still survival rate in our cases (25.0%), seems disappointing. As mentioned earlier, the reasons for low survival rate in our cases were- limited resources, unavailability of ICU and ventilator care when required, poor affordability of patients and high cost of prolonged stay and of large amount of sedative drugs required. The commonest cause of death in our patients was respiratory failure (57.1%). One case each died from shock, renal failure and cardiac arrest. In study by Patel *et al* in 8697 cases, commonest causes of death were respiratory failure (81.2%) and shock (6.7%), a finding similar to

our study.²³ In these days of ventilator era, respiratory failure should be a less common cause of death. When ventilator support is provided early, the causes of death are different. For example, study by Wasay *et al* in 96 patients, 13.5% died of cardiac arrhythmia, 7.3% died of respiratory failure and 1.0% died of shock.⁹ Among 24 cases of our study 11 cases left against medical advice. Among these 11 cases, 7 cases left because patients were deteriorating despite treatment and there was little hope of survival. Four cases left, though they were not deteriorating, because parents could not afford the cost of treatment and hospital stay. The mean duration of hospital stay among survivors was 21.5 days (SD±6.19) with a range of 14 to 28 days. It is comparable to study by Lau *et al* (mean = 21.4 days) and relatively shorter than study by Juma *et al* (3-7 Weeks).^{15,25} Those who died in hospital did so within first few days (Mean 3.75days) (Range 0.25-9days). This shows that risk of dying is highest within first few days of the illness.

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