

**Retrospective Study of the Outcome of Necrotizing Fasciitis in
Intensive Care Unit, Hospital Raja Perempuan Zainab 11,
Kota Bharu, Kelantan.**

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**Dissertation submitted in partial fulfilment of the requirements for the
Degree of Masters of Medicine (Anaesthesiology)**



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FOREWORD

In the name of Allah, the Most Gracious, Most Merciful. Praise to Allah, by His Grace, this manuscript is able to be finished and completed within the time frame provided.

This manuscript is unable to be produced successfully without assistance and guidance from many people. Therefore, I would like to offer my sincere thanks to all of them.

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To my dear husband Dr Mohd Azmi bin Yaacob who always accompany and support my endeavours, my adorable child Mohd Harith Nuruddin B Mohd Azmi, Zainab Bt Mohd Azmi, Muhammad Hadyan bin Mohd Azmi and all family members, thanks for their prayer and of course, the endless love, support and patience. May Allah (SWT) bless every one of us.

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ABBREVIATION

| | |
|--------|--|
| APACHE | Acute physiology and chronic health evaluation |
| Cr | Creatinine |
| ICU | Intensive care unit |
| IQR | Interquartile range |
| IV | Intravenous |
| MAP | Mean arterial pressure |
| MRSA | Methicillin resistant <i>Staphylococcus aureus</i> |
| MSSA | Methicillin sensitive <i>Staphylococcus aureus</i> |
| NSTI | Necrotizing soft tissue infection |
| ROC | Receiver operating characteristics |
| SBP | Systolic blood pressure |
| SIRS | Systemic inflammatory response syndrome |
| WBC | White blood count |

ABSTRACT

OBSERVATIONAL STUDY OF THE OUTCOME OF NECROTIZING FASCIITIS IN INTENSIVE CARE UNIT HOSPITAL RAJA PEREMPUAN ZAINAB 11 KOTA BHARU KELANTAN.

Background: Necrotizing fasciitis is a rapidly progressive soft tissue infection involving deep fascia which carries relatively high mortality rate worldwide. The aim of this study is to determine the mortality rate in our local general hospital and to investigate the factors that determine the primary outcome (mortality) of the necrotizing fasciitis patients treated in Intensive Care Unit.

Methods: This is retrospective cross sectional study involved 71 patients admitted to intensive care unit (ICU) HRPZ II from January 2012 to December 2015. Patients were analyzed for presence of co-morbidities, Acute Physiology and Chronic Health Evaluation (APACHE II score), factors important in pathogenesis and treatment, and mortality.

Results: The overall mortality was 22/71(31%). The mean APACHE II score was 19.2 (SD=6.57) and the median time to operation was 50 hours (IQR=70.0). Factors directly contributing towards mortality were higher APACHE II score (adjusted OR 1.41, 95%CI: 1.20, 1.66, $P < 0.001$) and an increase in time to surgical debridement (adjusted OR 1.03, 95%CI: 1.01, 1.05, $P=0.003$).

Conclusion: Early surgical debridement was crucial in the treating the necrotizing fasciitis. High APACHE 11 score during admission was associated with increase mortality.

ABSTRAK

KAJIAN PEMERHATIAN DARI HASIL PESAKIT NECROTIZING FASCIITIS YANG DIRAWAT DI UNIT RAWATAN RAPI HOSPITAL RAJA PEREMPUAN ZAINAB 11 KOTA BHARU KELANTAN

Objektif: “Necrotizing fasciitis” adalah jangkitan pada tisu badan yang melibatkan fascia dan membawa kadar kematian yang tinggi di seluruh dunia. Tujuan kajian ini adalah untuk menentukan kadar kematian “necrotizing fasciitis” di hospital besar tempatan kami dan untuk menyiasat faktor-faktor yang menyumbang ke arah kematian pesakit “necrotizing fasciitis” dirawat di Unit Rawatan Rapi.

Kaedah: Ini adalah kajian retrospektif yang melibatkan 71 pesakit yang dimasukkan ke Unit Rawatan Rapi (ICU) HRPZ II dari Januari 2012 hingga Disember 2015. Pesakit telah dianalisis untuk morbiditi, Acute Physiology and Chronic Health Evaluation (APACHE skor II), faktor-faktor penting dalam patogenesis dan rawatan, dan kematian.

Keputusan: Jumlah ematian keseluruhan adalah 22/71 (31%). min skor APACHE II adalah 19.2 (SD = 6.57) dan masa median untuk operasi adalah 50 jam (IQR = 70.0). Faktor-faktor yang secara langsung menyumbang kepada kematian adalah lebih tinggi APACHE II skor (adjusted OR 1.41, 95% CI: 1.20, 1.66, $P < 0.001$) dan kelambatan untuk melakukan pembedahan (adjusted OR 1.03, 95% CI: 1.01, 1.05, $P = 0.003$).

Kesimpulan: Kajian menunjukkan bahawa pembedahan awal adalah penting dalam pengurusan jangkitan tisu “necrotizing” kerana ia memberi kesan besar kepada keputusan pesakit dari segi kematian. Pesakit yang tinggi APACHE 11 skornya harus dimasukkan awal ke unit rawatan rapi untuk penjagaan yang lebih rapi dan sistematik kerana semakin tinggi skor kadar kematian akan meningkat.

CHAPTER 1

1.0 INTRODUCTION AND LITERATURE REVIEW

Necrotizing fasciitis is a rare but rapidly progressive soft tissue infection involving the subcutaneous tissue, fat and deep fascia, typically sparing muscle. This infection, which is usually induced by virulent, toxin producing bacteria, can occur in any region of the body but it is predominantly located in the abdominal wall, perineum and extremities.(1). It is associated with extensive soft tissue necrosis, profound septic shock and high morbidity and mortality.

On the basis of microbiological cultures Giuliano and colleagues divided the necrotizing fasciitis into two distinct groups.

- Type I infections are polymicrobial and involve non-group-A streptococci, aerobes and/or facultative anaerobic bacteria, usually seen in patients with comorbidities (eg, diabetes or peripheral vascular disease).
- Type II is usually caused by β -haemolytic group-A streptococci alone or in combination with staphylococci.(2).

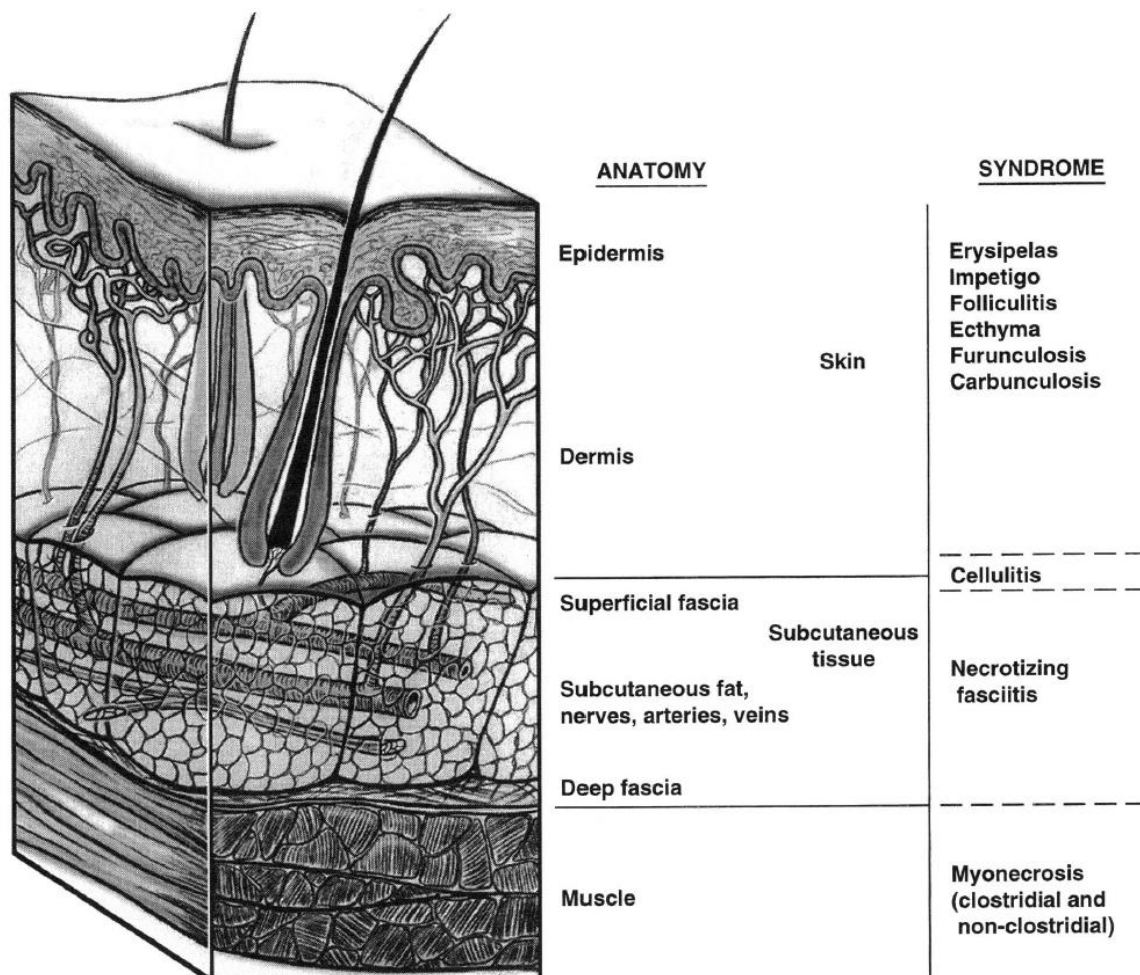


Figure 1.0 Anatomic and clinical classification of soft tissue infections

(Source : Chest Journal ,Volume 110, July 1996 “Necrotising Fasciitis”)

HISTORY

Hippocrates in the 5th century was the first who described necrotizing fasciitis as a complication of "erysipelas" (3). In the early 19th century, few names were used interchangeably to describe necrotizing fasciitis include the malignant ulcer, gangrenous ulcer, putrid ulcer, phagedena ("eating away"), phagedenic ulcer, phagedena gangraenosa, and hospital gangrene. By the mid 19th century, most of treating surgeon preferred to use hospital gangrene and phagedena to describe it (1).

Meleney reported a series of 20 patients in 1924 as having "hemolytic streptococcal gangrene," later called as Meleney's gangrene. The first description of necrotizing fasciitis was by a Confederate Army surgeon, Joseph Jones during the US Civil War 1871, who called it hospital gangrene (4). Wilson in 1952 was first who used the term necrotizing fasciitis, the most accurately described consistent with the nature of infection, facial necrosis (5).

The French venereologist Jean Alfred Fournier was first identified Fournier gangrene in 1883. He described a series in which 5 previously healthy young men suffered from a rapidly progressive gangrene of the penis and scrotum without apparent cause. This condition, which later described as Fournier gangrene, is defined as a polymicrobial necrotizing fasciitis of the perineal, perianal, or genital areas.(6)

PATHOPHYSIOLOGY

The pathogen enters the human body into subcutaneous tissue either through disruption of the overlying skin or by hematogenous spread from a distant site of infection. Polymicrobial necrotizing fasciitis (Type 1) is usually caused by enteric pathogens, whereas monomicrobial necrotizing fasciitis (Type 2) is usually due to skin flora.(1)

The release of endogenous cytokines and bacterial toxins are believed to result in tissue damage and systemic toxicity. Diagnosis is often extremely difficult due to the lack of skin findings early in the disease and it relies on a high index of clinical suspicion. Definitive diagnosis is made based on operative finding that is demonstration of a lack of resistance of normally adherent fascia to blunt dissection (1).

CLINICAL PRESENTATION

Retrospective study in New Zealand intensive care unit over 8.5 years showed swelling (83%) and severe pain (76%) were the most common presenting features , lower limb was the most frequent site of infection (53%) and Type 2 infection (52%) was more common than type 1 (43%).Mortality was 29% (7).

Study conducted in India between 1995-2005 showed the prevalence of this disease was higher in males than females with the rate of 2.6:1. Diabetes mellitus was the most common predisposing disease. Genital region was the most common site of involvement. Nonspecific erythema was the main dermatological manifestation (8).

One study in China involved forty six patient admitted from 2002-2008 showed the median patient age was 63 years (range, 22-85) with majority patients were male (76%). From this study, the most common affected site was lower limb (67.4%). The incidence more common in immunocompromised patient (74%), followed by diabetes mellitus (39%) and chronic renal failure, Cr >1.6mg/dL (19%) (9).

APACHE 11 SCORING

In modern medicine the use of scoring systems to predict risk of mortality and evaluating outcome in critically ill patients is important. Prognostic or general severity scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE) evaluate the risk based on clinical data available within the first 24 hours of ICU stay.(10).

The APACHE scoring was initially developed in 1982 based on the assumption that the severity of acute disease could be measured by quantifying the degree of abnormality of physiologic variables. The APACHE II model was developed and published in 1985 due to the complexity of the primary model and it has become the most frequently used.(10). The original number of physiologic variables was revised and reduced from 34 to 12 and some were re-weighted (11).

Study involving 67 patients presenting with NSTIs to the Department of General Surgery, Uludag University Medical Faculty between January 1986 and December 2002 showed the overall mean APACHE II score was 13.9 ± 1.01 . The mean APACHE II scores were 8.5 for survivors and 19.6 for non survivors. ROC analysis revealed a threshold APACHE II score for mortality of 13. The mortality rate for patients with an APACHE II score of 13 was 21%, whereas the mortality rate for patients with a score of 14 or higher was 86% ($p = 0.001$). All patients with an APACHE II score of 20 or higher ($n = 18$) died (12). Another retrospective review in New Zealand intensive care unit showed that APACHE II score, pre-existing renal impairment and gout were all independent predictors of mortality (13).

Certain markers predict those individuals at increased risk for multiple-organ failure and death and therefore assist in deciding allocation of intensive care resources(14). It is possible that the low mortality rate was due to a lower severity of illness, with a median APACHE II score of 14 (12–20). The only other study to report APACHE scores recorded a higher median score of 22.95 .However, only patients requiring ICU admission were included, 96% of patients met the SIRS/sepsis criteria, 71% met the criteria for severe sepsis or septic shock and 71% of patients required ventilatory and vasopressor support, all of which suggest severe illness.

ORGANISM ISOLATED DURING OPERATION

Study done in Ohio analysed sixty five patients with NSTIs secondary to postoperative wound complications , trauma , cutaneous disease , idiopathic causes , perirectal abscesses , strangulated hernias , and subcutaneous injections who were treated between January 1989 and June 1994. *Streptococcus pyogenes* infection was the most common cause of monomicrobial necrotising soft tissue infection, but was not associated with an increased mortality(15).

One study involving 65 patients in Ohio showed the most common infection was type 1 infection (polymicrobial) in 45 patients (69%). *Streptococcus pyogenes* was isolated in only 17% of the cases, but accounted for 53% of type 2 infections. From one study conducted in India from 1995 to 2005, the most common organism isolated was *Enterococcus faecalis* (8).

From another study in China, forty-six patients with monomicrobial necrotizing fasciitis were examined retrospectively from November 2002 to January 2008 Chang Gung Memorial Hospital at Chia Yi. Most of the patients (76.1%) were infected with gram-negative bacillus and *Vibrio* species were the most commonly isolated (65.7%) predominantly *Vibrio vulnificus*, followed by *K. pneumonia*, *Escherichia coli* and *Pseudomonas Stutzeri*. 23.9% were infected with gram-positive cocci with *Staphylococcus aureus* was the most commonly isolated (54.5%), followed by beta-hemolytic *Streptococcus* (36.3%) and *S. viridans*(9.1%). In six *Staphylococcus aureus*, four were *Methicillin-Sensitive Staphylococcus aureus* (MSSA), and two were *Methicillin-Resistant Staphylococcus aureus* (MRSA). *Prevotella* spp., an anaerobic gram-negative bacterium, was found in one (2.9%) patient (9).

MANAGEMENT

Necrotizing soft tissue infections was one of the highly lethal soft tissue infections which best treated by early and repeated aggressive debridement and broad-spectrum antibiotics. In some of the cases, hyperbaric oxygen therapy offers the advantage of early wound closure (14).

Treatment modalities in necrotizing soft tissue infection were include surgical debridement, antibiotics, supportive care, and hyperbaric oxygen. Early and adequate surgical debridement and fasciotomy have been showed to improved patient's survival. The initial antibiotic therapy should include broad spectrum coverage. Mortality rates are as high as 76%. Delays in diagnosis and/or treatment associated with poor outcome, with the main cause of death being overwhelming sepsis and multiorgan failure (17).

Sixty-five patients were identified between January 1989 and June 1994 from MetroHealth Medical Center Cleveland, Ohio. This patient were analysed for presentation, etiology, factors important in pathogenesis and treatment, and mortality. The result showed early debridement of necrotizing fasciitis was associated with a significant decrease in mortality (16).

The keys of successful in management of necrotizing soft tissue infection were include early diagnosis, aggressive surgical debridement, antibiotics, and intensive care unit support. The most common pitfall in treatment is delay in diagnosis followed by inadequacy of surgical debridement (18).

The main treatment of necrotizing soft tissue infections include early surgical debridement, fluid resuscitation, antibiotics, and general cardiorespiratory supportive care to maintain vital organ function (19). Surgical debridement should be early and extensive in which all necrotic tissue must be excised (16). Repeat debridement, sometimes on a daily basis, should be done until the local infectious process has been arrested. From one study in Ohio, an average of 3.3 operative debridement per patient and amputation in 12 patients were necessary to control infection (16). The coverage of the wound is usually obtained by skin grafting later once the sepsis is controlled (18).

The surgical debridement usually were repeated every 2 days until all necrotic tissue had been removed. Amputation may be required in some cases which generally was performed in two stages, initially leaving the tissues open after the initial debriding amputation and wound closure performed later once the tissue healthy and viable allowing reapproximation of the skin or skin grafting (14).

A retrospective case and chart review was performed in 58 patients with necrotising fasciitis admitted to the intensive care unit of a tertiary hospital in New Zealand between January 2000 and June 2008. The mean time from presentation to surgery was 17 hours (range:1 hour and 32 minutes to 5 days 12 hours and 33 minutes . Four patients did not undergone surgery — one patients refused, one died before surgery and two were considered moribund and received palliative care. From those who had surgery, 63% were operated on within the first 12 hours and 81% within 24 hours. The median number of operative procedures performed per patient was 4 (IQR, 1.75–6). Median length of stay in hospital was 31 days (IQR, 9–55 days). ICU length of stay was 65 hours (IQR, 15–194 hours) with most of the patients required ventilation (79%) and median duration of ventilation was 28.5 hours

(IQR, 3.5–91.25 hours). Renal replacement therapy was performed in 29% of patients. APACHE II scores ranged from 6 to 31 (median, 21 [IQR, 15.75–25]). Mortality rate was 29% (13).

Principles for managing septic shock such as intravenous fluid resuscitation, mechanical ventilation, and inotropic support should be instituted accordingly (20). Broad spectrum antibiotic and anaerobic coverage is essential. Many antibiotic combinations are acceptable. The usually combination were penicillin (or a cephalosporin), anaerobic coverage (clindamycin or metronidazole), and Gram-negative coverage (aminoglycoside, third-generation cephalosporin, or ciprofloxacin). Antibiotics are modified after Gram stains, culture and sensitivity results available. Blood cultures and wound cultures are both useful, but simple wound swabs are usually insufficient for proper culturing. Finally, antibiotic treatment is should also be guided by the finding gained during operation(18).

The risk factors for mortality include advanced age, underlying illness, hypotension, and bacteraemia. Based on this study, the results suggest that necrotizing soft tissue infections due to Group A streptococcus might be increasing in frequency and aggression. Overall mortality remains high (20% to 34% in larger series) (21-23). Clinical diagnosis requires a high index of suspicion upon presentation (24).

Despite aggressive therapy, and modern intensive care unit support, the mortality of necrotizing soft tissue infections still remains high in some countries (15–50%). Factors associated with increased mortality include extent of soft tissue involvement, delay in diagnosis, inadequate debridement, advanced age, and truncal involvement.

Early commencement of antibiotics is essential in the treatment of sepsis and necrotizing fasciitis, although early surgical debridement is the mainstay of treatment (25). One study conducted in Australia intensive care unit involving 20 patients showed that only 25% of patients had positive blood cultures, with most organisms being identified from the infected sites. The initial antibiotics given in this study were active against the subsequently cultured bacteria isolated from surgical site in 83% of cases. This highlights the importance of early clinical suspicion and compliance with empirical guidelines, as blood cultures alone may not aid with the diagnosis or administration of appropriate antibiotic therapy (26).

CHAPTER 2 : STUDY PROTOCOL

2.1 DISSERTATION PROPOSAL

TITLE

OBSERVATIONAL STUDY OF THE OUTCOME OF NECROTIZING FASCITIS IN
INTENSIVE CARE UNIT HOSPITAL RAJA PEREMPUAN ZAINAB 11 KOTA
BHARU KELANTAN.

NAME OF THE STUDENT:

Dr NOOR SHAZLINI BINTI MUSTAPA

NAME OF SUPERVISOR:

ASSOC. PROF. DR. SAEDAH BINTI ALI

NAME OF CO-SUPERVISOR:

PROF SHAMSULKAMARUJAN BIN HASSAN

DR MOHD NAZRI BIN ALI

STUDY DURATION

1ST DISEMBER 2014 – 30TH APRIL 2016

INTRODUCTION

Necrotizing fasciitis is a rare but life-threatening soft-tissue infection characterized by rapidly spreading inflammation and subsequent necrosis of the fascial planes and surrounding tissue. Infection typically follows trauma, although the inciting insult may be as minor as a scrape or an insect bite. Often caused by toxin-producing, virulent bacteria such as group A streptococcus and associated with severe systemic toxicity.

Necrotizing fasciitis is often initially misdiagnosed as a more benign soft-tissue infection. The single most important variable influencing mortality is time to surgical debridement. Thus, a high degree of clinical suspicion is necessary to avert potentially disastrous consequences. Orthopaedic surgeons are often the first to evaluate patients with necrotizing fasciitis and as such must be aware of the presentation and management of this disease.

Necrotizing fasciitis, the most extreme form of these infections, may be life-threatening. Consequently, physicians need to know how to diagnose and effectively treat this deep infection of the subcutaneous tissues. The diagnosis of necrotizing fasciitis is based on the history (i.e., predisposing factors to infection), gram staining and culture, radiography and, ultimately, surgical exploration. Timely diagnosis, broad-spectrum antibiotic therapy, and aggressive surgical debridement of affected tissue are keys to the treatment of this serious, often life-threatening infection.

Diabetes mellitus was the most common co-morbid. Pseudomonas, Staphylococcus, Streptococcus and Enterobacteriaceae were the common pathogens isolated.

LITERATURE REVIEW

Literature review was done by internet search using PUBMED, SPRINGERLINK, OVID, PROQUEST and Wiley Online Library via ESYPROXY USM. Keywords such as necrotizing fasciitis, soft tissue infection, and intensive care unit were used.

An article title “*Early diagnosis and treatment of necrotizing fasciitis can improve survival: an observational intensive care unit cohort study*” by Bucca K1, Spencer R, Orford N, Cattigan C, Athan E and McDonald A demonstrate one of the lowest reported mortality rates, with early surgical debridement being achieved in the majority of patients. The main delay was found to be in the diagnosis of Necrotising fasciitis.

A study conducted by Bingöl-Koloğlu M1, Yildiz RV, Alper B, Yağmurlu A, Ciftçi E, Gökçora IH, Ince E, Emiroğlu M, Dindar H from Department of Pediatric Surgery, Ankara University School of Medicine, Ankara, Turkey in paediatric population showed although these infections are rare in children, their lethal potential and early diagnostic signs must be recognized. All children with NF should undergo early surgical debridement to prevent delay in treatment. The mortality and morbidity associated with Necrotizing fasciitis in children can be decreased with clinical awareness, early diagnosis, and adequate and urgent surgical debridement followed by intensive supportive care and early wound resurfacing.

An article titled “ *Necrotizing fasciitis: an epidemiologic study of 102 cases*” by Fazeli MS¹, Keramati MR. from Department of Surgery, Imam Hospital, Tehran. They we evaluated prevalence of variables including predisposing factors, clinical and para clinical findings, distribution of tissue involvement and mortality rate in 102 patients of necrotizing fasciitis at our Hospital between the years 1995 and 2005. The results showed that the prevalence of this disease was higher in males than females with the rate of 2.6:1. Diabetes mellitus was the most common predisposing disease. Genital region was the most common site of involvement. Muscles were involved in 25.5% of cases. Nonspecific erythema was the main dermatological manifestation. The most common organism was *Enterococcus faecalis* and mortality rate was 10.8%.

Study conducted by Kwan MK¹, Saw A, Chee EK, Lee CS, Lim CH, Zulkifle NA, Saarey NH, Mohamad Hussien MN from Department of Orthopaedic Surgery, University of Malaya Medical Centre, Kuala Lumpur, Malaysia title “*Necrotizing fasciitis of the lower limb: an outcome study of surgical treatment*”. They did a retrospective review of 36 cases of necrotizing fasciitis of the lower limb treated in our center between 1998 and 2002. Only 19% of the cases were correctly diagnosed upon admission and 48.6% were initially diagnosed as 'cellulitis'. Diabetes mellitus was the most common co-morbid. *Pseudomonas*, *Staphylococcus*, *Streptococcus* and *Enterobacteriaceae* were the common pathogens isolated. Ten patients (27.8%) had major amputation as part of radical debridement. The overall mortality rate was 36% with laboratory parameters: high serum urea and creatinine, and low haemoglobin levels were predictors for higher mortality. Poor white cell response which is common in diabetic patients and a delay in surgical debridement were notable attributes to a higher mortality. Necrotizing fasciitis is a serious infection associated with significant

morbidity and mortality. A poor white blood cell response, high serum urea and creatinine, and low haemoglobin level were the predictors for mortality. Early diagnosis and prompt treatment are of paramount importance in the treatment of this infection.

OBJECTIVES

General objective:

To study the outcome of necrotizing fasciitis patient treated in intensive care unit Hospital Raja Perempuan Zainab 2

Specific objectives:

- 1.To determine mortality rate of patient with necrotizing fasciitis admitted to intensive care unit Hospital Raja Perempuan Zainab 2.
- 2.To determine factors that contribute to mortality in necrotizing fasciitis patient treated in intensive care unit Hospital Raja Perempuan Zainab 2.
- 3.To study the association between time to surgical debridement with hospital mortality of necrotizing fasciitis patient treated in intensive care unit HRPZ 2.

RESEARCH METHODOLOGY

Study type:

Observational study

Study design:

Retrospective record review.

Study setting:

Intensive Care Units Hospital Raja Perempuan Zainab 11

Study population:

Necrotising fasciitis patients that admitted to ICU Hospital Raja Perempuan Zainab 11

Time Frame:

1st January 2012 until 31st November 2015

Inclusion criteria:

Patient admitted to ICU with necrotizing fascitis

Exclusion criteria:

Patient that developed necrotizing fascitis as a post operative complication

DATA COLLECTION

Patient who fulfill the inclusion and exclusion criteria as above will in included in this study.

A serial of information will be obtained from patient database

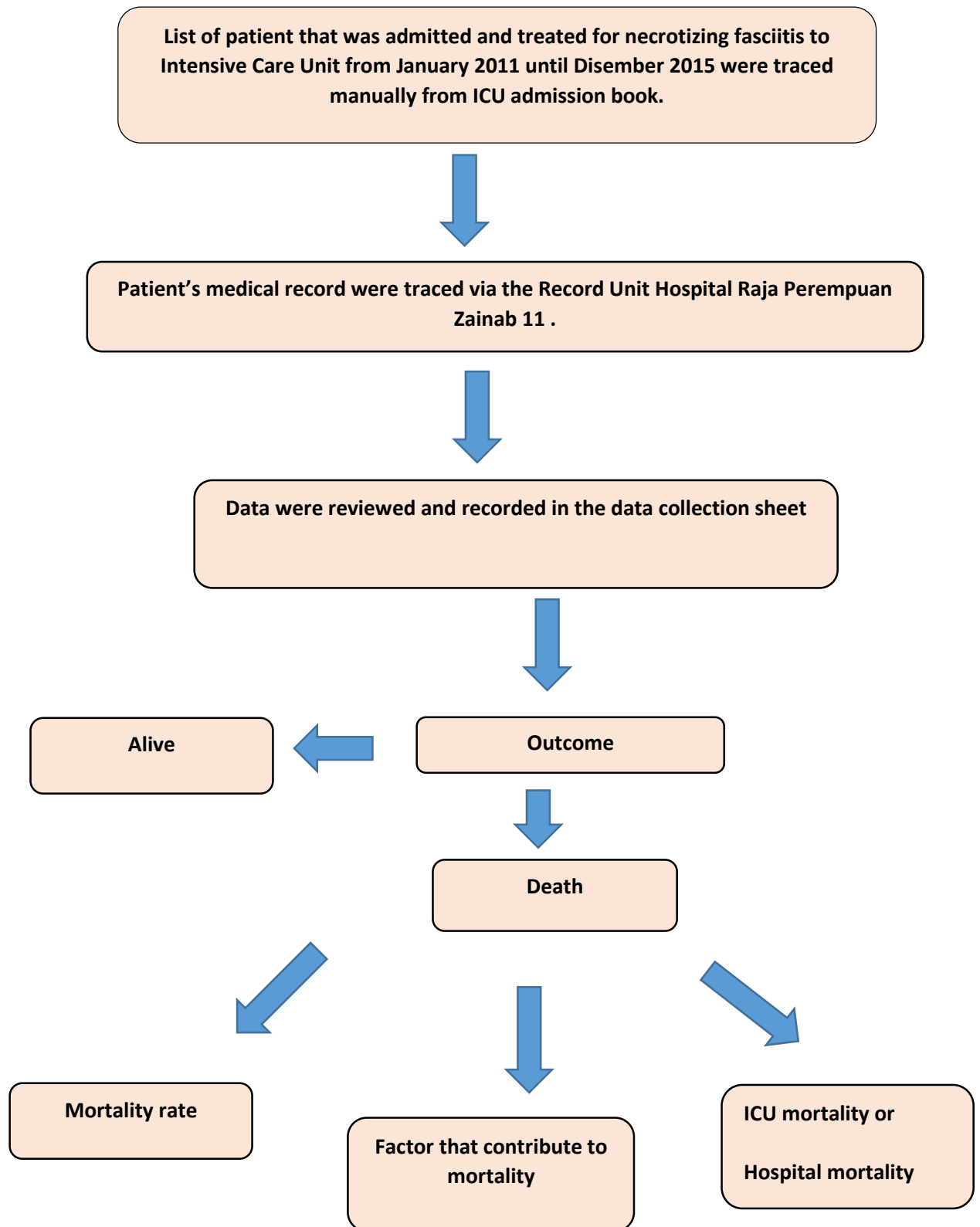
Information such as

- Patient's demographic data.
- Relevant comorbidities.
- Duration of illness prior to hospitalization
- APACHE 11 score
- Onset of systemic inflammatory response syndrome (SIRS)
- Criteria for severe sepsis
- Time to surgical debridement
- The number of operation done .
- Organism isolated (culture) during operation
- Duration of ventilation and ICU stay.
- Requirement of vasopressor
- Requirement of renal replacement therapy
- Outcome in term of mortality (alive and death)
- Outcome : ICU mortality or hospital mortality
- Duration of hospital stay

STUDY METHODOLOGY

- Sample size will be find out using ICU data, based on ICU admission of patient with necrotizing fasciitis
- Approval will be obtained from ethics committee and the need for informed consent will be waive.
- All patient with inclusion criteria will be identified from intensive care unit data base in year 2012-2015.
- Patient's record will be trace using tracer sheet.
- Record and ICU chart will be review and analyze manually.
- Clinical and demographic data that will be obtain from patient's chart include
 - age, gender, comorbidities, APACHE II scores, sepsis and systemic inflammatory response syndrome criteria met,
- Use of inotropes and vasopressors, requirement for and duration of ventilation, requirement of renal replacement therapy,
- Time of admission to surgical debridement, ICU and hospital length of stay (LOS) and patient's outcome (mortality rate)
- Data related specifically to identification and management of necrotizing fascitis will be obtained
- Data will be collected and enter into SPSS and will be analysed using appropriate statistical test.

FLOW CHART OF THE STUDY



STATISTICAL ANALYSIS

Data entry and analysis were done using SPSS software (SPSS, Chicago). The results are expressed in terms of numbers and percentages or the mean and standard deviation. Independent variables (factors) were screened one by one by using simple logistic regression. Only variables that statistically importance with p value <0.25 or clinically importance were included to proceed with Multiple Logistics Regression. Then proceed with variable selection to select the important independent variable from Multiple Logistic regression model. There were two methods used : Forward LR and Backward LR. The best model depends on: most fit, most parsimonious or most clinically sound. Multiple Logistics Regression (from simple logistics regression, all significant variables (p value<0.25) entered Multiple Logistics Regression, only variables with p-value <0.05 will be included in the final result.

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2.2 ETHICAL APPROVAL



JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(Medical Research & Ethics Committee)
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Ruj. Kami : (6) KKM/NIHSEC/P14-1302
Tarikh : 19hb Disember 2014

Noor Shazlini binti Mustapa,
Hospital Raja Perempuan Zainab II.

Tuan/Puan,

NMRR-14-1216-21038 (IIR)

Observational Study Of The Outcome Of Necrotising Fascitis In Intensive Care Unit.

Lokasi Kajian: Hospital Raja Perempuan Zainab II.

Dengan hormatnya perkara di atas adalah dirujuk.

2. Jawatankuasa Etika & Penyelidikan Perubatan (JEPP), Kementerian Kesihatan Malaysia (KKM) mengambil maklum bahawa projek tersebut adalah untuk memenuhi keperluan akademik **Sarjana Perubatan (Mmed Anesthesiology) di Universiti Sains Malaysia (USM)**.

3. Sehubungan dengan ini, dimaklumkan bahawa pihak JEPP KKM tiada halangan dari segi etika ke atas pelaksanaan projek tersebut. JEPP mengambil maklum bahawa kajian ini tidak melibatkan intervensi terhadap subjek dan hanya melibatkan penggunaan rekod perubatan sahaja dalam mengumpul data kajian. Segala rekod dan data adalah **SULIT** dan hanya digunakan untuk tujuan kajian ini dan semua isu serta prosedur mengenai **data confidentiality** mesti dipatuhi. Kebenaran daripada Pengarah Hospital di mana kajian akan dijalankan mesti diperolehi terlebih dahulu sebelum kajian dijalankan. Tuan/Puan perlu akur dan mematuhi keputusan tersebut.

4. Adalah dimaklumkan bahawa kelulusan ini adalah sah sehingga **19hb Disember 2015**. Tuan/Puan perlu menghantar dokumen-dokumen seperti berikut selepas mendapat kelulusan etika. Borang-borang berkaitan boleh dimuat turun daripada laman web MREC (<http://www.nih.gov.my/mrec>).

- I. 'Continuing Review Form' selewat-lewatnya 2 bulan sebelum tamat tempoh kelulusan ini bagi memperbaharui kelulusan etika.
- II. Laporan tamat kajian pada penghujung kajian.
- III. Laporan mengenai "All adverse events, both serious and unexpected"/Protocol Deviation atau Violation kepada Jawatankuasa Etika & Penyelidikan Perubatan, KKM jika berkenaan.
- IV. Memaklumkan jika terdapat pindaan keatas sebarang dokumen kajian.

5. Sila ambil maklum bahawa sebarang urusan surat-menyurat berkaitan dengan penyelidikan ini haruslah dinyatakan nombor rujukan surat ini untuk melicinkan urusan yang berkaitan.

Sekian terima kasih.

BERKHIDMAT UNTUK NEGARA

Saya yang menurut perintah,



(DATO' DR CHANG KIAN MENG)

Pengerusi

Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

CC

**Pengarah,
Hospital Raja Perempuan Zainab II.**

**Clinical Research Centre,
Hospital Raja Perempuan Zainab II.**