Original Article

Clinical and Microbiological Spectrum of Necrotizing Fasciitis in Surgical Patients at a Philippine University Medical Centre

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OBJECTIVE: The study describes the clinical characteristics, bacteriology and risk factors for mortality of patients with necrotizing fasciitis (NF), seen in a university medical centre.

METHODS: The medical charts of NF patients admitted to the institution from January 2004 to July 2007 were retrieved and reviewed retrospectively.

RESULTS: The majority of the 67 patients included in the study presented with localized nonspecific inflammatory manifestations: tenderness (94%), warmth (86%), oedema (76%), skin necrosis (75%), and ulceration (68%). Diabetes mellitus (22%) was the most common predisposing medical condition. The most frequent isolates were *Escherichia coli* (44%), *Acinetobacter baumannii* (19%), *Staphylococcus aureus* (15%) and *Enterococcus faecium* (15%). Overall mortality rate was 36%. Risk factors significantly associated with mortality were truncal involvement ($p = 0.034$), leukocytosis ($p = 0.038$), acidosis ($p = 0.001$), hypoalbuminaemia ($p = 0.004$), hypocalcaemia ($p = 0.000$) and hyponatraemia ($p = 0.023$). Logistic regression analysis revealed acidosis [$p < 0.05$, odds ratio (OR) = 9] and hypoalbuminaemia ($p < 0.05$, OR = 14) as significant independent risk factors for mortality.

CONCLUSION: The identified risk factors can inform clinicians of increased mortality risks for certain patients with NF. They should serve as a trigger for more aggressive surgical and critical care, and antimicrobial therapy for these patients. [*Asian J Surg* 2010;33(1):51–8]

Key Words: antimicrobial susceptability, bacteriology, complicated soft tissue infection, Fournier's gangrene, microbiologic spectrum, necrotizing fasciitis, Philippines, surgical patient

Introduction

Necrotizing fasciitis (NF) is a relatively rare but seriously fatal soft tissue infection. Mortality from this infection is significant if left untreated or if treatment is delayed. Early diagnosis and definitive management are paramount because of the rapidly progressing nature of the infection. Thus, it is important for physicians to have a high index of suspicion based on the initial clinical history and physical assessment. Studies that determine the clinical features, outcome and bacteriology of NF in patients seen in the Philippines and similar low-income, resource-poor settings are lacking. This study investigated the clinical characteristics of NF, its bacterial isolates in tissue/wound culture, and the risk factors that influence mortality in patients at the University of the Philippines-Philippine General Hospital (PGH), in a low-income country. It also provides information that could aid the

early recognition of NF and its risk factors for mortality, and improve management.

Early clinical recognition of NF can be challenging because of the paucity of clinical findings in the initial stage of the illness. Presenting local manifestations are nonspecific and include oedema, cellulitis, local anaesthesia and occasional crepitations.[1] The pathognomonic features of NF can rapidly develop. Redness, pain and oedema can quickly progress to central patches of dusky blue discoloration, with or without serosanguineous blisters within 24 to 48 hours. This eventually leads to gangrene of the affected tissues by the fourth or fifth day.[2,3] Concurrently, systemic manifestations of sepsis develop, including altered mental status, tachycardia, tachypnoea, leukocytosis, hyperglycaemia, oliguria, fever/chills and metabolic acidosis. Bacteraemia is rarely identified.[4]

Protocols for the empiric management of the infection emphasize early diagnostic procedures, prompt debridement of infected tissues, antimicrobial therapy, and resuscitation in an intensive-care setting.[5] The choice of empiric antibiotics should be based on expected pathogens and their known sensitivity.[4]

Characterizing the clinical features and outcome of patients with NF is an important step in devising the best management for treating this rare but highly fatal infection. By investigating the clinical features that predict mortality and the pathogenic organisms involved in the infection, possible recommendations can be made based on the presence of certain risk factors for predicting mortality and the most appropriate empiric antibiotics that should be used to treat the infection.

Patients and methods

Data collection

All medical records of NF patients between January 2004 and July 2007 in the Department of Surgery, PGH were obtained via chart review and queries of the departmental Integrated Surgical Information System (ISIS) database. The case definition used in diagnosing NF was taken from the 1997 prospective study of Kaul et al[6] in Ontario, Canada and the 2005 clinical review of Wong and Wang.[7] Patients who fulfilled the clinical, surgical and/or histopathological criteria for NF, either local or spreading, were included in the study. Demographic and clinical information was reviewed for the study population. The following search terms were used for the ISIS database: NF,

streptococcal NF, streptococcal gangrene, necrotizing gangrene, soft-tissue gangrene, Fournier's gangrene, necrotizing soft tissue infection, suppurative fasciitis, progressive bacterial synergistic gangrene, Meleney's gangrene, synergistic necrotizing cellulites, and gas gangrene. Corresponding microbiological data on wound or tissue biopsy cultures were retrieved for the same population from the Section of Microbiology, Department of Laboratories, PGH. Medical records were reviewed for age, sex, clinical findings, site of primary infection, predisposing factors, microbial cultures, laboratory work-ups, treatment and final outcome.

Statistical analysis

All data were encoded electronically in Microsoft Excel. Data obtained were subjected to statistical tests. The χ^2 test was used to determine which risk factors were significantly associated with death. Such risk factors were further evaluated by estimating the odds ratio (OR) and 95% confidence interval (CI). A p value of <0.05 was considered significant.

Results

A computer-generated search of the ISIS database, using the key search terms listed, yielded an initial 70 patients devoid of duplications and irrespective of the presence of any microbial culture studies done. The actual size of the study population was reduced to 67 patients when three patients with incompatible diagnoses were excluded.

Of the 67 patients included in this study, the greatest proportion (40%) of the patients belonged in the 41–60 years age group. The occurrence of NF was higher in men (84%) than in women (16%). Not all patients however, had records of the baseline clinical parameters considered in this study. As such, the rates for each of these parameters were computed based on available data. Bacteraemia was recorded in 3 (14%) of the 21 cases with available blood cultures. Shock (systolic blood pressure < 90 mmHg) was reported in 4 (8%) of 50 patients. Previous trauma was documented in 15 (44%) of 34 patients and spontaneous infection in 15 (50%) of 30 patients. Of the 15 patients with prior trauma, 11 were community acquired, which included penetrating injury, animal bite, gun-shot wound and blunt trauma; one had surgical wound infection and three had unspecified trauma. A large percentage of patients had surgical debridement, 75% (50 of 67 patients)

Table 1. Clinical manifestations in patients with necrotizing fasciitis

Clinical features	No. of patients with records*	Cases (%)
Tenderness	47	44 (94)
Warmth	22	19 (86)
Oedema	41	31 (76)
Skin necrosis	36	27 (75)
Ulcerations	28	19 (68)
Temperature > 38°C	54	34 (63)
Vesicles, bullae	23	8 (35)
Purple discoloration of involved area	21	7 (33)
Local anaesthesia	20	4 (20)
Crepitus	14	2 (14)
Confusion	32	4 (13)
Jaundice	24	3 (13)
Systolic blood pressure < 90 mmHg†	50	4 (8)
Coma	31	1 (3)

*Total number of patients considered for every parameter was based on the availability of the information as a pertinent negative or positive sign/symptom; †systolic blood pressure < 90 mmHg referred to the lowest recorded blood pressure for the entire duration of the study.

Table 2. Predisposing conditions and skin lesions in patients with necrotizing fasciitis ($n = 67$)

Predisposing conditions	No. of patients (%)
Underlying medical condition	
Diabetes mellitus	15 (22)
Chronic systemic diseases*	9 (13)
Pulmonary diseases†	2 (3)
Malignancy‡	2 (3)
Haematologic disease§	2 (3)
Immunosuppressive illness‖	1 (1)
None	39 (58)
Predisposing skin lesions	
Abscess formation	27 (40)
Penetrating trauma	8 (12)
Minor wounds	4 (6)
Pustular lesions	3 (4)
Inflammation/swelling	3 (4)
Burns	2 (3)
Laceration	2 (3)
Surgery	1 (1)
Chronic skin conditions¶	1 (1)
Blunt trauma	1 (1)
Mass/tumour	1 (1)
None	12 (18)

*Chronic systemic diseases include chronic heart diseases, peripheral vascular diseases, liver diseases and renal failure; †pulmonary diseases include pneumonia, tuberculosis, chronic obstructive pulmonary diseases and asthma; ‡malignancy refers to gastrointestinal cancer and pulmonary cancer; §haematologic diseases include anaemia, leukaemia and other haematologic abnormalities; ‖immunosuppressive illnesses include chronic corticosteroid use, solid organ transplant, HIV infection and asplenia; ¶chronic skin conditions include decubitus ulcers, dermatitis and psoriasis.

as a component of their treatment. Overall mortality rate was 36%.

Although there were 67 patients in total, the number with documented clinical features varied, depending on whether they were mentioned as pertinent positive, negative or not at all. Hence, the cases were expressed as a percentage of the total number of patients with available information for the parameter being considered. The most common clinical manifestations of patients with NF were tenderness (44/47, 94%), warmth (19/22, 86%), oedema (31/41, 76%), skin necrosis (27/36, 75%), ulcerations (19/28, 68%), and fever (34/54, 63%). Table 1 shows the clinical manifestations of patients with NF. The prevalence of coma and hypotension was low in the spectrum of patients seen.

As shown in Table 2, the majority of the 67 patients did not have any previously identified predisposing medical conditions (58%), while 42% did have. Of the medical conditions considered, diabetes mellitus (22%) remained the leading associated illness, followed by chronic systemic diseases (13%), pulmonary diseases (3%), malignancy

(3%), haematological diseases (3%) and immunosuppressive illness (1%). The predisposing skin lesion for most cases was abscess formation (40%), which was followed by penetrating trauma (12%). Eighteen percent of the cases had no documented predisposing skin condition.

Forty-five percent of the NF patients in this study had Fournier's gangrene in which the primary lesions were in the perineal area (Table 3). Involvement of the lower extremities and the trunk was seen in 22% and 15% of all cases, respectively. A combination of lesions in the perineal and lower extremities was only documented in 4% of the cases.

Table 4 summarizes the bacterial isolates in the study. Among the 67 patients, mono- and polymicrobial isolates were identical in prevalence. Among the Gram-positive

Table 3. Anatomic location of primary site of infection ($n = 67$)

Anatomic location	No. of patients (%)
Perineum	30 (45)
Lower extremities	15 (22)
Chest and abdomen	10 (15)
Perineum and lower extremity	3 (4)
Upper extremities	2 (3)
Head and neck	1 (1)
Upper and lower extremities	1 (1)

Table 4. Bacteria recovered in wound/tissue cultures of patients with necrotizing fasciitis*

Isolates	No. of patients (%) with cultures ($n = 48$)
No growth	1 (2)
With growth	
Monomicrobial	24 (50)
Polymicrobial	23 (48)
Gram-positive organisms	
Staphylococcus aureus	7 (15)
Enterococcus faecium	7 (15)
Methicillin-resistant *Staphylococcus aureus*	2 (4)
Staphylococcus epidermidis	2 (4)
Enterococcus sp.	2 (4)
Gram-negative organisms	
Escherichia coli	21 (44)
Acinetobacter	9 (19)
Klebsiella pneumonia	5 (10)
Proteus mirabilis	4 (8)
Hafnia alvei	3 (6)
Alcaligenes faecalis	2 (4)
Klebsiella sp.	2 (4)
Enterobacter cloacae	2 (4)
Proteus rettgeri	1 (2)
Pseudomonas aeruginosa	1 (2)
Enterobacter aerogenes	1 (2)
Citrobacter sp.	1 (2)
K. pneumoniae ss. ozaenae	1 (2)
Burkholderia mallei	1 (2)
K. pneumoniae ss. rhinoscleromatis	1 (2)
Proteus vulgaris	1 (2)
Pantoea (Entero.) *agglomerans*	1 (2)
Gram-variable organisms	
Achromobacter	1 (2)

*Of the 67 patients, culture studies were done only in 48 patients (72%). Results are from after 4 days of incubation. There were 19 patients with no culture studies noted from the hospital records retrieved.

organisms, *Staphylococcus aureus* and *Enterococcus faecium* were documented to be the most frequently isolated (15%) among the patients with NF. *Escherichia coli* (44%) was the leading Gram-negative pathogen in patients with NF, which was consistent with the high incidence of Fournier's gangrene. The combinations of *E. coli* and *Klebsiella pneumonia* (6%) and *E. coli* and *Acinetobacter baumannii* (6%) were commonly seen among the polymicrobial isolates (Table 5).

A breakdown of antimicrobial susceptibility for each of the representative bacterial isolates is shown in Table 6. Both *E. coli* and *Proteus mirabilis* were highly sensitive to piperacillin-tazobactam, ceftazidime and gentamicin. Nosocomially acquired *A. baumannii* was highly sensitive to carbapenems but resistant to gentamicin and piperacillin-tazobactam. *S. aureus* remained sensitive to clindamycin, oxacillin and ampicillin-sulbactam.

Thirteen risk factors were assessed for a correlation with mortality: age ≥ 65 years, chronic illness, hypotension, delay in surgical debridement, truncal involvement, anaemia (< 10 mg/dL), thrombocytopenia ($< 100 \times 10^9$/L), leukocytosis ($> 12 \times 10^9$/L), acidosis (pH < 7.35), hypoalbuminaemia (< 30 g/L), hypocalcaemia (< 2.2 mmol/L), hyponatraemia (< 135 mmol/L), and azotemia (blood urea nitrogen > 5.4 mmol/L). Table 7 summarizes the risk factors that influenced mortality among patients with NF. It was identified that truncal involvement ($p = 0.034$), leukocytosis ($p = 0.038$), acidosis ($p = 0.001$), hypoalbuminaemia ($p = 0.004$), hypocalcaemia ($p = 0.000$), hyponatraemia ($p = 0.023$) were significantly associated with death.

Independent predictors of mortality were assessed and summarized in Table 8. Logistic regression analysis showed that acidosis ($p < 0.05$; 95% CI: 1.9–44.9) and hypoalbuminaemia ($p < 0.05$; 95% CI: 1.5–658.7) were the significant individual independent risk factors for death. Patients with acidosis were nine times more likely to die than patients without. Patients with hypoalbuminaemia were 14 times more likely to die than those without.

Discussion

Most patients with NF present with signs of inflammation such as tenderness, warmth and erythema.[8] The

Table 5. Frequency of monomicrobial and polymicrobial isolates*

Isolates	No. of patients (%) with cultures ($n = 48$)
Monomicrobial	24 (50)
E. coli	9 (19)
Klebsiella sp.	2 (4)
MRSA[†]	2 (4)
S. aureus	2 (4)
Others[‡]	9 (19)
Polymicrobial	23 (48)
E. coli + *Klebsiella pneumoniae*	3 (6)
E. coli + *A. baumannii*	3 (6)
E. coli + *S. aureus*	2 (4)
S. aureus + *Staphylococcus epidermidis*	2 (4)
Enterococcus faecium + *A. baumannii*	2 (4)
Others[§]	11 (23)

*Of the 67 patients, culture studies were only done in 48 patients (72%). [†]MRSA isolates were distinguished from *S. aureus* to signify their presence among the isolates; [‡]others refer to the least common monomicrobial isolates; [§]others refers to the least common polymicrobial combinations. *E. coli* = *Escherichia coli*; MRSA = methicillin-resistant *Staphylococcus aureus*; *S. aureus* = *Staphylococcus aureus*; *A. baumannii* = *Acinetobacter baumannii*.

Table 6. Antimicrobial susceptibility for the isolates*

Isolates	Antimicrobial susceptibility rates (%)
Escherichia coli ($n = 21$)	
Piperacillin-tazobactam	100
Cefuroxime	100
Ceftriaxone	100
Ceftazidime	100
Ampicillin	100
Gentamicin	100
Acinetobacter baumannii ($n = 9$)	
Imipenem	100
Chloramphenicol	50
Amikacin	40
Gentamicin	33
Piperacillin-tazobactam	20
Staphylococcus aureus ($n = 7$)	
Ampicillin-Sulbactam	100
Clindamycin	100
Oxacillin	100
Klebsiella pneumoniae ($n = 5$)	
Cefuroxime	100
Ceftriaxone	100
Proteus mirabilis ($n = 4$)	
Amikacin	100
Ceftazidime	100
Gentamicin	100
Imipenem	100
Piperacillin-tazobactam	100
Ampicillin	50
Chloramphenicol	50
Enterobacter cloacae ($n = 2$)	
Amikacin	100
Ceftazidime	100
Imipenem	100
Ampicillin-sulbactam	50

*The antimicrobial panels available were not used uniformly for each of the isolates. Shown above are the antimicrobial agents tested for every isolate.

authors found similar common clinical characteristics as exemplified by previous studies. Hassell et al[9] have reported that the most common clinical manifestations at presentation were pain in the affected area, induration and swelling of the affected area, extensive erythema in 29% of patients, and systemic complaints of fever and rigor. In a 10-year retrospective study of NF in Oman, all patients had local pain that was out of proportion with the signs, and fever.[8] Similarly, in the present study, other clinical manifestations observed were oedema (63%), temperature > 38°C (63%), purple discoloration of involved area (33%), local anaesthesia (20%), and crepitus (14%). The infection can be present without an obvious portal of entry such as a wound or ulceration, therefore, clinical suspicion of its presence in a patient with severe pain and local signs of inflammation should be higher.

Diabetes mellitus (22%) was the leading associated medical illness. Diabetes as the most common predisposing medical condition also has been reported by others, with ranges from 32% to 62%.[10-12] The presence of diabetes has been associated with increased mortality, as

shown by Rouse et al.[10] The most common aerobes isolated from NF patients with diabetes were *E. coli* (21%) and enterococci (18%).[10]

In other studies, the most common predisposing skin lesion was trauma, but in some cases, no prior skin lesion was documented. In the present study, 18% of the cases had no documented predisposing skin condition. In an

Table 7. Risk factors for mortality in patients with necrotizing fasciitis

	Number (%)*	Died (%)	$p^{\dagger}$
Acidosis (pH < 7.35)	13 (19)	9 (69)	0.001‡
Thrombocytopenia (< 100 × 10⁹/L)	5 (7)	3 (60)	0.151
Truncal involvement	10 (15)	6 (60)	0.034‡
Age ≥ 65 yr	7 (10)	4 (57)	0.179
Hypotension (< 90/60 mmHg)	4 (6)	2 (50)	0.496
Hypocalcaemia (< 2.2 mmol/L)	10 (15)	5 (50)	0.000‡
Anaemia (< 10 mg/dL)	21 (31)	10 (48)	0.052
Hyponatraemia (< 135 mmol/L)	14 (21)	6 (43)	0.023‡
Delay in surgical debridement (> 24 h from admission)	20 (30)	8 (40)	0.073
Azotemia (blood urea nitrogen > 5.4 mmol/L)	28 (42)	11 (39)	0.093
Leukocytosis (> 12 × 10⁹/L)	41 (61)	14 (34)	0.038‡
Chronic illness	22 (33)	7 (32)	0.953
Hypoalbuminaemia (< 30 g/L)	24 (36)	6 (25)	0.004‡

*Expressed as percentage of the total number of patients ($n = 67$); $^{\dagger}\chi^2$ test; $^{\ddagger}p < 0.05$.

Table 8. Odds ratio (OR) and 95% confidence interval (CI) of risk factors significantly associated with mortality in patients with necrotizing fasciitis

Risk factors	OR	95% CI
Truncal involvement	4.2	(0.8, 22.6)
Leukocytosis (> 12 × 10⁹/L)	4.0	(0.9, 23.8)
Acidosis (pH < 7.35)*	9	(1.9, 44.9)*
Hypoalbuminaemia (< 30 g/L)*	14	(1.5, 658.7)*
Hypocalcaemia (< 2.2 mmol/L)	NA	NA
Hyponatraemia (< 135 mmol/L)	4.2	(0.9, 18.4)

*Of note is that hypoalbuminaemia and acidosis are recognized risk factors for mortality, but only the resolution of acidosis has shown to be associated with improvements in mortality; $^{\dagger}p < 0.05$. NA = not available.

earlier study by Freeman et al,[13] it was documented that 14% of the patients had no history of trauma.

The majority of NF patients in our study had their primary lesions in the perineal area (45%), which is similar to previous studies.[11,12] In an earlier case series by Rouse et al,[10] as many as 78% of the infections involved the abdomen, groin or perineum. A number of previous studies have emphasized that a higher mortality rate is associated with infection at these sites. The increased mortality rate could represent inadequate examination and treatment of obscure suppurative processes in this region, particularly in the perirectal spaces.[10]

The predominance of isolated Gram-negative bacilli in the study population could be accounted for by the high prevalence of Fournier's gangrene in which the most commonly isolated bacteria are *E. coli*, *K. pneumonia* and enterococci. Among patients with comorbidity, of which diabetes mellitus is the most common, *E. coli* (36%) was still the most frequently isolated organism followed by *E. faecium* (18%), *K. pneumonia* (18%), *P. mirabilis* (9%) and *S. species* (9%).

Our findings are similar to those in an earlier case series by Freeman et al,[13] which reported that Gram-negative bacilli accounted for 86% of the isolated pathogens. The presence of *S. aureus* as a common pathogen in the present study could be accounted for by surgical wound infection. This is in contrast to the published literature where this bacterium is not reported as a common cause of NF, but rather, the cause of NF is frequently attributed to beta-hemolytic streptococcus. Another study by Brook and Frazier[14] has shown that *S. aureus, E. coli* and group A streptococci as predominant aerobic isolates in patients with NF. A similar pattern of bacterial isolates has been reported in a case series by Majeski and Alexander,[15] where *E. coli*, *S. aureus* and haemolytic streptococci were the most frequently isolated bacteria.

Penetration was the most frequent cause of injury among trauma patients with NF in the present study. Other patients had injuries that were sustained from burns, laceration, crushing and vehicular accidents. Among trauma patients who eventually had NF, the most frequently isolated organism was *E. coli, S. aureus, K. pneumoniae, Pantoea agglomerans, A. baumanii* and *E. faecium. S. aureus* was present in one burn patient.

Numerous studies have reported that an increasing incidence of methicillin-resistant *S. aureus* (MRSA) is

responsible for rapidly progressive diseases including NF.[11,16] This finding is consistent with the present study, which showed the potential emergence of community-acquired MRSA in the Philippines, because none of the MRSA patients were previously hospitalized or in the postoperative phase.

E. faecium is another common nosocomial pathogen in NF, with an increasing incidence of acquired resistance to antimicrobial agents including vancomycin.[17,18] In the present study, the relatively high proportion of entero-cocci isolated reflects the high prevalence of Fournier's gangrene. Furthermore, in NF patients who have had a previous surgery, the most frequent isolates were *E. coli*, *A. baumanii* and *E. faecium*.

The present study showed that *A. baumannii* is a common co-isolate with *E. coli* in patients with NF. However, to our knowledge, no studies to date have shown possible synergism between the two organisms or the incidence of *Acinetobacter*-related NF.

Although it has been reported previously that single-organism NF commonly is caused by group A strepto-cocci, the incidence of NF caused by other organisms is increasing.[19] Wong et al[19] have shown that single-organism NF caused by *Klebsiella* spp. is associated strongly with predisposing conditions such as diabetes mellitus. This was also reflected in the present study. This could explain the increasing incidence of other causative organisms, depending on their predisposing conditions or comorbidity. One case report[20] of monomicrobial NF in a pregnant woman has been published with *S. aureus* as the causative microorganism.

No anaerobic organisms were recorded since anaerobic culture was not routinely done at our study site. However, anaerobes have been isolated in many previous studies.[10,13–15,21,22] *Bacteroides* (20%) and peptostreptococci (11%) were the most frequently isolated anaerobes in a case series by Giuliano et al.[23] Variation in the isolates between studies is most probably explained by the use of different antibiotics and culture techniques. Since a number of bacteria can lead to NF, the disease must be considered as a clinical entity and not a specific bacterial infection.[2]

Saini et al[24] reported the polymicrobial causes of surgical infections, and isolated *Streptococcus pyogenes* in a small proportion of cases. They were also able to identify the following as the most common organisms in surgical infections: *E. coli*, *S. aureus*, *Klebsiella* spp., *Pseudomonas aeruginosa*, *Bacteroides fragilis* and *Peptostreptococcus* spp.[24]

Based on the antimicrobial susceptibility patterns in the present study, the suggested empiric antibiotic regimen should include drugs with Gram-negative, Gram-positive and anaerobic coverage. Specifically, the following have been shown to be highly effective against the aerobic organisms isolated in our study: piperacillin-tazobactam, ampicillin-sulbactam, cefuroxime, ceftazidime, ceftriaxone, imipenem and gentamicin. The empiric antibiotic regimen must be chosen by taking into consideration the underlying clinical setting of the necrotizing infection, with the most probable antimicrobial susceptibility of the organisms involved.

In a recent retrospective study[25] of 89 patients with NF, it has been reported that advanced age, presence of two or more associated comorbidities, and a delay of > 24 hours from admission to surgery were significantly associated with increased mortality ($p < 0.05$). Among the three factors, a delay of > 24 hours from admission to surgery was the only independent predictor of mortality after adjusting for age, sex, diabetes and hypotension.[25] This is in contrast to the result of the present study that showed that only hypoalbuminaemia and acidosis were independent risk factors that predicted mortality. In a prospective, population-based surveillance by Kaul et al,[6] a high mortality rate of 34% was reported, and mortality was significantly correlated with increasing age ($p = 0.006$), hypotension ($p = 0.01$) and bacteraemia ($p = 0.03$).

As a result of the substantial mortality associated with NF, a high index of suspicion is important. However, given the preponderance of nonspecific initial manifestations, early diagnosis is difficult. Disease outcome is affected adversely by host immunity and bacterial isolates. Due to the myriad of bacterial isolates involved, empiric antibiotics must have an adequate spectrum against the typical bacteria involved. Certain clinical markers could be used to predict adverse outcomes. Still, aggressive surgical debridement is the cornerstone treatment of this devastating soft tissue infection. Broad-spectrum antimicrobial regimen tends to mask the severity of the infection and its clinical presentation, thus may delay hospital admission.[25]

This descriptive study was limited largely by the quality of the study site's electronic database, microbiology laboratory, and possible concerns with extrapolating findings to other patient populations. The clinical characteristics, microbial cultures and risk factors identified and analyzed were limited by the availability of data in the electronic database. The clinical manifestations described

were dependent on the presence or absence of the pertinent positive or negative signs or symptoms, as recorded in the electronic patient records. In terms of bacteriology, not all patients had microbial cultures performed. Furthermore, anaerobic cultures are not performed routinely in the institution, which prevented their categorical enumeration in the present study. Standard discs for antimicrobial susceptibility testing of all potential antimicrobials for NF were not available at the study site. This limited the reported susceptibilities to those for antimicrobials with available suseptibility discs only. The extrapolation of the risk factors for mortality could also be influenced by the unique characteristics of the study population (i.e. high prevalence of Fournier's gangrene). The use of arterial pH to assess the severity of NF is suboptimal and ill-advised, as better measures of systemic hypoperfusion have been found to be predictive of mortality for the critically ill (lactate and/or superior vena cava oxygen saturation [ScVO$_2$])[26] and because arterial pH can be misleadingly normal due to respiratory compensation. Determining the accuracy of the risk factors should be tested in a prospectively designed study.

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