

Snakebite mortality at Port Moresby General Hospital, Papua New Guinea, 1992–2001

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The estimated snakebite mortality in Papua New Guinea (3.5/100 000 population per year) is about 100-fold higher than in Australia.¹ There are concerns that this rate is increasing, perhaps because of inadequate antivenom supplies — an international problem that is particularly acute in the Indo-Pacific region.^{2–4} Detailed studies of the problems of snakebite in PNG were last carried out a decade ago; however, such investigations were generally restricted to patients receiving antivenom and were not specifically focused on mortality.^{1,5–11}

Port Moresby General Hospital (PMGH) has the largest caseload of seriously envenomed patients in PNG. Between 1990 and 1992, snakebite is said to have accounted for about 50% of all patients requiring ventilation at this hospital.⁵ Enzyme-linked immunoassays attributed 94% of serious snakebites to two species: 83.2% to Papuan taipans (*Oxyuranus scutellatus canni*) and 10.8% to death adders (*Acanthophis* spp.).¹

The aim of our study was to investigate snakebite mortality at PMGH as a means of identifying factors that currently contribute to poor clinical outcomes after snakebite. This should provide the basis for developing sustainable initiatives to improve the prognosis for snakebite across PNG.

METHODS

We conducted a retrospective analysis of snakebite admissions to PMGH between 1 January 1992 and 31 December 2001. Our focus was on snakebite mortality within the intensive care unit (ICU).

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ABSTRACT

Objective: Fatal snakebites at Port Moresby General Hospital (PMGH), Papua New Guinea (PNG), were examined to identify interventions that may improve patient survival.

Design: Retrospective case series.

Subjects and setting: Inpatients at PMGH who presented with snakebite, had evidence of envenomation, and died as inpatients between 1 January 1992 and 31 December 2001.

Outcome measures: Number and cause of fatalities; ventilation bed-days; antivenom timing, dose and price.

Results: 87 deaths occurred among 722 snakebite admissions to the intensive care unit (ICU). Of these 722 patients, 82.5% were ventilated, representing 45% of all ventilated ICU patients and 60% (3430/5717) of all ICU ventilator bed-days. The median duration of ventilation in fatal snakebite cases was significantly less than in non-fatal cases for children (3.0 v. 4.5 days) and adults (3.0 v. 5.0 days). The case-fatality rate for children (14.6%) was significantly greater than that for adults (8.2%). Sixty fatalities were examined in detail: 75% received blood products; 53% received antivenom (mostly a single ampoule of polyvalent), but only 5% received antivenom \leq 4 hours post-bite. Major causes of death included respiratory complications (50%), probable intracerebral haemorrhage (17%), and renal failure (10%). Antivenom unit costs increased significantly over the decade; in 2000 an ampoule of polyvalent antivenom was 40-fold more expensive in PNG than in Australia on a gross domestic product (A\$) per capita basis.

Conclusions: Management of severe snakebite is a major challenge for PMGH. Improved antivenom procurement and use policies (including increased use of appropriate monovalent antivenoms), combined with targeted snakebite education interventions (community- and hospital-based), are key interventions to reduce the ongoing toll from snakebite.

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Patient identification

Hospital logbooks were examined by hand, and available data for each snakebite patient were retrieved. A diagnosis of snakebite envenomation was defined by:

- *Evidence of neurotoxicity:* Specific signs of venom-induced neurotoxicity (including ptosis, dysphagia, dyspnoea).

for 20 minutes remains unclotted) and/or spontaneous bleeding; or

- *Evidence of neurotoxicity:* Specific signs of venom-induced neurotoxicity (including ptosis, dysphagia, dyspnoea).

Patients were excluded if another obvious cause of death (unrelated to snakebite) was described in the notes.

Data collection

Data were obtained regarding the age, sex, duration of admission, duration of ventilation and outcome for each snakebite patient treated in the ICU. Examination of records from the high dependency unit identified additional deaths. Fatalities were identified and all available medical records were reviewed. Clinically relevant data in medical records were recorded on structured case report forms for each patient by either of two trained researchers, according to predetermined clinically relevant definitions. Rel-

evant epidemiological and demographic data were also collected. A random sample comprising 20% of the total was simultaneously analysed by two of the researchers to ensure agreement of interpretation and thus inter-rater reliability.

Patients were classified as children (<15 years) or adults (≥15 years).

Seasonal occurrence was recorded as either the “rainy” (November to April) or “dry” (May to October) season, consistent with previous definitions.⁵

Locality was defined as “urban” (within a 20 km radius of Port Moresby) or “rural” (>20 km from Port Moresby).

Antivenom costs

Data on antivenom costs were obtained from the PNG Department of Health.

1 Signs and symptoms in 60 patients who died of snakebite, 1 January 1991 to 31 December 2001

Symptom or sign	Present		Not documented
	Absent	Present	
Abdominal pain	4	48	8
Vomiting	13	40	7
Headache	9	38	13
Collapse within 30 min	45	7	8
Neurotoxicity*	0	60	0
Tender lymph nodes	2	49	9
Spontaneous bleeding	15	35	10
Muscle pains	6	25	29
WBCT ≥20 min	11	45	4

* Defined by one or more of ptosis, dysphagia or dyspnoea. WBCT = whole blood clotting test

Statistical analysis

Summary statistics were obtained using Microsoft Excel. Analysis of mean ventilator bed-days was performed using Student's *t* test for equal variances. The Mann-Whitney *U* test was used to compare median ventilation times in both fatal and non-fatal cases, and the χ^2 test was used to compare the adult and child case-fatality rates.

Ethics approval

Ethics approval was obtained from the PNG Medical Research Advisory Council.

RESULTS

Inpatient deaths

We identified 722 patients as being admitted to PMGH ICU for snakebite envenomation during the study period: 260 (36%) children and 462 (64%) adults. Eighty-nine of these people died. Two adults were excluded: one who died from burns incurred after snakebite, and another because no snakebite was documented in the medical file. Sixty medical files from the 87 fatalities (32 adults; 28 children) were available for detailed study.

Demographics

Most fatal bites originated in rural areas (73%), and occurred during the rainy season (60%). Time-of-bite data were available for 70 patients: 42 of these bites occurred in the afternoon. The location of the bite site was recorded for 86 patients: 77 were bitten on a lower limb.

Sex and age distribution

Forty-six patients were male (53%), and 22 of these (48%) were children. Of the 87 fatalities, 41 (47%) involved children. The ratios of males to females were the same in both adults and children.

First aid

Pre-hospital management was reported in 19 of 60 patients. Pressure bandages had been applied in six, and 13 had scarified the bite site. The use of tourniquets was recorded in two instances.

Symptoms and signs

Key clinical features from the 60 patients for whom medical files were available are shown in Box 1.

Blood defects

20WBCT results were recorded for 56/60 patients. Blood was incoagulable after 20 minutes in 45 patients (80%). Spontaneous bleeding was reported in 35/60 patients (58%). One patient had thrombocytopenia, and four had post-bite anaemia (haemoglobin decrease >30 g/L).

Blood products

Blood products were given to 45/60 patients (75%): all 45 received fresh frozen plasma (modal dose, 2 units; range, 1–9 units); 20 also received whole blood (modal dose, 2 units; range, 1–4 units) and four received packed cells (2 units each).

Renal function

Renal impairment (defined by serum creatinine level rising from <0.10 mmol/L to >0.20 mmol/L) occurred in 22/60 (37%) patients who died, and renal failure (defined by anuria) was present in four (7%).

Antivenom administration

Antivenom was administered to 32/60 (53%) patients, but only three (5%) received antivenom within 4 hours of the bite (Box 2). Twenty-one patients received blood products as well as antivenom. Of the children who were ventilated in the ICU and died, 13/26 (50%) received antivenom, but only two of these received it within 4 hours of the bite.

Dose and type of antivenom

With one exception, all patients who received antivenom were treated with a single ampoule. Twenty-two patients received CSL polyvalent antivenom; eight more received CSL taipan antivenom; and one received CSL death adder antivenom. One patient received an ampoule each of CSL polyvalent and CSL black snake antivenoms. No formal snake identifications were documented and the CSL Venom Detection Kit (VDK) was not used.

2 Use of antivenom in 60 patients who died of snakebite

Time after bite (hours)	Clinic records (n=29)		PMGH records (n=60)	
	Number of patients*	Number given antivenom†	Number of patients*	Number given antivenom†
<4	24	1	19	2
4–10	4	1	22	10
>10	1	2	19	16
Total	29	4	60	28

* Number who arrived at a primary health clinic or Port Moresby General Hospital (PMGH) within the stated time. † Number who received antivenom within the stated time.

3 Ventilation times and total ventilator bed-days for fatal and non-fatal snakebites

	Fatal snakebites			Non-fatal snakebites		
	Children	Adults	Total	Children	Adults	Total
Number of admissions	38	38	76	222	424	646
Number ventilated	36 (95%)	38 (100%)	74 (97%)	186 (84%)	336 (79%)	522 (81%)
Median (95% CI) ventilation time (days)	3.0 (2–5)	3.0 (1–4)	3.0 (2–4)	4.5 (4–5)	5.0 (5–6)	5.0 (5–5)
Number of ventilation bed-days	164	171	335	943	2152	3095
Proportion of snakebite ventilation bed-days (%)	4.8%	5.0%	9.8%	27.5%	62.7%	90.2%

Duration of ventilation

Over the decade, the most common reasons for ventilation at PMGH did not alter, apart from one month when the Australian (Surgical) Heart Team was at the hospital (data not shown). Of the ICU snakebite patients, 596/722 (82.5%) were ventilated, including 222 (85.4%) children and 374 (81.0%) adults (Box 3). Snakebite accounted for 45.0% of all 1325 patients ventilated during the study period, but took up 60.0% (3430/5717) of all ventilator bed-days (total number of days ventilated) (Box 4). The median duration of ventilation was significantly longer ($P < 0.005$) for snakebite patients (5.6 days) compared with all other ventilated patients (3.1 days).

For the 222 ventilated children, the median ventilation time for those who died (3.0 days) was significantly shorter ($P < 0.02$) than for those who survived (4.5 days). Similarly, considering the 374 ventilated adult patients, the median ventilation time for those who died (3.0 days) was significantly shorter ($P < 0.001$) than for the others (5.0 days).

Mechanism of death

Respiratory causes were implicated in half the fatalities. Respiratory arrest occurred in 17/60 patients (28%), with median time to hospital presentation of 13 hours, and median intubation of 14 hours. Eleven of these 17 patients had received antivenom; but only one received it within 4 hours of being bitten. Another three patients suffered cardiorespiratory arrest during hand-ventilation by relatives. Three deaths resulted from self-extubation, and another patient died from sudden loss of supplemental oxygen. Six patients died from pneumonia, and two other deaths were attributed to acute respiratory distress syndrome.

The deaths of 10 patients with uncoagulable blood (20WBCT ≥ 20 min), spontaneous bleeding and deteriorating neurological status were attributed to intracranial haemorrhage. Although the Glasgow Coma Score was recorded, focal neurological signs were not. Renal failure was reported as the cause of six deaths, including two patients undergoing peritoneal dialysis. Profound respiratory depression and renal failure were coexistent contributors in five deaths, and another five patients had presumed intracranial haemorrhage and concurrent renal failure. Two deaths were attributed to overwhelming sepsis.

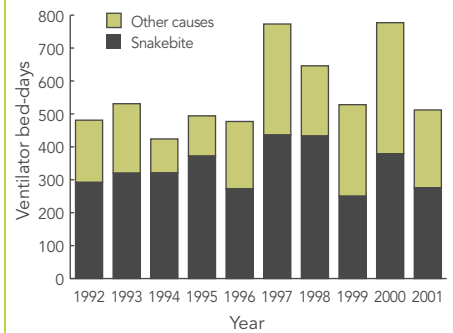
ICU case-fatality rates

The overall ICU case-fatality rate was 10.5% (76/722), with a significant difference ($P < 0.01$) between the case-fatality rates for children (14.6%; 38/260) and adults (8.2%; 38/462). Similar results ($P < 0.05$) were obtained comparing deaths between ventilated children (16.2%; 36/222) and ventilated adults (10.2%; 38/374).

Antivenom costs

The unit cost to the PNG Health Department, on a per-ampoule basis, of taipan monovalent and polyvalent antivenom over the study period is presented in Box 5. Between 1992 and 2000, the local price of CSL polyvalent antivenom almost quadrupled and the price of CSL taipan antivenom more than doubled. Comparing PNG and Australian polyvalent antivenom prices in terms of GDP/capita per ampoule, costs increased from being 19 times more expensive in PNG in 1992 to 38 times more expensive in 2000. It should be noted that this does not represent the price for those wanting to purchase direct from the importer or local pharmacy, where a pre-

4 Ventilator bed-days: snakebite compared with all other causes



Data were extracted from Port Moresby General Hospital Intensive Care Unit logbooks.

mium is charged above the PNG Health Department price.

DISCUSSION

This is the first study that specifically examined snakebite mortality in PNG. Previous reports on this subject have overwhelmingly focused on morbidity among patients receiving antivenom in an era of lower antivenom prices.^{1,5-11} Unfortunately, the reality over the past decade has changed from a situation where most snakebite patients received antivenom to one of restricted antivenom availability and its delayed administration.¹³

Financial constraints mean that many investigations considered routine for snakebite in Australia are often unavailable at PMGH, and cultural factors result in low autopsy rates.^{14,15} One consequence is that studies such as ours are limited to information available in medical notes. Moreover, hospital records are not always readily available, impeding access to meaningful data. Despite these limitations, we were able to demonstrate that envenomation places a greater burden on PMGH ICU ventilators than all other conditions and that the duration of dependency for snakebite was significantly longer than for other diagnoses, undoubtedly adding to treatment costs. This represents the highest proportional ventilator load reported for snakebite in any hospital worldwide.

The second major finding of our study related to the worsening outcomes for children. A study during the 1980s found that 29.6% of children admitted to PMGH ICU with envenomation required intubation, 91% received antivenom, and the case-fatality rate was 7.7%.⁶ In contrast, in our study,

5 Prices (per ampoule) for CSL polyvalent and taipan antivenoms to the Papua New Guinea Department of Health

Year	Reference	CSL polyvalent		CSL taipan		Polyvalent antivenom cost (GDP per capita) [†]
		Kina	A\$*	Kina	A\$*	
1985	16	212	300	173	245	Not available
1987	16	367	580	352	556	Not available
1992	18	803	1180	730	1073	0.88
1995 [‡]	18	1739	1758	1604	1620	1.20
1998 [§]	18	2352	1811	2338	1800	1.36
2000	18	2960	1835	1740	1079	1.52
2003 [¶]	18	3575	1833	3075	1577	Not available

* Equivalent cost in Australian dollars. † Cost of one ampoule of polyvalent antivenom as a multiple of the PNG GDP (A\$) per capita.¹² In 2000, the Australian GDP (A\$) per capita was \$33 000,¹² and the polyvalent antivenom cost as a multiple of GDP (A\$) per capita was 0.04 (2.5% of the PNG value). ‡ The kina was deregulated in 1995. § Before 1998, antivenom was purchased directly from CSL Ltd; since then, it has been purchased from a wholesaler. ¶ In 2003, the costs to Australian hospitals of CSL polyvalent and taipan antivenoms were \$1270 and \$1160, respectively (excluding GST) (Victorian Hospital and Government Price List).

85.4% of children admitted to the ICU were intubated and ventilated, antivenom use was only documented for 50% of the children who died, and the paediatric case-fatality rate was 14.6%. Ventilation was also a key feature in the management of the adult ICU admissions.

Increased reliance on ventilation may be a consequence of inadequate antivenom supplies due to rising costs, influenced partly by the floating of the kina and its subsequent devaluation against the Australian dollar.^{2,3,16} The cost issue is even more extreme when considering direct antivenom purchases from Port Moresby pharmacies by individuals when PMGH stocks have been depleted. However, comparison of year 2000 GDP/capita antivenom costs shows that antivenoms cost less in India (which produces its own antivenoms) than in Australia, indicating that not all developing nations suffer the same fate as PNG.¹⁷ Since 1998, PNG has purchased antivenom from a wholesaler instead of directly from the manufacturer.¹⁸ Direct purchasing from CSL of less expensive monovalent antivenoms in combination with appropriate diagnostic use of the simple 20WBCT and CSLs VDK should not only generate significant unit cost savings, but also result in increased stock availability.

Previous studies have found that delays in the administration of antivenom significantly increase the necessity to intubate snakebite patients at PMGH.^{7,9} Patients who received antivenom within 4 hours of being bitten were three times less likely to require intubation, exhibited more rapid resolution of neurotoxicity, and had shorter hospital

stays.⁷ Unfortunately, even though many patients in our study arrived at a health facility (either a peripheral clinic or PMGH) within 4 hours of the bite, very few received antivenom within that period (Box 2).

Despite clear guidelines for appropriate antivenom administration, their relevance becomes questionable in the absence of adequate antivenom supplies. Consequently, antivenom is often reserved for moribund patients, and its use may be delayed until significant deterioration has occurred.^{19,20} During the 1960s, patients who developed paralysis often received up to four ampoules each.^{21,22} Since then, antivenom use has become more frugal, although in the 1980s and early 1990s most patients received at least one ampoule.^{5,9} This study shows that the treatment focus has switched from high antivenom availability and use with lower rates of ventilation to one of low antivenom availability and consequent high rates of ventilation. This is despite clear advice that snakebite deaths in PNG may be prevented by more widespread availability of antivenom.²³

This is the first study to detail the use of blood products in envenomed patients in PNG. Given the concern about intracranial haemorrhage in the context of a bleeding diathesis, use of products such as fresh frozen plasma might appear reasonable. However, blood products are scarce and expensive, their value in the treatment of snakebite coagulopathy is unclear, and they are potentially hazardous. Moreover, previous studies have demonstrated that systemic bleeding generally resolves rapidly after

administration of appropriate amounts of specific antivenom.⁹

Previous studies have found that the positive predictive value (PPV) of a 20WBCT ≥ 20 minutes for diagnosis of Papuan taipan envenoming is 96%.⁷ In our study, 75% of patients had a 20WBCT ≥ 20 minutes, but only 25% of those who received antivenom received taipan monovalent. Given the gap between the cost of polyvalent and monovalent antivenoms, the recommendations that all envenomed PMGH patients with incoagulable blood should receive monovalent taipan antivenom, and that CSL Venom Detection Kits be used to enable monovalent antivenom selection in cases without coagulopathy, remain relevant.⁷ Such protocols should significantly reduce per-patient antivenom costs and increase overall antivenom availability.

Our study confirms previous findings that about 20% of snakebite patients present to hospital more than 10 hours after the bite.⁷ While some of these patients may consult traditional healers before seeking medical services, transportation difficulties on poorly maintained roads are probably a more important factor, with many rural health centres lacking functioning ambulances and communications infrastructure.^{24,25} Potentially dangerous first aid techniques, such as scarification, also persist in PNG and are reported more frequently than the application of pressure bandaging.^{9,24,25} Infrequent use of pressure immobilisation is a continuing challenge for community education in Australia and PNG, but it is encouraging to note an apparent reduction in tourniquet use reported at PMGH since the 1980s.^{1,5,26}

System failures and equipment deficiencies contributed to several of the deaths, and included ICU bed and staff shortages that led to intubated patients spending lengthy periods in the emergency department, where they could not be adequately monitored and, on occasion, self-extubated as a result. Ventilator shortages often resulted in relatives being required to rotate hand-ventilation of paralysed patients. Even in a well-equipped Australian ICU, snakebite can be a challenging condition to manage. The difficulties of managing venom-induced multi-system failures are compounded in PNG by precarious health infrastructure²⁰ and increasing antivenom costs, which are further exacerbated by economic instability and a devaluing currency.

Development of protocols that increase availability of less expensive monovalent

antivenoms, in conjunction with appropriate diagnostic criteria for their use, may improve prognoses; however, resources also need to be committed to ensuring that adequate life support facilities and other infrastructure are available. We reinforce recent calls for wider public snakebite first aid education, and the development and implementation of appropriate snakebite management protocols for both rural clinics and urban hospitals.^{2-5,9}

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COMPETING INTERESTS

None identified.

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