

Necrotising fasciitis: an 8.5-year retrospective case review in a New Zealand intensive care unit

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Invasive soft tissue infections were first described in the 5th century BCE, but the term *necrotising fasciitis* was first used in 1952.¹ It describes a rapidly progressive soft tissue infection involving the subcutaneous tissue, fat and fascia, but typically sparing muscle. It is associated with extensive necrosis, profound shock and high morbidity and mortality.

Incidence has been reported at 500–1500 cases per year in the United States and 500 cases per year in the United Kingdom.² Early diagnosis is notoriously difficult, yet essential, as patients require aggressive resuscitation, early surgery and optimal antimicrobial therapy for the best chance of survival.^{3–5}

Infection is classified as:

- type 1 — polymicrobial, usually seen in patients with comorbidities (eg, diabetes or peripheral vascular disease), and involving anaerobic and/or aerobic bacteria; or
- type 2 — due to group A β -haemolytic streptococci and/or *Staphylococcus aureus*.

Most patients require multiorgan system support in an intensive care unit and repeated surgical procedures for aggressive debridement of necrotic tissue. Survivors may require extensive rehabilitation and have marked residual disability. Fiscal impact on health care systems is significant.⁶

Non-steroidal anti-inflammatory drug (NSAID) use has been implicated as a risk factor for necrotising fasciitis, but this remains controversial. Biological plausibility exists and published literature suggests a possible association, but this is unproven.^{7–14}

Middlemore Hospital is a tertiary hospital that serves a catchment population (Counties Manukau District Health Board [CMDHB]) of 473 000 in South Auckland, New Zealand. The catchment population has high proportions of Maori (17%) and Pacific Islander (21%) people. More than a third of the population (34%) live in areas rated as “very deprived” on the New Zealand Deprivation Index.^{15,16}

In this study, we aimed to determine the incidence and clinical characteristics of those patients presenting to our ICU with necrotising fasciitis, with a view to highlighting comorbidities associated with mortality. In addition, we aimed to ascertain any significant association with NSAIDs.

Methods

We performed a retrospective review of all patients with a diagnosis of necrotising fasciitis admitted to Middlemore

ABSTRACT

Background: Necrotising fasciitis is a rare, rapidly progressive soft tissue infection associated with extensive necrosis, profound shock and high morbidity and mortality. Incidence worldwide is thought to be increasing.

Objective: To investigate the demographics, comorbidities, microbiological features, resource use and outcome of patients with necrotising fasciitis. We aimed to identify factors associated with mortality.

Design, participants and setting: A retrospective case and chart review was performed in consecutive patients with necrotising fasciitis admitted to the intensive care unit of a tertiary hospital between January 2000 and June 2008.

Results: 58 patients with necrotising fasciitis were admitted during the study period. Pacific Islander and Maori peoples were overrepresented. Comorbidities were consistent with previous studies except for a high incidence of gout. Lower limb was the most frequent site of infection (53%). Swelling (83%) and severe pain (76%) were the most common presenting features. Type 2 infection (52%) was more common than type 1 (43%). Mortality was 29%. Recent non-steroidal anti-inflammatory drug use was reported by 43% of patients but not associated with mortality. Logistic regression modelling identified Acute Physiology and Chronic Health Evaluation (APACHE) II score, pre-existing abnormal renal function and gout to be associated with mortality.

Conclusions: There is an higher incidence of necrotising fasciitis at our hospital in South Auckland than reported elsewhere. Maori and Pacific Islander people are at increased risk. In our patient sample APACHE II score, pre-existing abnormal renal function and gout were associated with mortality.

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Hospital ICU between January 2000 and June 2008. Ethics committee approval was obtained from the Northern X Regional Ethics Committee. As the study was classified a retrospective audit, no ethics review was deemed necessary and the need for informed patient consent was waived by the ethics committee.

Table 1. Demographics of 58 patients with necrotising fasciitis, Middlemore Hospital intensive care unit, January 2000 – June 2008

Characteristic	
Mean age in years (SD); range	51.3 (17); 18–79
Male sex, no. (%)	36 (62%)
Ethnicity, no. (%)	
Pacific Islander	25 (43%)
European	20 (34%)
Maori	13 (22%)

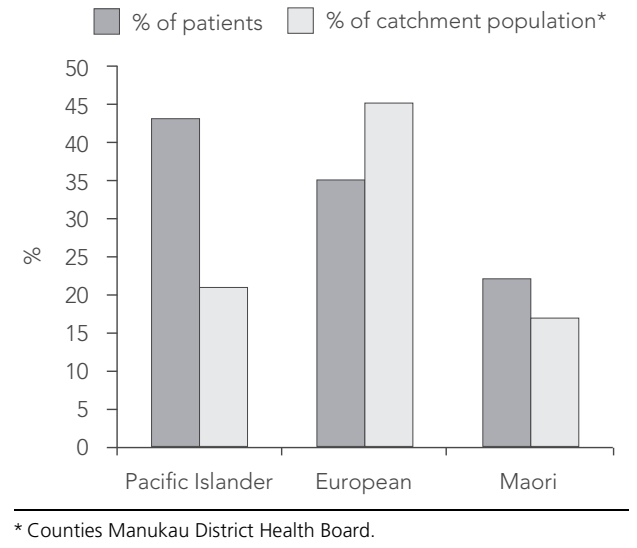
Table 2. Comorbidities of 58 patients with necrotising fasciitis, Middlemore Hospital intensive care unit, January 2000 – June 2008

Comorbidity	No. (%)
Impaired glucose tolerance	20 (34%)
Diabetes, insulin-dependent	6 (10%)
Diabetes, treated with oral hypoglycaemics	7 (12%)
Glycated haemoglobin > 6.0%; no treatment	7 (12%)
Obesity	18 (31%)
Gout	16 (28%)
Respiratory disease	14 (24%)
Congestive cardiac failure	13 (22%)
No comorbidity	12 (21%)
Renal impairment	11 (19%)
Previous cellulitis	7 (12%)
Heavy alcohol consumption	4 (7%)
Peripheral vascular disease	3 (5%)

Patients with a diagnosis of necrotising fasciitis, necrotising soft tissue infection or cellulitis were identified from the ICU database. Patients were included in the analysis if: (i) they had a confirmed diagnosis of invasive soft tissue infection with tissue necrosis at surgery or autopsy; or (ii) if treated non-operatively, a clinical and microbiological picture that supported the diagnosis. Patients were excluded if they were aged under 15 years, transferred to our institution from another hospital, or if the diagnosis of necrotising fasciitis was unclear.

Data were collected using a standardised data collection form that included demographics, comorbidities, history of recent NSAID use, laboratory results, surgical management, ICU management and outcome. A digitally integrated patient information system, patient clinical notes and daily ICU charts were all used to gather information. Pre-existing

Figure 1. Ethnicity of 58 patients with necrotising fasciitis, Middlemore Hospital intensive care unit, January 2000 – June 2008



renal impairment was recorded if there was a documented abnormal serum creatinine level (>120 $\mu\text{mol/L}$) or micro-albuminuria (> 30 mg/mmol) before the index admission.

The microbiological results from any samples collected at the time of admission or surgery were recorded. Results from wound, aspirate or tissue samples were recorded separately to blood culture results.

Data were analysed using SPSS, version 14.0 (SPSS Inc, Chicago, Ill, USA) and presented as mean (SD) or median (interquartile range [IQR]), as appropriate. Parametric data were analysed using the Student *t* test. Non-parametric data were analysed with the Mann–Whitney test or, in the case of contingent data, χ^2 or the Fischer exact test, as appropriate. Comorbidities were evaluated, along with Acute Physiology and Chronic Health Evaluation (APACHE) II score and time to surgery, in a multivariable logistic regression model. The model was used to generate a receiver operating characteristic (ROC) curve. This was used to assess the model's fit to the observed outcome.

Results

Demographics

Fifty-eight patients were admitted to the ICU during the study period with a diagnosis of necrotising fasciitis (mean, 6.8 patients/year). Data on one patient were limited. Patient demographics are displayed in Table 1.

Figure 1 shows patient ethnicity and population ethnicity within the CMDHB catchment area.

Table 3. Clinical features of 58 patients with necrotising fasciitis, Middlemore Hospital intensive care unit, January 2000 – June 2008

Clinical feature	No. (%)
Site of infection	
Lower limb	31 (53%)
Trunk including axilla	13 (22%)
Perineum/buttocks	9 (16%)
Upper limb	3 (5%)
Face/scalp	1 (2%)
Symptoms and signs	
Swelling	48 (83%)
Severe pain	44 (76%)
Necrosis	29 (50%)
Blistering	19 (33%)
Ulceration	17 (29%)
Rigors	10 (17%)
Potential precipitant	
Recent trauma without skin breach	11 (19%)
Recent trauma with skin breach	8 (14%)
Recent invasive procedure	4 (7%)

Clinical features

Patient comorbidities are displayed in Table 2. Obesity, gout and impaired glucose tolerance were the most common comorbidities.

Presenting clinical features, symptoms and signs, and potential precipitants identified are presented in Table 3.

A history of recent trauma was documented in 23/58 patients (40%); 12 of these cases involved a skin breach, including four patients who had undergone a recent operative procedure. All patients who had the capacity to feel pain at the site and were well enough to communicate effectively reported severe pain (44/58; 76%). The other 14 patients (24%) either had a sensory neurological deficit or a decreased Glasgow Coma Scale score.

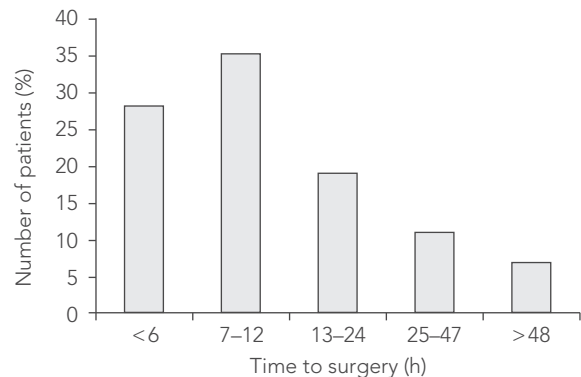
Clinical course

Patient triage categories at presentation to the emergency department were recorded as:

- T1 (seen immediately) — 1 patient (2%)
- T2 (seen within 10 minutes) — 11 patients (19%)
- T3 (seen within 30 minutes) — 31 patients (53%)
- T4 (seen within 60 minutes) — 12 patients (21%)
- T5 (seen within 120 minutes) — 1 patient (2%)

Two patients were not triaged as they were admitted directly to a ward.

Figure 2. Time from presentation to surgery for 58 patients with necrotising fasciitis, Middlemore Hospital intensive care unit, January 2000 – June 2008



Time from presentation to surgery ranged from 1 hour and 32 minutes to 5 days 12 hours and 33 minutes (mean, 17 hours and 5 minutes [SD, 26.7 hours]). Four patients did not have surgery — one declined, one died before theatre and two were considered moribund and received palliative care. Of the patients who had surgery, 63% were operated on within the first 12 hours and 81% within 24 hours (Figure 2).

The median number of operative procedures performed per patient was 4 (IQR, 1.75–6). Amputation of the affected limb was necessary in 10% of cases.

Median hospital length of stay was 31 days (IQR, 9–55 days). ICU length of stay 65 hours (IQR, 15–194 hours). Most patients required ventilation (79%) with a median duration of 28.5 hours (IQR, 3.5–91.25 hours). Renal replacement therapy was performed in 29% of cases. APACHE II scores ranged from 6 to 31 (median, 21 [IQR, 15.75–25]). Mortality was 29%.

Microbiology

Positive microbiological results (either from wound swab or blood culture) were seen in 55 patients (94%) and are displayed in Table 4. One patient, considered moribund, had no samples sent, and two patients showed no growth. Blood cultures were sent for 50 patients (86%) and were positive for 17 patients. Three patients had positive blood culture results that were inconsistent with aspirate, swab or tissue samples and were consistent with skin contamination — these patients were grouped according to their tissue sample results. Type 1 and type 2 infection were associated with 36% and 20% mortality, respectively.

Table 4. Microbiological features of 58 patients with necrotising fasciitis, Middlemore Hospital intensive care unit, January 2000 – June 2008

Microbiological feature	No. of patients (%)
Type 2 infection	30 (52%)
Type 1 infection	25 (43%)
Growth from swab/tissue sample	
<i>Streptococcus pyogenes</i>	20 (34%)
<i>S. pyogenes</i> + <i>Staphylococcus aureus</i>	7 (12%)
<i>S. aureus</i>	3 (5%)
Methicillin-resistant <i>S. aureus</i>	1 (2%)
Pure gram-negative growth*	6 (10%)
Pure anaerobic growth	1 (2%)
Mixed growth	8 (14%)
Blood culture	
Positive blood culture	17 (29%)
<i>S. pyogenes</i>	7 (12%)
<i>Aeromonas hydrophila</i>	2 (3%)
<i>S. aureus</i>	1 (2%)
Streptococcus group G	1 (2%)
<i>Vibrio vulnificus</i>	1 (2%)
Mixed growth/contaminant	4 (7%)

* *Escherichia coli*, *Citrobacter freundii*, *A. hydrophila*, *V. vulnificus*, *Klebsiella pneumoniae*.

Non-steroidal anti-inflammatory drug use

Twenty-five patients (43%) reported recent NSAID use. On univariate analysis, no association was demonstrated between NSAIDs and mortality.

Logistic regression

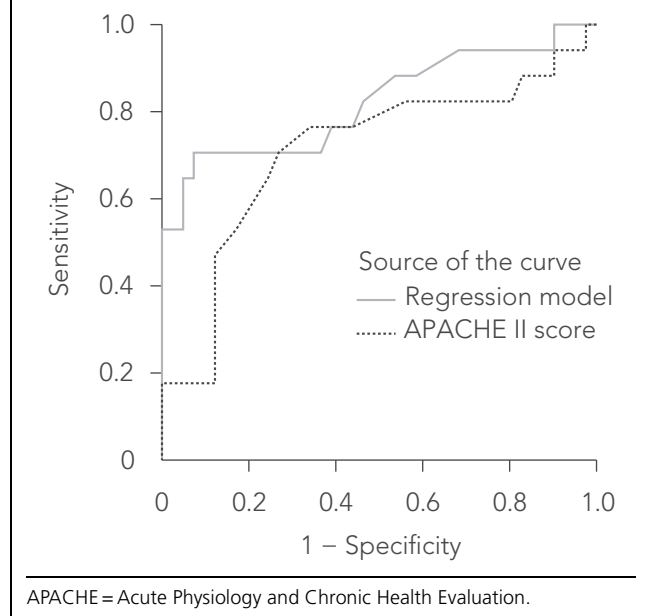
Logistic regression modelling was used to evaluate interactions between premorbid factors. The model that best described the data contained APACHE II score, preadmission renal impairment and previous diagnosis of gout.

The model's discrimination was assessed by comparing the ROC curve for the model's prediction with that from APACHE II score alone. The area under the ROC curve for APACHE II score is 0.71. The area under the curve for the model is 0.82 (Figure 3).

Discussion

Our catchment population produced a mean of 6.8 ICU admissions due to necrotising fasciitis per year over 8.5 years — the equivalent of 2–3 times the published incidence of necrotising fasciitis in other developed nations. Patient presentation and clinical course were comparable

Figure 3. Receiver operating characteristic (ROC) for regression model and APACHE II score



with known studies. APACHE II score, pre-existing renal impairment and gout were all independent predictors of mortality. In addition, ethnicity and socioeconomic factors may also be associated with severity in our population. Recent NSAID usage was not associated with mortality.

Maori and Pacific Islander people comprise 65% of cases while making up only 38% of our catchment area, as previously noted.^{4,17} The patients' spectrum of comorbidities is similar to that seen in other case series, with the exception of gout.^{2,4,17-24}

All our patients with intact sensation, and who were able to express themselves, complained of severe pain. Those who did not were either obtunded or had sensory deficits in the affected area. This highlights that pain out of keeping with visual appearance of the affected area is a common symptom in the vast majority of patients.² The extremities, especially lower limbs, were the most common site for infection, with an average of 4.5 surgical procedures per patient and an amputation rate of 10%, in keeping with other institutions.^{4,5,20-24}

Time from admission to surgery was similar to published literature.^{4,23,24} It is interesting to note that 75% of patients were triaged as T3 or T4 (not critical), although the cohort had a relatively high mortality rate of 29%, supporting previous observations that necrotising fasciitis is often difficult to diagnose and its severity difficult to assess.^{2,4,18-24}

Type 2 infection was more common than type 1, as seen previously in our hospital,¹⁷ but contrary to other published data, which report type 1 to be the more common form of

necrotising fasciitis.⁴ Type 2 patients had a trend to higher mortality.

The mortality rate of 29% is similar to published data. This mortality rate is notably higher than the 12% recorded on our ICU database for deaths from sepsis (all types) in a similar period (unpublished data). Hospital length of stay and ICU resource use are similar to other studies.

The potential relationship between NSAIDs and necrotising fasciitis has been debated for over 20 years and remains controversial.⁷⁻¹⁴ In our sample, 43% of patients gave a history of recent NSAID use. Data for prevalence of NSAID use in the community are not available. Recent NSAID use was not an independent risk factor for mortality in the patients admitted to the ICU.

Previous studies do not report gout as a comorbidity for necrotising fasciitis, but the 28% incidence seen in our sample seems noteworthy. The prevalence of gout in the CMDHB catchment area is not accurately reported. A New Zealand study of 657 patients reported an overall prevalence of 4.7%. The prevalence among Maori was significantly higher than among Europeans (6.4% v 2.9%), with Maori men having the highest prevalence (13.9%).²⁵ Gout has previously been reported as a risk factor for cardiovascular mortality in the general population, and in renal dialysis patients,²⁶ and hyperuricaemia itself may also be related to mortality.^{27,28}

In the critical care setting, Chuang and colleagues measured uric acid concentration levels in 73 patients presenting with severe sepsis and in 76 healthy controls. They concluded that there was a significant increase in uric acid levels in patients with severe sepsis and septic shock and that uric acid levels correlated significantly with APACHE II scores.²⁹ However, any direct association between uric acid levels and outcome in sepsis remains unclear.³⁰⁻³² Alternatively, it may also be that patients suffering from gout do not easily differentiate between the early symptoms of gout and that of necrotising fasciitis, or that gouty tophi represent a ready route for invasive infection.

Ethnicity has previously been described as a potential risk factor for sepsis. A study in Auckland in 2005 demonstrated that Polynesian and Maori children had a significantly higher risk of developing osteomyelitis than their peers.³³ Similarly, a study at Alice Springs Hospital in central Australia demonstrated significant racial disparities in infection-related mortality in the Indigenous population.³⁴ Other studies also suggest that ethnicity may influence susceptibility to, and outcome from, sepsis;^{35,36} however, confounding issues such as socioeconomics must always be considered.

Little published research has specifically examined any link between socioeconomic factors and sepsis. Poor housing conditions; density of population within accommoda-

tion; limited health knowledge; and lack of access to health care, or barriers to that access, could contribute to increased incidence or severity of sepsis. Our catchment has several areas that are socioeconomically deprived, with many of these factors potentially contributing to sepsis.

It is possible, however, that the incidence found in our population represents the true incidence of necrotising fasciitis in the developed world. Necrotising fasciitis is notoriously difficult to diagnose and may be confused with more common diagnoses. Underreporting may be significant; the true incidence may be changing, and collection and dissemination of statistics lagging behind this change. A US study using data from the 2000–2004 US Healthcare Cost and Utilization Project National Inpatient Sample studied the discharge diagnoses from more than 1000 acute care hospitals over 4 years. Over the study period, the incidence of necrotising fasciitis increased by 30%.³⁷

Overinterpretation of our results must be avoided — although this was a relatively large case series for necrotising fasciitis, our numbers were small. Data were retrospectively collected and, in some cases, incomplete. Patient identification was reliant on clinical coding and therefore may have yielded an incorrect prevalence. Definition of comorbidities, especially obesity (which was not always based on measurement of body mass index) lacked precision.

Summary and conclusions

We present a retrospective case series of intensive care patients with necrotising fasciitis. The incidence of this disease in our population is 2–3 times greater than that reported in other developed countries. Pacific Islander and Maori patients are at increased risk. APACHE II score, pre-existing renal impairment and gout were associated with mortality. The association of gout with mortality was an unexpected finding. We are planning a further prospective study to determine the ongoing incidence of necrotising fasciitis in South Auckland and whether gout is a true independent predictor of mortality.

Competing interests

None declared.

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