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CASE SERIES

Neonatal Tetanus Case Series: A Tale of Survival and Tragedy at St Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia

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Background: Neonatal tetanus remains a significant threat in regions with limited healthcare access, despite being preventable through vaccination. The case-fatality rate of untreated neonatal tetanus is close to 100%. Even one case of neonatal tetanus regarded as a failure of the healthcare system, making it essential to remain mindful of this disease's relevance to public health. Two cases of neonatal tetanus are presented, highlighting the severe consequences of the disease. One infant survived after ICU treatment, while the other succumbed despite medical intervention.

Conclusion: These cases underscore the critical need for clean delivery practices and Tetanus anti-toxoid vaccination for women of reproductive age. Improving access to quality antenatal healthcare and promoting clean birth practices are essential in reducing the incidence of neonatal tetanus and preventing unnecessary deaths.

Keywords: neonatal tetanus, home delivery, Ethiopia

Introduction

Neonatal tetanus is a form of generalized tetanus that affects infants under 28 days old. It is primarily contracted by babies born to mothers who were either unvaccinated or inadequately vaccinated. The World Health Organization (WHO) defines a confirmed case of neonatal tetanus as an illness that occurs in infants between three and twenty-eight days old. During this time, affected infants may exhibit stiffness and muscle spasms, hindering their ability to suckle or cry.[1,2]

Tetanus is caused by the bacterium Clostridium tetani, which produces toxins affecting the nervous system. While C. tetani spores are ubiquitous in the environment, the most common cause of neonatal tetanus is the use of non-sterile tools during umbilical cord cutting or applying traditional medicines to the cord stump without proper sterilization. Risk factors for maternal and newborn tetanus (MNT) include deliveries on contaminated surfaces or by individuals with unclean hands. Therefore, stringent measures must be taken to prevent bacterial transmission, especially during childbirth.[2]

Transmission of the bacteria occurs when they come into contact with dead or damaged tissues, such as the wound resulting from cutting the umbilical cord. Factors like unsanitary practices, lack of sterilized delivery instruments, poor hygiene conditions, and limited medical access increase the risk of neonatal tetanus during labor.[2,3]

Although tetanus is preventable through vaccination, it remains a significant cause of morbidity and mortality among children under five years old, particularly in low-resource settings. The under reporting of neonatal tetanus cases, estimated to be less than 5%, suggests that the actual death toll may be higher than documented in many countries. The majority of neonatal tetanus cases are concentrated in 16 African nations, accounting for 90% of global incidents.[4]

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Symptoms of neonatal tetanus typically manifest between 3 and 28 days after birth, with an average onset of 7 days. Initial signs include difficulty in breastfeeding, excessive crying, lockjaw, risus sardonicus (a forced grin with raised eyebrows), opisthotonos (backward arching of the spine), and autonomic nervous system dysfunction leading to respiratory failure. Untreated neonatal tetanus has a near 100% fatality rate, which can be reduced to 10–20% with intensive care.[2,5,6]

The majority of tetanus cases are concentrated in low-resource nations, where the mortality rate is significantly higher due to factors such as inadequate injury care, ineffective immunization, and decreasing levels of protective antibodies.[7] In 2018, neonatal tetanus was responsible for 1% of neonatal deaths, a significant decrease from 7% in 2000.[8] Every year, approximately 3.3 million newborns lose their lives, with neonatal tetanus emerging as one of the primary causes. This disease contributes to 40% of child deaths and a staggering 57% of infant deaths under the age of five. On a daily basis, around 9000 infants succumb to various causes within the first 28 days of life, highlighting the urgent need for effective prevention and treatment strategies.[9.]

In Ethiopia, neonatal mortality rates rose by 1% between 2016 and 2019, with tetanus responsible for 9% of these deaths, translating to 4.5 deaths per 1000 live births.[9]

Neonatal tetanus management does not follow a standardized protocol but aligns closely with the approach for generalized tetanus. Access to intensive care unit (ICU) resources and expertise is vital for the successful treatment of neonatal tetanus cases. Treatment strategies include neutralizing the toxin before it enters the nervous system through human tetanus immunoglobulin (HTIG) and Tetanus antitoxin administration, and inhibiting further toxin production with antibiotic therapy like Metronidazole. Effective muscle relaxation and sedation are typically achieved with benzodiazepines or baclofen. While medications like lorazepam, Midazolam, and Diazepam are commonly used in resource-limited settings, Phenothiazines such as Chlorpromazine are also employed for sedation.[10–12]

Research suggests that administering diazepam alone or in combination with traditional anticonvulsants like phenobarbitone and chlorpromazine may lead to a milder clinical course and shorter hospital stay for neonatal tetanus patients. Additionally, comprehensive care including autonomic instability management, general ICU support, feeding assistance, and ventilatory support is crucial for optimal patient care.

This case series illustrates a neonatal tetanus case with successful treatment and recovery as well as a tragic outcome.

Materials and Methods

This case series was reported from St. Paul Hospital Millennium Medical College in Addis Ababa, Ethiopia, a renowned institution with a workforce exceeding 2800 individuals encompassing clinical, academic, administrative, and support roles. The hospital caters to patients from across the nation, offering specialized medical services and engaging in fundamental and applied research. With a capacity exceeding 700 beds for inpatient care, the facility attends to an average of 1200 emergency and outpatient cases daily.

Both cases were treated at the Pediatric ICU in the Pediatrics department, which admits aged 7 days to 14 years.

Ethical Approval and Consent

St Hospital Millennium medical college has granted approval prior to conducting the case series. The authors notified parents of both neonates about the case series before the investigation. Written informed consent was obtained and verified by parents' signature to include their child in the case series. To protect the privacy of the children, all identifying information has been removed prior to writing this article.

Case 1

Patient Information

- Female neonate.
- Age: 11 days
- Delivery: Home delivery with unsterilized instruments and with traditional birth attendants.

Case Presentation and Hospital Course

An 11-day-old female infant, delivered to a mother without antenatal care, was assisted by a traditional birth attendant at home. The umbilical cord was cut and tied with an unsterilized material. The newborn initially cried and breastfed well but started showing signs of distress on the 9th day, including reduced feeding and a high fever. Additionally, she exhibited abnormal body movements characterized by stiffness in her limbs and loss of consciousness.

Upon arrival at the emergency department, the infant appeared severely unwell, displaying an elevated heart rate, respiratory rate, and fever. Physical examination revealed concerning signs such as a flat fontanelle, respiratory retractions, audible grunting, and hypertonic limbs with rigidity. However, capillary refill was normal, and the pulse was strong. The infant showed depressed neonatal reflexes and presented with a diffuse papular rash on the abdomen.

Tests were conducted, including a complete blood count (CBC), serum electrolyte, organ function test, cerebrospinal fluid analysis (CSF), and C-reactive protein (CRP). Blood culture was also sent. The infant was initially treated with intranasal oxygen and antibiotics for suspected meningitis with Ampicillin and ceftriaxone at anti-meningeal doses, calcium gluconate, and phenobarbitone. She was then transferred to the Pediatric Intensive Care Unit (PICU). Result for cerebrospinal fluid analysis (CSF), and C-reactive protein (CRP). Blood culture came back to be in normal range, negative, and no growth respectively.

Neonatal tetanus was considered due to the characteristic nature of the spasms, and tetanus antitoxin was administered. Metronidazole was initiated, and Diazepam 0.75mg IV was alternated with chlorpromazine (CPZ) 7mg IV four times a day. On the second day of admission, Diazepam was changed to a continuous infusion at 15mg/kg/day, and the infant was placed on continuous positive airway pressure (CPAP) with an FiO2 of 35% and positive end-expiratory pressure (PEEP) of 5.

On the 7th day, the spasms began to decrease in frequency, allowing for the tapering of the diazepam infusion, and Ceftriaxone was discontinued. On the 9th day, the infant developed abdominal distension, with gaseous bubble seen on abdominal ultrasound, which improved with erythromycin for gastrointestinal motility. After 12 days in the PICU, the infant was transferred to the ward and showed continued improvement. Phenobarbitone and diazepam were tapered, then discontinued, and the infant was discharged with a follow-up appointment. Detailed in Table 1.

Case 2

- Male neonate.
- Age: 8 days.
- Delivery: Home delivery with unsterilized instruments and without skilled birth attendants.

Clinical Presentation and Hospital Course

An 8-day-old male neonate, born to a 20-year-old primiparous mother with no antenatal follow-up, was delivered at home with the assistance of a traditional birth attendant. The infant initially cried and fed well but on the fifth day, he developed floppiness and exhibited abnormal body movements characterized by extremity and back stretching. Additionally, he presented with cough and watery diarrhea. Upon presentation to a local hospital, the diagnosis of neonatal tetanus was made, and treatment with Diazepam, cefepime, Tetanus Anti-Toxin (TAT), Ampicillin, and Metronidazole was initiated. Following a three-day hospitalization, the infant was referred to our facility.

Upon admission to PICU of St Paul hospital Millennium medical hospital, the neonate was promptly assessed. He experienced frequent induced and spontaneous spasms, necessitating Diazepam infusion. The infant was intubated and placed on mechanical ventilation in SIMV mode in a darkened environment. Chlorpromazine was administered four times a day, and Phenobarbitone therapy was initiated. Electrolyte analysis revealed hypernatremia at a level of 167, which was promptly corrected through deficit therapy.

On the third day of PICU admission, the neonate developed abdominal distension with coffee ground gastric aspirate. Vitamin K was administered, and a transfusion of fresh frozen plasma (FFP) was initiated. Peripheral pulses were weak,

Table 1 Hospital Course of Case 1

			Admission to PICU	**Day 1**	**Day 3**	**Day 5**	**Day 7**	**Day 8**	**Day 9**	**Day 12**	**Day 13**	**Day 14**	**Day 15**
Vital sign	PR		200	180						110	150	135	148
	RR		64	60						54	52	40	46
	T		40.1	39.8						36.3	36	36.8	36.7
	SaO2		95% with INO2		99% With CPAP O2	98% with INO2		92% with INO2	98% with INO2	97%	94%	93%	92%
Physical Exam	Respiratory system	IC and SC retraction	Severe	Moderate		Mild			None	None			
		Chest sound	Transmitted			Clear			Clear	Clear			
		Other		Grunting		Moderate grunting			Abdominal distension				
	Nervous system	Neonatal reflexes	Depressed,	Absent		Suckling sustained	Spasm decreases	1 episode of spasm, no seizure	Intact	Intact			
		Tone	Hypotonic			Normotonic in LL &Hypertonic in UL			Normotonic	Normotonic			
		Position and spasm	Arched/ opisthotonos, frequent spasm	Arched/ opisthotonos, frequent spasm		1 episode of spasm			No spasm	No spasm			
	Integumentary system		Diffuse papular rush										
		-CSF= normal	Normal										
		CBC= WBC	21.5K mm3						10.36K mm3				
		Blood culture	No growth										
		CRP	Neg										
		Other	Normal Range						Normal range				

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Treatment		CPAP O2 with Fio2 2535%, PEEP=5	Same	INO2	INO2	INO2					
	Calcium gluconate QID							Phenobarbital BID		Phenobarbital BID	
	Ampicillin and Ceftriaxone anti-meningeal dose	Ampicillin and Ceftriaxone anti-meningeal dose		Ceftriaxone anti-meningeal dose	Ceftriaxone anti-meningeal dose			CPZ BID		CPZ BID	
	Loaded with Phenobarbital	Phenobarbital		Phenobarbital BID	Phenobarbital BID	Phenobarbital BID		Metronidazole BID		Diazepam PRN	
	TAT	Paracetamol			CPZ BID	CPZ BID		Diazepam BID		Feeding 35 mL Q 2 hourly	
	Metronidazole TID	Metronidazole TID		Metronidazole BID	Metronidazole BID	Metronidazole BID		Erythromycin daily			
		Feeding 28mL QID		Feeding 24mL QID	Feeding 24mL QID	Feeding 24mL Q 2 hourly		Feeding 27mL po QID			
		Diazepam with CPZ alternatively		Diazepam to continuous infusion PLUS CPZ BID	Diazepam to continuous infusion	Diazepam to continuous infusion		Enema daily			
Plan	Add Diazepam with CPZ alternatively	Follow VS and Spasm	D/c Ampicillin and change CPAP to INO2		D/c Ceftriaxone	Change INO2 to surface O2	Deescalate feeding and Start Maintenance fluid and Enema TID	Transfer to ward	D/C Metronidazole, D/c Erythromycin, D/C Enema	Descalate phenobarbital to Daily dose	D/C Phenobarbital
	-Follow Vital signs	Change Metronidazole to BID	Change Diazepam to continuous infusion.				Start Erythromycin. Change Diazepam IV infusion to QID the to BID after 1 day		Change Diazepam to PRN, Escalate feeding to 25 mL Q 2hourly		

Abbreviations: PR, pulse rate; RR, respiratory rate; SaO2, saturation of oxygen; CPAP, continuous positive airway pressure; INO2, Intranasal oxygen; BID, bis in die; twice a day; TID, ter in die: three times a day; QID, quarter in die four times a day; PRN, pro re nata; As per needed; IC, Intercostal; SC, Sub-costal; LL, lower limb; UL, Upper limb; CPZ, Chlorpromazine; IV, Intravenous; TAT, Tetanus anti-toxoid; WBC, white blood cell; CBC, complete blood count; hg, Hemoglobin; hct, Hematocrit; Cr, Creatinine; RFT, Renal function test; BUN, Blood urea Nitrogen; Na, sodium; K, potassium; Cl, chlorine; CSF, cerebro-spinal fluid; CRP, C reactive protein; D/C, Discontinue; PEEP, Positive end-expiratory pressure.

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prompting a normal saline bolus. Due to an inadequate response and suspicion of septic shock, an adrenaline drip was commenced, followed by the addition of dopamine, resulting in improved palpable pulses. Antibiotics were switched to Meropenem, adjusted for renal function due to anuric status with a creatinine level of 2.02. Anuria persisted for two days, necessitating a Lasix challenge once the child emerged from shock, leading to the initiation of urine output on the second day of the challenge. Concurrently, anemia was identified with Hgb/HCT levels of 10/29, prompting a packed red blood cell (PRBC) transfusion alongside Lasix administration.

On the fifth day of admission, the neonate's pulses began to weaken once more, accompanied by bradycardia readings ranging from 88 to 95. Adrenaline drip was started, while mechanical ventilation parameters were maximized with an Fio2 of 100%. Despite being on maximum mechanical ventilation parameters, the neonate experienced desaturation. The bradycardia persisted, dropping to the 60s and eventually falling below 60. Cardiopulmonary resuscitation (CPR) was promptly initiated and continued for a total of 20 minutes, necessitating the administration of three doses of adrenaline. Tragically, despite all efforts, the neonate could not be revived. The likely immediate cause of death was determined to be multiorgan failure secondary to severe sepsis and neonatal tetanus, as outlined in detail in Table 2.

Discussion

Both cases outlined in this report are in line with existing literature underscoring the significance of unsterile birthing practices in the transmission of neonatal tetanus. The neonates were delivered at home by traditional birth attendants who utilized non-sterile instruments, highlighting the ongoing challenges in promoting hygienic birthing procedures, particularly in areas with limited healthcare access. Despite global initiatives, cultural and logistical obstacles persist, contributing to unhygienic deliveries that pose substantial risks for neonatal tetanus.

The clinical presentations of the two cases showcased the diverse progression of neonatal tetanus. Although both neonates initially exhibited a contaminated cord and displayed feeding and crying abilities, their subsequent trajectories diverged. Case 1 manifested spasms and neurological symptoms, showing positive responses to treatment, whereas Case 2 experienced a more severe course culminating in fatality due to tetanus and uncontrolled sepsis with septic shock. This variability in outcomes underscores the intricate and unpredictable nature of neonatal tetanus, underscoring the literature's assertion that individual cases can exhibit significant variations in severity and responsiveness to interventions.[1,4–9]

The literature review indicates that intensive care can significantly reduce the rate of neonatal tetanus mortality. Case 1 serves as a compelling example, demonstrating the positive response to antitoxin therapy, respiratory support, and care in the PICU. In contrast, Case 2, despite aggressive intervention, resulted in a tragic outcome, shedding light on the challenges involved in managing neonatal tetanus. These challenges include the unavailability of human tetanus immunoglobulin (HTIG) and blood gas analyzers, as well as the high cost of frequent laboratory investigations in Ethiopia. This comparison underscores the critical importance of early recognition and comprehensive care, as well as the ongoing need for advancements in treating severe cases to enhance overall outcomes.[1,4–10]

The literature highlights that neonatal tetanus has a greater impact on low resource regions globally. The cases presented in the literature exemplify this disparity, emphasizing the need for targeted interventions in high-risk areas. Efforts to eliminate neonatal tetanus must address not only the medical aspects but also the socio-economic and cultural factors that contribute to its prevalence, taking a holistic approach to ensure sustained progress in the fight against this preventable disease.[2,3,13]

It is crucial for the global community to maintain a focus on addressing the root causes that drive the prevalence of neonatal tetanus. Enhancing access to quality healthcare, expanding vaccination coverage, and boosting awareness of the risks and outcomes of this preventable disease are essential steps in eliminating it from the most at-risk populations worldwide. By deploying tailored interventions that consider the specific requirements and obstacles encountered by diverse communities, we can progress towards a future where neonatal tetanus no longer claims the lives of children.

Table 2 Hospital Course of Case 2

		Admission to PICU	Day 1	Day 3	Day 4	Day 5	Day 6
CBC	WBC		20.08K mm3			11.71Kmm3	
	Platelet		402k			146k	
	Hg		14.5			11.2	
	Htc		42.5			31.2	
RFT	Cr		1.7	2.02		2.19	
	BUN		61.9	70.6		95.5	
Electrolyte	Na		147	149		147	
	k		-	5.45		5.97	
Treatment		Cefepime	MV Simu mode FiO2 40 FEEP5	MV Simu mode FiO2 40 FEEP5	Same	SIMV FiO2 40 FEEP5	Death
			Diazepam to continuous infusion	Diazepam continuous infusion		Phenobarbital	
		Ampicillin and Ceftriaxone anti-meningeal dose	Ampicillin and Ceftriaxone anti-meningeal dose	Ampicillin and Ceftriaxone anti-meningeal dose		Adrenalin, Nor-adrenaline, and Dopamine infusion	
		Loaded with Phenobarbital	Phenobarbital	Phenobarbital BID		Maintenance fluid	
		TAT	CPZ PRN	CPZ QID		Meropenem	
		Metronidazole TID	Metronidazole TID	Metronidazole BID		Hydrocortisone	
		Diazepam	Feeding 32 mL QID	Feeding 32 mL QID		FFP and vitamin K	
		Feeding 32mL Q2 hourly		Maintenance fluid		CPZ and Lasix	
Plan			Put on deficit therapy for sodium	Add adrenalin infusion	Add nor adrenaline		
				Add Calcium gluconate QID	Change antibiotic to meropenem		
					Transfuse with PRBC and FFP		
					Add Lasix		
					Give diazepam BID Stat		

Abbreviations: PR, pulse rate; RR, respiratory rate; SaO2, saturation of oxygen; CPAP, continuous positive airway pressure; INO2, Intranasal oxygen; BID, bis in die; twice a day; TID, ter in die: three times a day; QID, quarter in die four times a day; PRN, pro re nata; As per needed; IC, Intercostal; SC, Sub-costal; LL, lower limb; UL, Upper limb; CPZ, Chlorpromazine; IV, Intravenous; TAT, Tetanus anti-toxoid; WBC, white blood cell; CBC, complete blood count; hg, Hemoglobin; hct, Hematocrit; Cr, Creatinine; RFT, Renal function test; BUN, Blood urea Nitrogen; Na, sodium; K, potassium; Cl, chlorine; CSF, cerebro-spinal fluid; CRP, C reactive protein; D/C, Discontinue; PEEP, Positive end-expiratory pressure.

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Conclusion

Neonatal tetanus is a fatal disease that can be prevented, but unfortunately, it mostly affects developing countries due to unsanitary birthing practices and limited access to healthcare. The mortality rate associated with this disease is extremely high. In this case series, the tragic stories of the fatal and devastating consequences of the disease could be attributed to delayed presentation that in turn lead to delayed ICU admission, while the success story demonstrates the potential for positive outcomes with early presentation, which in turn lead to prompt ICU intervention. Therefore, it is crucial to take preventive measures, ensure hospital delivery, provide early intervention and ICU management, and offer extensive health education regarding Neonatal tetanus. Moreover, emphasis should be given to improved vaccination coverage and sterile delivery practices in Ethiopia and other developing countries.

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Disclosure

The authors report no conflicts of interest in this work.

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