

NEONATAL TETANUS: THE CURRENT CONTEXT OF CASES IN TAWAU, SABAH, MALAYSIA

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Abstract

Objective: To study the demographic, clinical features, management and outcome of neonatal tetanus treated at Tawau Hospital. **Method:** A retrospective study of neonatal tetanus admitted to a district hospital in Sabah was conducted. **Results:** In 2015, the hospital handled 18 cases of babies with neonatal tetanus in the Tawau Hospital. This implies an occurrence of 1.5 cases per month. All the mothers were non-citizens and did not have any proper antenatal follow up. All the tetanus babies required invasive mechanical ventilation with a median of 20 days (range, 5 to 32 days). The survival rate was 94.4%. **Conclusion:** Despite the promotion of maternal and childhood vaccination along with hygienic practices of delivery, neonatal tetanus still remains a threat to babies born in Sabah.

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Introduction

Tetanus is a long recognized disorder since the 5th century, as described by Hippocrates using the Greek word “tetanos” meaning muscular spasm. There was no means to prevent tetanus until World War I when passive immunization was introduced [1]. Since the introduction of tetanus toxoid vaccination, there has been a decline in tetanus incidence globally.

Tetanus is characterized by a clinical triad of rigidity, muscle spasms, and autonomic dysfunction [2]. *Clostridium tetani*, a gram-positive spore producing obligate anaerobe whose potency lies in its highly lethal toxin tetanospasmin, which is a neurotoxin, causes

tetanus. The spores are resistant to heat and are found ubiquitous in nature mainly in soil, animal intestine and feces [1].

Neonatal tetanus, a rare disease in the developed countries, still accounts for 1% of global neonatal death in 2013, particularly in Southern Asia and sub-Saharan Africa [3]. This is attributed to the absence of passive immunization in babies born to unimmunized mothers; as well as unhygienic delivery and cord cutting practices in rural areas.

Since The Maternal and Neonatal Elimination Initiative by the World Health Organisation (WHO) and its partners in 1989, the proportion of global death from

neonatal tetanus decreased from 14% in 1993 to 1.7% in 2008 [3]. Despite the worldwide effort to advocate adequate immunization and clean delivery practices, neonatal tetanus still accounts for an estimated 49,000 neonatal deaths in 2013 globally [4]. In Malaysia, there were only 0.01 to 0.05 cases per 100,000 of Malaysia's population documented from 2006 till 2010.

Yet Sabah was noted to have the highest incidence and prevalence of neonatal tetanus in the country. Within the 5 years duration from 2006 till 2010, an average of 9.2 cases was reported annually in Sabah, accounting nearly 90% of the total cases reported in the country [5-9] (Table 1).

Table 1. The number of cases and incidence rate of neonatal tetanus in Sabah and Malaysia from 2006 till 2010

	Number of Cases		Incidence Rate (per 100 000 Population)	
	Sabah	Malaysia	Sabah	Malaysia
2006	10	11	0.32	0.04
2007	13	14	0.41	0.05
2008	10	13	0.22	0.03
2009	3	4	0.06	0.01
2010	10	10	0.18	0.02

Background of Study

Tawau is located in the South East coast of Sabah, in close proximity with the Malaysia-Indonesian-Philippines border, hence giving rise to the unique population demographics of different racial, cultural and socioeconomic diversity that is not seen in other parts of Malaysia. Up to 24.5% of Sabah's population are non-citizens [10].

Tawau Hospital is the only multi-specialty hospital in the town of Tawau, with the capacity of 401 beds. It is also the referral centre for several district hospitals in the east coast of Sabah (Tawau, Kunak and Semporna), providing its services to nearly 600,000 of the Malaysian population in the region [11]. The paediatric department of Tawau Hospital currently provides neonatal and general paediatric health care services, through the neonatal and paediatric intensive care unit to general inpatient wards, as well as outpatient specialist clinic.

The paediatric receives more than 5,000 patients per year with approximately 100 patients in the paediatric intensive care unit.

Methods

This study was conducted in Tawau Hospital, Tawau, Sabah, Malaysia. This is a retrospective observational study on neonatal tetanus patients admitted to the neonatal ward between January and December 2015. A total of 18 cases were compiled and analysed.

Dakar score was used to determine the severity and prognosis of the diseases during the respective admissions. It is a prognostic score by a team from Senegal (Dakar, 1975) [12] which can be established after the third day following the first clinical signs: Score 0-1: mild (<10% mortality), score 2-3: moderate (10-20% mortality), score 4: severe (20-40% mortality) and score 5-6: very severe (>50% mortality).

Results

Table 2. Weight, nationality, ethnic group, number of maternal antenatal visit, age of presentation and umbilical cord cutting method of patients with tetanus in Tawau Hospital, Tawau, Sabah in year 2015

Case	Weight (Kg)	Nationality	Ethnic Group	Maternal Antenatal Visit	Age of Presentation	Umbilical Cord Cutting Method
1	3.2	Indonesia	Bajau	No	Day 7	Razor blade
2	2.5	Filipino	Bajau	No	Day 6	Unsterile scissors
3	2.8	Indonesia	Bajau	No	Day 5	Razor blade
4	2.5	Unkpown	Bajau	No	Day 5	Unsterile scissors
5	2.6	Indonesia	Bugis	No	Day 5	Unsterile scissors
6	2.3	Unkpown	Bajau	No	Day 7	Razor blade
7	2.7	Indonesia	Bugis	No	Day 7	Unsterile scissors
8	2.9	Filipino	Bajau	1 visit	Day 3	Razor blade
9	3.4	Unknown	Bajau	No	Day 7	Unsterile scissors
10	2.3	Unknown	Suluk	No	Day 5	Unsterile scissors
11	2.7	Filipino	Suluk	No	Day 3	Unsterile scissors
12	2.6	Indonesia	Bugis	No	Day 6	Razor blade
13	2.9	Indonesia	Bajau	No	Day 4	Razor blade
14	3.1	Unkpown	Bugis	No	Day 5	Unsterile scissors
15	2.7	Unknown	Bugis	No	Day 5	Razor blade
16	2.4	Unknown	Suluk	No	Day 6	Unsterile scissors
17	2.5	Unknown	Bajau	No	Day 5	Razor blade
18	2.7	Filipino	Suluk	No	Day 7	Razor blade

All the mothers were undocumented immigrants. The babies weighed between 2.3 kg to 3.4 kg (mean: 2.7 kg). Out of the eighteen cases, only one Filipino immigrant had one antenatal visit, while the others did not have any visits prior to delivery.

The mean of age of presentation was 5 days (ranging between 3 to 7 days). Every single one of the babies was delivered at home by untrained birth attendants who used either unsterile scissors (50%) or razor blade (50%) to cut the umbilical cord.

Table 3. Laboratory investigations of the patients with tetanus in Tawau Hospital, Tawau, Sabah, Malaysia in the year 2015

Case	Hb (g/dL)	TWBC (x10 ⁹ /L)	Platelet (x10 ⁹ /L)	Sodium (mmol/L)	Potassium (mmol/L)	Urea (mmol/L)	Creatinine (mmol/L)	Dextrostix (mmol/L)
1	14.5	11.7	394	147	5.0	7.0	53	0.7
2	13.7	11.4	389	147	5.2	5.3	70	5.3
3	17.6	14.3	301	154	4.6	6.6	65	2.4
4	12.7	12.4	335	139	6.3	4.1	48	5.3
5	20.4	11.4	280	142	5.6	4.0	52	2.3
6	17.3	19.3	325	144	4.7	6.2	20	2.4
7	16.8	16.8	378	138	6.3	2.2	30	4.7
8	10.4	25.7	490	143	6.0	13.4	140	2.0
9	18.5	15.0	606	137	4.3	2.6	37	5.6
10	19.7	9.1	189	143	4.2	2.7	35	5.0
11	17.2	11.0	319	145	5.2	3.1	51	3.4
12	16.8	14.1	537	141	5.5	7.0	31	3.6
13	12.3	13.5	445	140	5.8	5.0	45	2.8
14	14.3	17.6	332	134	4.5	3.2	31	5.0
15	15.4	12.8	287	137	3.9	2.1	43	4.1
16	16.9	15.4	332	133	4.7	3.7	56	3.8
17	12.6	11.2	450	145	5.1	4.3	66	3.2
18	15.4	19.3	321	138	4.1	3.4	45	2.7

Five babies had hypoglycaemia (dextrostix < 2.6mmol/L) upon arrival to the emergency department. The umbilical swabs which were taken did not yield any *Clostridium tetani*. Lumbar puncture was done in all

patients except for cases 2 and 12 as the mothers did not consent to the procedure.

All the blood and cerebrospinal fluid cultures were negative as well.

Table 4. Umbilical swab, blood and cerebrospinal fluid results of patients with tetanus in Tawau Hospital in Year 2015

Case	Umbilical Swab	Blood C&S	CSF			
			Protein (g/L)	Glucose (%)	Cells	Culture
1	Proteus mirabilis	No growth	3.00	63	Nil	No growth
2	Not taken	No growth	#	#	#	#
3	K. Pneumoniae, Acinobacter calcoaceticus	No growth	0.45	88	Nil	No growth
4	No growth	No growth	1.06	66	Nil	No growth
5	Not taken	No growth	2.70	67	Nil	No growth
6	No growth	No growth	1.00	45	Nil	No growth
7	K. Pneumoniae, E. coli	No growth	*	*	*	No growth
8	Proteus mirabilis	No growth	4.00	69	RBC loaded, WBC loaded (Neu90%, Lym10%)	No growth

9	E. coli, Staph aureus	No growth	0.60	70	Nil	No growth
10	Bacillus	No growth	2.00	60	Nil	No growth
11	Not taken	No growth	1.90	96	Nil	No growth
12	Not taken	No growth	#	#	#	#
13	Proteus mirabilis	No growth	0.60	66	Nil	No growth
14	K.Pneumoniae	No growth	0.70	54	Nil	No growth
15	Staph aureus	No growth	1.10	65	Nil	No growth
16	Not taken	No growth	1.40	77	Nil	No growth
17	Staph aureus	No growth	0.30	80	Nil	No growth
18	Not taken	No growth	1.00	78	Nil	No growth

* Sample not suitable for processing; # Procedure not consented

Table 5. The duration of invasive ventilation, maximum dose of midazolam to control spasm, onset of feeding intolerance and autonomic dysfunction of the patients with tetanus in Tawau Hospital in Year 2015

Case	Duration of Invasive Ventilation (Days)	Maximum Dose of Midazolam to Control SPASM (mcg/kg/min)	Onset of Feeding Intolerance (Day of Illness)	Autonomic Dysfunction
1	5	20	Nil	Absent
2	30	8	18	Present
3	18	10	Nil	Present
4	8	15	Nil	Present
5	26	12	15	Present
6	23	10	Nil	Present
7	12	16	Nil	Present
8	24	10	6	Present
9	29	24	Nil	Present
10	22	16	6	Present
11	32	20	7	Present
12	11	4	8	Absent
13	13	8	Nil	Present
14	21	16	13	Present
15	19	10	Nil	Present
16	25	20	10	Present
17	11	8	Nil	Present
18	9	10	Nil	Absent

All the tetanus babies required invasive mechanical ventilation with a median of 20 days (range, 5 to 32 days). They also received sedation in the form of intravenous infusion of midazolam with a mean of

maximum dose of 13mcg/kg/min in order to control the spasm. 8 (44%) patients developed feeding intolerance while 15 (83%) of them had autonomic dysfunction.

Table 6. Dakar score of the patients with tetanus in Tawau Hospital in Year 2015

Case	Incubation Period (Days)	Period of Onset (Days)	Spasm	Fever (°C)	Tachycardia (BPM)	Entry Site	Dakar Score
1	5 (<7)	< 2	Present	38.3 (< 38.4)	186 (>150)	Umbilicus	5
2	5 (<7)	< 2	Present	38.5 (>38.4)	187 (>150)	Umbilicus	6
3	5 (<7)	< 2	Present	39.0 (>38.4)	178 (>150)	Umbilicus	6
4	4 (<7)	< 2	Present	37.3 (< 38.4)	167 (>150)	Umbilicus	5
5	5 (<7)	< 2	Present	39.6 (>38.4)	144 (<150)	Umbilicus	5
6	5 (<7)	< 2	Present	36.8 (<38.4)	156 (>150)	Umbilicus	5
7	5 (<7)	< 2	Present	36.1 (<38.4)	210 (>150)	Umbilicus	5
8	2 (<7)	< 2	Present	39.3 (>38.4)	172 (>150)	Umbilicus	6
9	6 (<7)	< 2	Present	36.6 (<38.4)	178 (>150)	Umbilicus	5
10	4 (<7)	< 2	Present	36.8 (<38.4)	150	Umbilicus	4
11	2 (<7)	< 2	Present	36.1 (<38.4)	177 (>150)	Umbilicus	5
12	4 (<7)	< 2	Present	38.0 (<38.4)	136 (<150)	Umbilicus	4
13	3 (<7)	< 2	Present	38.1 (<38.4)	168 (>150)	Umbilicus	5
14	4 (<7)	< 2	Present	38.9 (<38.4)	143 (>150)	Umbilicus	5
15	4 (<7)	< 2	Present	39.1 (<38.4)	181 (>150)	Umbilicus	6
16	5 (<7)	< 2	Present	39.7 (<38.4)	158 (>150)	Umbilicus	6
17	4 (<7)	< 2	Present	38.0 (<38.4)	159 (>150)	Umbilicus	5
18	4 (<7)	< 2	Present	38.0 (<38.4)	159 (>150)	Umbilicus	5

The median Dakar score at presentation was 5 (range 4 to 6).

Table 7. Outcome, duration of admission, follow up and complications of the patients with tetanus in Tawau Hospital in Year 2015

Case	Outcome	Duration of Admission (Days)	Follow Up	Complications
1	DAMA	6	Loss to follow up	Nil
2	Alive	52	Loss to follow up	<i>K. pneumoniae</i> sepsis, occipital sore (<i>P. aeruginosa</i>), thigh abscess (ESBL <i>K. pneumoniae</i>)
3	Alive	40	Loss to follow up	ESBL <i>E.coli</i> (tracheal C&S), occipital sore
4	Expired	8	Expired	ESBL sepsis (Intracardiac and LP post mortem C&S: ESBL <i>K. ozaenae</i>)
5	Alive	42	Loss to follow up	Nosocomial pneumonia
6	Alive	35	Loss to follow up	Aspiration pneumonia
7	Alive	27	Developmental up to age	Nosocomial pneumonia
8	Alive	41	Only two follow ups	Aspiration pneumonia
9	Alive	30	Developmental up to age	Nosocomial sepsis
10	Alive	38	Loss to follow up	ESBL <i>K. pneumoniae</i> sepsis (blood C&S)
11	Alive	52	Only one follow up	Occipital sore (<i>P.aeruginosa</i>), MRSA sepsis (blood C&S), aspiration pneumonia
12	Alive	14	Loss to follow up	Aspiration pneumonia
13	Alive	44	Loss to follow up	Aspiration pneumonia

14	Alive	53	Loss to follow up	Nosocomial pneumonia
15	Alive	35	Loss to follow up	Occipital sore
16	Alive	47	Loss to follow up	Nosocomial sepsis
17	Alive	41	Loss to follow up	Occipital sore
18	Alive	28	Loss to follow up	Nosocomial pneumonia

DAMA: Discharge against medical advice; *K. pneumoniae*: *Klebsiella pneumoniae*; *P. aeruginosa*: *Pseudomonas aeruginosa*; *E.coli*: *Escherichia coli*; ESBL: extended spectrum beta lactamase, C&S: culture and sensitivity; LP: lumbar puncture; *K.ozaenae*: *Klebsiella ozaenae*; MRSA: methicillin-resistant *Staphylococcus aureus*

The median duration of admission was 19 days (range, 6 to 53 days). The common complications observed were nosocomial sepsis (6 cases), aspiration pneumonias (5 cases), nosocomial pneumonias (4 cases) and occipital sores (5 cases).

Out of the 18 neonatal tetanus cases that were admitted, 17 (94.4%) were discharged alive. One patient succumbed due to sepsis after eight days of hospital stay. One patient was discharged against medical advice (DAMA). 13 patients defaulted follow up and only 4 patients came to the hospital for review. Out of the four, only two patients consistently came for their clinic appointments while another two subsequently defaulted as well.

Discussion

Neonatal tetanus is a clinical diagnosis as there are no laboratory tests that provide a gold standard for diagnosis. Most of the babies in this series were presented with typical symptoms such as poor sucking, muscle spasm, and fever [13]. Five of them had hypoglycaemia during presentation to the emergency department and this is most probably due to poor sucking and feeding. It is known that the time between getting the infection and manifesting the symptoms is usually between three and ten days [13]; as indicated in this study, from three to seven days. All the babies were delivered at home by untrained birth attendants and the cords were cut via unsterile methods, which we believe is the point of entry for the causative agent i.e. *Clostridium tetani*. A tetanus score (Dakar) was calculated (Table 6), with higher scores being indicative of more severe disease. The patients had a score of 4 to 6, which indicates moderate to severe neonatal tetanus.

Once a diagnosis of neonatal tetanus has

been established, the babies were given high doses of intramuscular human tetanus immunoglobulin of 4,000 units to neutralize the unbound toxin. They were then nursed in incubators covered by cloth, to protect them from any stimulation of light or sound. Every single one of the babies required invasive mechanical ventilation in less than 24 hours upon admission, mainly due to uncontrolled spasms, hypoxia ($SpO_2 < 95\%$) or apnoea. Lumbar puncture was also performed as one of the main differential diagnoses for neonatal tetanus is meningitis.

All the babies received intravenous benzylpenicillin 100,000 units/kg/dose 6 hourly and intravenous metronidazole 7.5mg/kg 8 hourly to eliminate *Clostridium tetani* (as per hospital protocol) because penicillin still remains a standard therapy in many parts of the world; although metronidazole seems to be replacing it and is being considered as first line therapy [14]. Furthermore, in a study conducted by Yen et al, 533 patients randomized to metronidazole required fewer muscle relaxants and sedatives compared with 572 patients randomized to penicillin [15].

To control the autonomic disturbances (diagnosed in the presence of labile blood pressure, tachy- or bradycardia) and muscle spasms in these patients, sedatives, anticonvulsants and muscle relaxants such as midazolam, morphine, phenobarbitone, phenytoin, chlorpromazine, baclofen, and atracurium were used. Some of the babies required high doses of sedatives and anticonvulsants to achieve adequate control of spasms; in case nine for example, the baby required as high as 24 mcg/kg/min of intravenous midazolam infusion.

The majority of these babies developed many complications such as pneumonia, occipital sores, and nosocomial sepsis. They

are often attributable to prolonged periods of immobility, ventilation, critical illness and intensive care [16]. Although the mortality rate was high (based on the Dakar score) in these babies, a survival rate of 94.4% was achieved despite the limited resources in the Tawau Hospital.

The limitation of this study includes the inability to conduct a long-term neurological follow-up review on 15 of the patients as they did not attend their scheduled clinic appointments. Only two survivors returned for treatment consistently, and fortunately, their developmental assessments were appropriate to the age. There were no obvious neurological sequelae. However, significant sequelae such as cerebral palsy, microcephaly, mental retardation, and seizures, were described by Khoo et al. in two of his 17 neonatal tetanus patients [17]. All the patients with sequelae had severe tetanus with frequent and prolonged apnoeic episodes suggesting that brain damage in neonatal tetanus is due mainly to the severity of cerebral hypoxia [18].

Neonatal tetanus is absolutely preventable through immunization and hygienic practices during delivery. Despite the wide availability of maternal and childhood vaccination services to confer protection against tetanus, Malaysia still fails to eliminate neonatal tetanus completely as the majority of the cases appear to be occurring primarily in undocumented immigrants in Sabah, as were reported in the Sandakan [19] and Kota Kinabalu [20] studies respectively.

The reason for the high incidence rate of neonatal tetanus in Sabah is thought to be multifactorial. Sabah is one of the most under developed states in Malaysia. Its mountainous lands with dense rain forest coverage cause a large part of the state to be

inaccessible. Therefore, access to the healthcare services is very difficult despite the continuous effort from the government to expand the public healthcare network.

Furthermore, the immigrant mothers may not be fully aware of the antenatal services provided by the public health care services or they may be fearful of facing deportation to their homeland if they were to show up in the existing government clinics. Should our Malaysian health care design a programme to reach out to those immigrant mothers to provide antenatal care and subsequently curb the onslaught of neonatal tetanus in Sabah? This concern requires further deliberation.

Conclusion

WHO estimated that in 2013, 49,000 newborns died from neonatal tetanus, which is a 94% reduction from the situation in the late 1980s [4]. Despite the promotion of maternal and childhood vaccination along with hygienic practices of delivery, neonatal tetanus still remains a threat to babies born in Sabah. However, changes in the healthcare and its reach out systems may contribute to the eradication of neonatal tetanus in Malaysia, especially in Sabah.

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