

# Factors Related to Mortality from Necrotizing Fasciitis at Sawanpracharak Hospital

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## Abstract

**Objective:** To determine the factors associated with necrotizing fasciitis at Sawanpracharak Hospital, Nakhonsawan.

**Materials and Methods:** Data were collected from medical records of patients who were diagnosed with necrotizing fasciitis during the period between January 2016 and December 2017. Logistic regression analysis was used to analyze the association between risk factors and mortality.

**Results:** Factors affecting mortality included hemorrhagic bleb (33.9% vs 66.7%,  $p$  value 0.02), hypotension (5.5% vs 40.0%,  $p$  value < 0.01), alteration of conscious (3.7% vs 40.0%,  $p$  value < 0.01), and acidosis (52.3% vs 86.7%,  $p$  value 0.01). Alteration of conscious increased the odds of mortality by 19.2 times (odds ratio 19.2, 95% CI 3.15-117,  $p$  value < 0.01).

**Conclusion:** Factors associated with necrotizing fasciitis at Sawanpracharak Hospital were related to the severity of the disease such as sepsis. It is imperative that there is a quick diagnosis of the infection, followed by an appropriate administering of antibiotic and surgical interventions to reduce the rate of mortality.

**Keywords:** Risk factors, Mortality, Necrotizing fasciitis

## INTRODUCTION

Necrotizing fasciitis (NF) is a serious infection of the skin and soft tissue. NF is a disease with a high mortality rate of 6 to 67%<sup>1</sup>. Some of the symptoms include mild to severe edema and redness at the affected area, with high-grade fever or sepsis<sup>2</sup>. Patients who have underlying conditions such as diabetes mellitus, cirrhosis, obesity, chronic alcohol drinking, malignancy, and immunocompromised host, may experience greater severity of these symptoms at the onset of NF<sup>3</sup>. The most common pathogen for this infection is staphylococcus group A but is often polymicrobial, including bacteria species such as staphylococcus, bacteroides, and clostridium species<sup>4,5</sup>.

Sawanpracharak hospital is a tertiary care center of Public Health Region 3 of Thailand. In the years 2007 to 2008, the hospital received one hundred and forty-nine patients with the diagnosis of NF. In these patients, there was a 22%<sup>6</sup> mortality rate—which is considerably high. Based on previous studies, the rate of mortality should be lower. This may be due to a variety of factors, such as the response of the pathogens to antibiotics, which may have changed with time. Therefore further studies are needed.

The result of treatment for NF is primarily based on the duration of diagnosis, duration of administering the antibiotic, surgical debridement, and the overall

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conditions of the patient<sup>7</sup>. According to previous studies, patients with advanced age (> 60 years), advanced clinical presentation, aeromonas infection, vibrio infection, liver cirrhosis, cancer, hypotension, and rising serum creatinine, have shown to be independent predictors of mortality from NF<sup>8,9</sup>. The present study aimed to identify risk factors associated with the mortality from NF, in order to provide better treatment for future patients.

### MATERIALS AND METHODS

This was a retrospective cohort study on patients who were diagnosed with NF in the surgical ward and treatment facility at Sawanpracharak hospital from January 2016 to December 2017. An electronic search was made for all patients having been discharged from Sawanpracharak Hospital with the diagnosis of and treatment for necrotizing fasciitis (International Statistical Classification of Diseases 10<sup>th</sup> revision version 2010, code M72.6).

Data collected included, but not limited to: patient's age, gender, underlying conditions, anatomical location of infection, clinical signs and symptoms, time-onset of infection prior to treatment, laboratory values on admission, and tissue culture. Qualitative variables are presented as counts and percentages. Numeric variables are presented as mean and standard deviation. Logistic regression analysis was used to examine the relationship between risk factors and mortality. Any association was considered significant if the p-value was less than 0.05.

### RESULTS

According to the medical records, there were 124 patients who were diagnosed with NF at Sawanpracharak hospital between January 2016 until December 2017. Of these, 61% were male, 53% were over the age of 60, 49% had pre-existing diabetes mellitus. The mortality rate was 12% in these patients. The most common site of the infection was in the lower extremities, particularly the feet and lower leg. Common symptoms exhibited by the patients included pain, erythema, and swelling (Table 1).

Laboratory values on admission were collected and analysed. Acidosis was present in 87%, and white blood cell counts more than 15,000 / uL or less than 5,000 / uL were present in 73% of patients who died.

Most patients underwent a single operation. The most common surgical procedure was excision and debridement, which was performed 127 times (Table 2).

**Table 1** Patient characteristics and comorbidities.

| Data                                 | Number (%)<br>( N = 124 ) |
|--------------------------------------|---------------------------|
| <b>Sex</b>                           |                           |
| Male                                 | 76 (61)                   |
| Female                               | 48 (39)                   |
| <b>Age</b>                           |                           |
| < 60 years                           | 58 (47)                   |
| ≥ 60 years                           | 66 (53)                   |
| <b>Underlying diseases</b>           |                           |
| Diabetes mellitus                    | 61 (49)                   |
| Chronic kidney disease               | 10 (8)                    |
| Cirrhosis                            | 4 (3)                     |
| Peripheral vascular disease          | 1 (1)                     |
| <b>Location of infection</b>         |                           |
| Upper extremities                    | 110 (88)                  |
| Lower extremities                    | 14 (12)                   |
| <b>Presenting signs and symptoms</b> |                           |
| Erythema                             | 90 (73)                   |
| Pain                                 | 88 (71)                   |
| Fever                                | 59 (48)                   |
| Skin necrosis                        | 57 (46)                   |
| Hemorrhagic bleb                     | 47 (38)                   |
| Hypotension                          | 12 (10)                   |
| Alteration of conscious              | 10 (8)                    |

Abbreviations: CKD; Chronic kidney disease, PAD; Peripheral arterial disease.

**Table 2** Types of operations

| Type of operation          | Number |
|----------------------------|--------|
| Excisional debridement     | 127    |
| Toe amputation             | 29     |
| Transmetatarsal amputation | 8      |
| Above-knee amputation      | 3      |

For patients with symptoms, the average time till diagnosis ( $\pm$  standard deviation) was  $3.7 \pm 3.1$  days for the recovery group, and  $3.4 \pm 2.4$  days for the deceased group. The average time to the administration of antibiotics was  $108.7 \pm 93.5$  minutes for the recovery group and  $72.9 \pm 44.7$  minutes for the deceased group. The waiting time for surgery was  $432.1 \pm 304.2$  minutes for the recovery group and  $1031.9 \pm 199.8$  minutes for the deceased group (Table 4).

On univariable analysis, clinical factors associated with mortality included hemorrhagic bleb (34% vs 67%;

**Table 3** Comparison between patients who died and those who survived

|  | <b>Alive<br/>(n = 109)<br/>N (%)</b> | <b>Dead<br/>(n = 15)<br/>N (%)</b> | <b>p-value</b> |
|--|--------------------------------------|------------------------------------|----------------|
| <b>Characteristics and co-morbidity</b>          |                                      |                                    |                |
| Sex: Male  | 68 (62)                              | 8 (53)                             | 0.58           |
| Age (≥ 60 years)                                 | 56 (51)                              | 10 (67)                            | 0.29           |
| <b>Co-morbidities</b>                            |                                      |                                    |                |
| Diabetes mellitus                                | 53 (45)                              | 8 (53)                             | 0.79           |
| Chronic kidney disease                           | 10 (9)                               | 0 (0.0)                            | 0.61           |
| Cirrhosis  | 6 (6)                                | 0 (0.0)                            | 0.99           |
| Peripheral vascular disease                      | 1 (1)                                | 0 (0.0)                            | 0.99           |
| <b>Clinical presentation</b>                     |                                      |                                    |                |
| <b>Location of infection</b>                     |                                      |                                    |                |
| Lower extremities                                | 98 (90)                              | 12 (80)                            | 0.38           |
| Upper extremities                                | 11 (10)                              | 3 (20)                             |                |
| <b>Signs and symptoms</b>                        |                                      |                                    |                |
| Pain   | 78 (72)                              | 10 (67)                            | 0.76           |
| Erythema   | 76 (70)                              | 14 (93)                            | 0.07           |
| Hemorrhagic blebs                                | 37 (34)                              | 10 (67)                            | 0.02           |
| Skin necrosis                                    | 53 (49)                              | 4 (27)                             | 0.17           |
| Fever  | 48 (44)                              | 11 (73)                            | 0.05           |
| Hypotension                                      | 6 (6)                                | 6 (40)                             | < 0.01         |
| Alteration of conscious                          | 4 (4)                                | 6 (40)                             | < 0.01         |
| <b>Laboratory data</b>                           |                                      |                                    |                |
| Hematocrit < 30%                                 | 53 (49)                              | 9 (60)                             | 0.58           |
| Platelets < 100,000 /uL                          | 6 (6)                                | 2 (13)                             | 0.25           |
| WBC > 15,000 or < 5,000 /uL                      | 64 (59)                              | 11 (73)                            | 0.40           |
| Serum creatinine > 2 mg/dL                       | 23 (21)                              | 6 (40)                             | 0.12           |
| Serum sodium < 135 mEq/L                         | 67 (62)                              | 9 (60)                             | 0.99           |
| Serum potassium < 3.5 mEq/L                      | 26 (24)                              | 3 (20)                             | 0.99           |
| Acidosis   | 57 (52)                              | 13 (87)                            | 0.01           |
| <b>Time to diagnosis (days) [Median (range)]</b> | 3 (1-14)                             | 2 (1-7)                            | 0.73           |
| <b>Time to antibiotic (min) [Median (range)]</b> | 85 (16-675)                          | 73 (15-180)                        | 0.15           |
| <b>Time to operation (min) [Median (range)]</b>  | 394 (56-2,880)                       | 319 (178-7,200)                    | 0.32           |

**Table 4** Multivariable logistic regression analysis of factors associated with mortality from NF

|                         | <b>Adjusted odds ratio<br/>(95% confidence interval)</b> | <b>p-value</b> |
|-------------------------|--|----------------|
| Hemorrhagic blebs       | 3.30 (0.72-15.0)   | 0.841          |
| Hypotension             | 4.14 (0.78-22.1)   | 0.096          |
| Alteration of conscious | 19.2 (3.15-117)  | 0.001          |
| Acidosis                | 2.54 (0.44-14.6)   | 0.296          |

Table 5 Adjusted odd ratio for predictors of mortality from NF

|                         | Adjusted odd ratio<br>(95% confidence interval) | P-value |
|-------------------------|---|---------|
| Hemorrhagic blebs       | 3.30 (0.72-15.03)                               | 0.841   |
| Hypotension             | 4.14 (0.78-22.10)                               | 0.096   |
| Alteration of conscious | 19.20 (3.15-116.70)                             | 0.001   |
| Acidosis                | 2.54 (0.44-14.64)                               | 0.296   |

Table 6 Microbiology

| Organisms                                 | No. |
|---|-----|
| Not culture                               | 59  |
| <i>Streptococcus</i> spp.                 | 18  |
| <i>Staphylococcus</i> -coagulase negative | 9   |
| <i>A. Baumannii</i>                       | 9   |
| <i>E. coli</i>                            | 5   |
| <i>Enterococcus</i> spp.                  | 5   |
| <i>S. aureus</i>                          | 4   |
| <i>Klebsiella</i> spp.                    | 4   |
| <i>Pseudomonas</i> spp.                   | 3   |
| <i>Aeromonas</i> spp.                     | 2   |
| <i>Corynebacter</i> spp.                  | 2   |
| <i>Proteus</i> spp.                       | 1   |

*p*-value 0.02), hypotension (6% vs 40%, *p*-value < 0.01), alteration of consciousness (4% vs 40%, *p*-value < 0.01), and acidosis (52% vs 87%, *p*-value 0.01) (Table 3).

Multiple logistic regression analysis showed that only alteration of conscious significantly increased the risk of mortality, by 19.2 times (odds ratio 19.2, 95% CI: 3.15-117, *p*-value 0.001) (Table 4). There were 65 wounds from which tissue culture was taken, of which 62 showed identifiable organisms. Of these, *Streptococcus* species were identified in 18 cases, *Staphylococcus* coagulase-negative bacteria in 9 cases, and *Acinetobacter baumannii* in 9 cases.

Analyzed risk factors relating to patients with NF, followed by death by using Logistic regression multiple variables, it has been found that patients who have an alteration of conscious increased the risk of mortality by 19.2 times (odds ratio 19.20, 95% CI 3.15-116.70, *p*-value 0.001) (Table 5).

There were sixty-five cases of tissue culture, and sixty-two cases were identified. *Staphylococcus* spp. 18 cases, *Staphylococcus* coagulase-negative 9 cases, and *A. Baumannii* 9 cases (Table 6).

## DISCUSSION

At Sawanpracharak Hospital, NF is one of the most common soft tissue infections. The estimated incidence is 7.45 cases per 100,000 population, which is considered high when compared to that of developed countries, which is approximately 4 cases per 100,000 population<sup>10,11</sup>. Important factors affecting the results of treatment of NF include: a timely diagnosis, the proper surgical procedure, the administration of antibiotics, the severity of the disease, and the identified pathogen<sup>1,3,12,13</sup>. The diagnosis of NF is usually based on the clinical signs and symptoms, such as swelling, redness, and pain at the infected site. But sometimes it can be difficult to determine whether the infection is necrotic fasciitis or cellulitis<sup>3,14,15</sup>. It is important to rely on other signs to make a proper diagnosis. These additional signs, unfortunately, usually indicate a more advanced or progressive stages of the infection. These signs include crepitus, hemorrhagic bleb, skin necrosis, hypotension, and alteration of conscious<sup>12</sup>. In the present study, the most common signs and symptoms continued to be erythema, seen in 90% of cases, and pain seen in 88%. Based on the findings of a recent study<sup>16</sup>, if a patient has hypotension, loss of consciousness, or kidney and liver failure within 24 after diagnosis, better care and treatment could lower the risk of the patient's death.

NF is a soft tissue infection caused by toxin-producing bacteria, which can spread to venous and lymphatic channels. The infections are often associated with severe sepsis and can turn rapidly fatal. Hemorrhagic bleb occurs secondarily to the involvement of small vessels supplying the skin or results from infection with a gas-forming strain of bacteria<sup>3,17</sup>. The presence of hemorrhagic bleb and skin necrosis is often seen in the later stages of NF<sup>18,19</sup>. It has been reported that hemorrhagic bleb was an independent predictor of mortality in patients with NF<sup>9</sup>.

In addition to looking for the signs and symptoms of NF, doctors should also rely on laboratory results for early recognition and accuracy of the diagnosis: laboratory risk indicator for necrotizing fasciitis (LRINEC) score, in conjunction with C-reactive protein level, WBC, hemoglobin level, serum calcium level, serum creatinine and serum glucose levels<sup>20</sup>. In the present study, there was no laboratory factor listed in the LRINEC score which was associated with NF mortality. However, we found that patients who have acidosis – which is a condition associated with hypotension, alteration of consciousness, and sepsis – is significantly associated with mortality. Further, from other previous studies, it has been shown that sepsis is the leading cause of death by way of NF<sup>21</sup>. After being diagnosed with NF, patients who undergo surgery within 24 hours have a better recovery rate<sup>3</sup>. Patients who received their surgery after 24 hours have a higher mortality rate, and tend to exhibit unstable vital signs and abnormal laboratory test results, which need to be corrected before surgery.

Necrotizing fasciitis is classified into 2 types, depending on the microbial cause. Type 1 necrotizing fasciitis is a polymicrobial infection, a combination of aerobic and anaerobic bacteria, and is the most common type. Type 2 necrotizing fasciitis is caused by Gram-positive bacteria such as *Streptococcus* spp<sup>22</sup>. In the present study, type 1 NF could not be diagnosed because of the lack of anaerobic culture facilities, a limitation of our institute. However, available tissue culture showed that the most common organisms were Gram-positive bacteria, so the choice of empirical antibiotics should cover Gram-positive bacteria.

### CONCLUSION

Factors related to mortality from necrotizing fasciitis included hemorrhagic bleb, hypotension, alteration of consciousness, and acidosis. It is imperative to diagnose the infection as soon as possible, followed by appropriate administration of antibiotics and surgical intervention to reduce the rate of mortality.

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**บทคัดย่อ** ปัจจัยที่มีผลต่อการเสียชีวิตในภาวะเนื้อเน่าตาย ในโรงพยาบาลสวรรค์ประชารักษ์  
กรกฤษณ์ เลาหศักดิ์ประสิทธิ์, พบ.

กลุ่มงานศัลยกรรม โรงพยาบาลสวรรค์ประชารักษ์ จังหวัดนครสวรรค์

**วัตถุประสงค์:** ศึกษาหาปัจจัยที่เกี่ยวข้องต่อการเสียชีวิตในภาวะเนื้อเน่าตายของผู้ป่วยในโรงพยาบาล  
สวรรค์ประชารักษ์ จังหวัดนครสวรรค์

**วัตถุประสงค์และวิธีการ:** ทบทวนเวชระเบียนระหว่างเดือนมกราคม 2559 ถึงเดือนธันวาคม 2560 เปรียบเทียบ  
ปัจจัยที่ศึกษาโดยใช้สถิติในการวิเคราะห์แบบถดถอย (Logistic regression analysis)

**ผลการศึกษา:** มีผู้ป่วยภาวะเนื้อเน่าตาย 124 ราย เป็นผู้ป่วยชายร้อยละ 61.3 อายุมากกว่า 60 ปี ร้อยละ 53.2  
และมีโรคประจำตัวเป็นเบาหวานร้อยละ 49.2 อัตราการเสียชีวิตร้อยละ 12.1 ตำแหน่งของรอยโรคส่วนใหญ่อยู่ที่  
รยางค์ส่วนล่างร้อยละ 87.7 อาการและอาการแสดงที่พบบ่อยที่สุดคือ บวมแดง และปวดบริเวณรอยโรค ปัจจัย  
ที่มีผลต่อการเสียชีวิต ได้แก่ ตุ่มน้ำพองข้างในมีเลือด (33.9% vs 66.7%,  $p$ -value 0.02) ความดันโลหิตต่ำ (5.5%  
vs 40.0%,  $p$ -value < 0.001) มีความรู้สึกตัวเปลี่ยนแปลง (3.7% vs 40.0%,  $p$ -value < 0.001) และภาวะความเป็น  
กรดในเลือด (52.3% vs 86.7%,  $p$ -value 0.01) เมื่อทำการวิเคราะห์แบบ Logistic regression multiple variable  
พบว่าหากมีความรู้สึกตัวเปลี่ยนแปลงโอกาสเสียชีวิต 19.20 เท่า (Odd ratio 19.20, 95% CI 3.15-116.70,  $p$ -value  
0.001) มีการส่งเพาะเชื้อจากเนื้อเยื่อ 65 ราย *Streptococcus* spp. เป็นเชื้อก่อโรคที่พบบ่อยที่สุด

**สรุปผลการศึกษา:** ปัจจัยที่มีผลต่อการเสียชีวิต ได้แก่ ตุ่มน้ำพองข้างในมีเลือด ความดันโลหิตต่ำ ความ  
รู้สึกตัวเปลี่ยนแปลง และภาวะความเป็นกรดในเลือดซึ่งสัมพันธ์กับความรุนแรงของโรคที่มากขึ้นตามระยะเวลา  
ที่เพิ่มขึ้น ดังนั้น จึงควรให้คำวินิจฉัยและการรักษาอย่างเหมาะสม เพื่อลดอัตราการเสียชีวิต

**คำสำคัญ:** ปัจจัยเสี่ยง, การเสียชีวิต, ภาวะเนื้อเน่าตาย