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FINAL RESEARCH PAPER ON DETERMINANTS AND OUTCOME OF  
NECROTIZING FASCITIS IN JMC:ONE YEAR RETROSPECTIVE

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JIMMA ,ETHIOPIA

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# CHAPTER ONE:INTRODUCTION

**Background;** Necrotizing fasciitis is a serious infection of the skin, subcutaneous tissue, and fascia. It can be caused by several different types of bacteria, and the infection can arise suddenly and spread quickly. The first clear description of necrotizing fasciitis was given by Joseph Jones, a surgeon in the Confederate Army of the United States in 1871. He described it as “hospital gangrene” in 2,642 soldiers with a mortality of 46 % during the Civil War. Necrotizing fasciitis itself was described in 1952 by Wilson when he observed edema and necrosis of subcutaneous fat and fascia with sparing of the underlying muscle in a series of 22 patients. Symptoms often begin within and typically include intense pain and tenderness over the affected area. If the infection continues to spread, the patient may experience dehydration, high fever, fast heart rate, and low blood pressure. Pain may improve as tissues and nerves are destroyed. As the infection spreads, vital organs may be affected and the patient may become confused or delirious. If not successfully treated, necrotizing fasciitis can lead to shock and eventual death.

Despite the advanced medical treatment, the rate of mortality is higher. Studies show that mortality in NF patients primarily depends upon the time of the medical and surgical interventions , extent of spread of infection to the primary site and elderly age. Mortality is up to 80% with no intervention, and 30-50% with intervention.

Management of necrotizing fasciitis places significant demands upon hospital and medical resources. According to study done in Australia, Alfred Hospital, a mean cost per patient was \$64,517 (range, \$1025 to \$514)

A retrospective cross-sectional study was conducted by reviewing

medical records of patients who developed necrotizing fasciitis from January 1, 2011 to December 31, 2015 in JUSH. Overall, 78 patients were diagnosed with necrotizing fasciitis and mortality rate was 19.23% even if factors associated with such high mortality rate are not studied by the time. The common comorbid condition was diabetes mellitus.

The finding of this study will benefit us to know outcome of NF in our hospital set up and based on that we will have an alertness and thorough attention to the diseases. It helps us to identify the associated factors that increase mortality and to combat it and as baseline data for further study in the study area. This study also adds the values to the scientific literatures.

## CHAPTER TWO: LITERATURE REVIEW

Necrotizing fasciitis(NF) is a rare soft tissue infection primarily involving the superficial fascia, and resulting in extensive undermining of the surrounding tissue.

If untreated it is invariably fatal and thus a high index of suspicion for diagnosis is required. Adults are more affected than children even if no age limit. The trunk was the most commonly involved anatomical region of the body (50.0%) in children, while in adults it was the lower limb (54.2%). The worldwide incidence is at 0.4 per 100,000. Mortality is up to 80% with no intervention, and 30-50% with intervention. Delay in intervention is associated with poor outcome(4). During a 14-year period, 331 NF patients were admitted with a mean age of  $50.8 \pm 15.4$  years and 74 % of them were males Non-survivors (26 %) were 14.5 years older ( $p = 0.001$ ) and had lower frequency of pain ( $p = 0.01$ ) and fever ( $p = 0.001$ ) than survivors (74 %) at hospital presentation(5).

Mortality still remains high despite the use of powerful antimicrobial agents and advances in care of critically ill patients (1). A retrospective cross-sectional study design was conducted by reviewing medical records of patients who developed necrotizing fasciitis during the period between January 1, 2011 and December 31, 2015 in Jimma University specialized hospital. Overall, 78 patients were diagnosed with necrotizing fasciitis and mortality rate was 19.23%(5)

It can affect all parts of the body and the lower extremities are the common site of infection followed by trunk, perineum and scrotum. predisposing factors are Diabetes mellitus, liver cirrhosis, alcoholism hypertension chronic renal insufficiency and malignancy(6)

## ***EPIDEMIOLOGY***

NSTIs are an exceedingly rare clinical entity, with an estimated 1000 cases annually in the United States; however, it appears that this incidence has been increasing. The cause for this increase is unclear, but it may be a result of greater awareness of the problem leading to higher rates of reporting, increasing bacterial virulence, increased antimicrobial resistance, or all 3. Most physicians will see only 1 case of NSTI throughout their career. This rarity prevents most physicians from maintaining sufficient clinical suspicion important for establishing the diagnosis early and initiating appropriate treatment.

There is no age or gender predilection, but higher rates of NSTIs are seen in obese, diabetic, and immunocompromised patients, as well as alcoholics and patients with peripheral vascular disease. However, NSTIs can (and do) occur in young, otherwise healthy patients with none of these predisposing factors. Geographic differences in etiology and microbiology have been shown on the national and regional level. Variance in patient risk factors, environmental levels and types of bacteria, and exposures related to factors such as the quality and purity of intravenous (IV) drugs may contribute to regional differences. There have been reports in the literature suggesting a link between nonsteroidal antiinflammatory drug (NSAID) usage and NSTIs. However, given the widespread usage of NSAIDs overall, and the use of NSAIDs for pain relief during the early phases of the disease process, this association does not necessarily represent a causal pathway. NSAIDs inhibit the conversion of arachadonic acid via cyclooxygenase-1 (COX1) or COX2 into thromboxane or other prostaglandins, respectively. COX1 is constitutively expressed at significantly higher levels than COX2, but in times of inflammation, expression of COX2 is increased to levels significantly higher than COX1. Therapeutically, NSAIDs inhibit

conversion of arachadonic acid by COX2 into prostaglandin E2, which is thought to be responsible for pain and fever associated with inflammation. Various other prostaglandins produced via COX2 pathway have been shown to be involved in gastrointestinal epithelial cell migration in animal models, modulate activity of myofibroblasts and collagen

deposition in wounds, and have immunomodulatory effects on leukocyte adhesion and granulocyte functions, including chemotaxis, oxidative burst, and bacterial killing. Therefore, it is possible that use of NSAIDs in the setting of NSTI may be associated with a worsened clinical course owing to alterations in the immune response(7). In a study of 161 patients with NF were included, the most common underlying disease was diabetes mellitus (66 cases, 41.0%).(8)

## ***DIAGNOSIS***

Necrotizing fasciitis is a devastating infection of the fascia and subcutaneous tissue. The presentation of the disease is nonspecific and variable. It is important to recognize early stage of the diseases which will present with minimal cutaneous manifestation making prompt diagnosis difficult(6). Delay in recognition and effective treatment increases the mortality.

Classic symptoms include severe pain out of proportion to local findings, erythema, mottling, crepitus, skin.

The laboratory findings in a study involving 115 patients shows leukocytosis (52%), leukopenia (8%), thrombocytopenia (40%) of the patients. Hemoglobin <10mg/dl is observed in 37% of the patients. There are also a record of ARF and coagulation profile derangement.

Image tools to complement diagnosis include magnetic resonance imaging (MRI), computed tomography (CT), ultrasonography (US) and



plain radiography. CT findings encompasses fatstranding and fascial thickening with fluid or gas collections over the fascial planes. MRI is useful to differentiate NF from cellulitis and is 100% sensitive and 86% specific in the diagnosis, although an overestimation extent of the infection has been described. Studies have showed that the use of ultrasound (US) for early diagnosis, US report a sensibility and specific of 88.2% and 93.3% respectively, findings include diffuse subcutaneous thickening, fluid layer of >4 mm along the deep fascia and gas in the soft tissues, which is pathognomonic(9)

### ***MICROBIOLOGICAL PATHOGENS***

The most common organisms identified are group A streptococcus followed by MRSA and MSS.E coli was identified in some of the patients and it is the commonest gram negative cocci.(6) Type 1 necrotizing fasciitis is caused by polymicrobial organisms commonly non-group A streptococcus,other aerobics and anaerobic organisms. Patients with type I NSTIs are typically older, with more medical comorbidities such as diabetes, and often have no history of trauma(7). Type 2 necrotizing fasciitis are caused by polymicrobial organisms,streptococcus pyogenes alone or with staphylococci (6). GAS infections of soft tissue have a significant potential for aggressive local spread, as well as systemic toxicity including toxic shock syndrome. When compared with type I NSTIs, patients with type II infections tend to be younger, healthier, and more commonly have a history of trauma, surgery, or IV drug use.(7) Type III NSTIs are caused by gram-negative marine organisms, most commonly *V.vulnificus*.Type IV NF is caused fungal infections. Although not as widely accepted as a class of NSTI compared with types I and II,type III infections have been reported along warm-water coastal regions in the southeastern United States, Central and South America, and

Asia. Infection can occur via exposure through an open wound or other break in the skin, but infection has also been reported via ingestion of colonized oysters by patients with cirrhosis. Type III infections clinically present and manifest progression of disease similar to that of type II infections in that there is early evidence of significant systemic toxicity. Multisystem organ failure and cardiovascular collapse occur very early and have been observed without any localized cutaneous evidence of infection(7).

### ***TREATMENTS***

Early antibiotic therapy must be established against a wide range of microorganisms. Hunter *et al.* suggest the combination of a carbapenem with clindamycin. Otherwise, If cultures demonstrate sensitive *Streptococcus pyogenes*, there is a general agreement that a combination of penicillin G and clindamycin (high doses) is the preferred option. Surgery is the crown jewel of NF treatment. It is imperative to perform an aggressive exploration and excision of all the necrotic and devitalized area, with margins of 5–10 mm. The average cost to treat NF approaches US\$50 000–100 000 per case(10)

Multiple operations are often necessary. Although some studies did not find significant correlation between early surgical debridement and clinical outcomes, it is globally accepted that any delay in diagnosis and surgery is associated with a clear increase in mortality. The rule of thumb is if deep soft tissue is suspected based on epidemiological, clinical and seminal local inflammatory data, is much better to perform surgical exploration than wait and see (9). Hyperbaric oxygen (HBO) therapy has also been proposed as an adjunctive therapy for NSTI.(11)

## **CHAPTER THREE:OBJECTIVES**

### ***General objective***

*To assess prevalence, and treatment outcome of necrotizing fasciitis in JMC 2021*

### ***Specific objectives***

*To assess the prevalence of necrotizing fasciitis in JMC 2021*

*To assess the treatment outcome of necrotizing fasciitis in JMC 2021*

*To assess factors associated with treatment outcome of necrotizing fasciitis in JMC 2021*

## **CHAPTER FOUR:METHODS AND MATERIALS**

Institutional based Retrospective study is conducted from Feb 1, 2020 - Feb 1, 2021. All patients diagnosed with necrotizing fasciitis in JMC within this specified period are included but those who left the hospital before completing the treatment are excluded. Questionnaire is prepared and data is collected from patients chart. Data collectors were trained on how to collect the data before starting data collection Sociodemographic characteristics and associated comorbid conditions are assessed. The collected data was checked for completeness and entered into the Epi-data 4.0.2 Version and then exported to SPSS Version 26 for analysis.

## **CHAPTER FIVE:RESULT**

This study is conducted on 48 patients treated in JMC over one year duration and 36 patients are male while 12 patients are females. The age distribution is ranging from 4days old newborn to 75years of age.The common presenting symptoms are pain, fever and swelling (95%, 91% and 81.3% ) respectively. The common signs on presentation are, tachycardia ((91.3%),fever(70.6%) ,tachypnea(43.6%) while few patients presented with low blood pressure(16.7%) and change in mental ststus(2.1%).

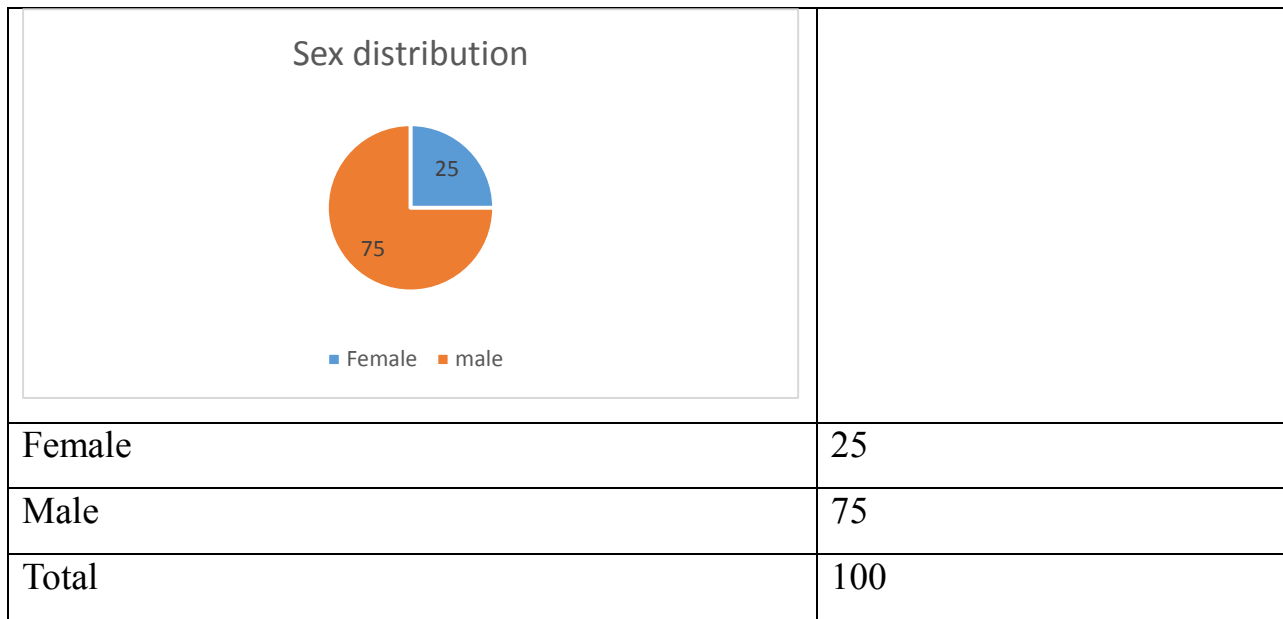
The anatomic distribution of the diseases include lower extremity, trunk,lower extremity with trunk,lower extremity with perineum in decreasing order of frequency.majority of the patients are presented to the hospital with in the first ten days of the illness(90%).The remaining patients came with in 10-15 days of the illness.All of the patients were given antibiotics with different regimens.The commonly given antibiotics were ceftraxone and metronidazole, the others being vancomycin,ceftazidime,and gentamycin.All of the patients were offered surgical intervention atleast once,the commonest being debridement and skin grafting for tissue loss.Amputation (BKA) is done for one patient.Thirty five percent of the patients were admitted to ICU while the remaining in the general ward.

Of all the patients under study seven patients had comorbid conditions like five patients with diabetes,two patients with hypertension,and one patient is diagnosed with COVID-19.The average duration of hospital stay was 30 days with minimum stay of two days and maximum of 120 days.

From fourty eight patients studied 33(68.75%) patients were treated and discharged,14 (29.16%) patients were died and one patient is left against medical advice.From fourteen patients who died,eight patients were males and six patients were females.According to the age distribution children of less than three years are

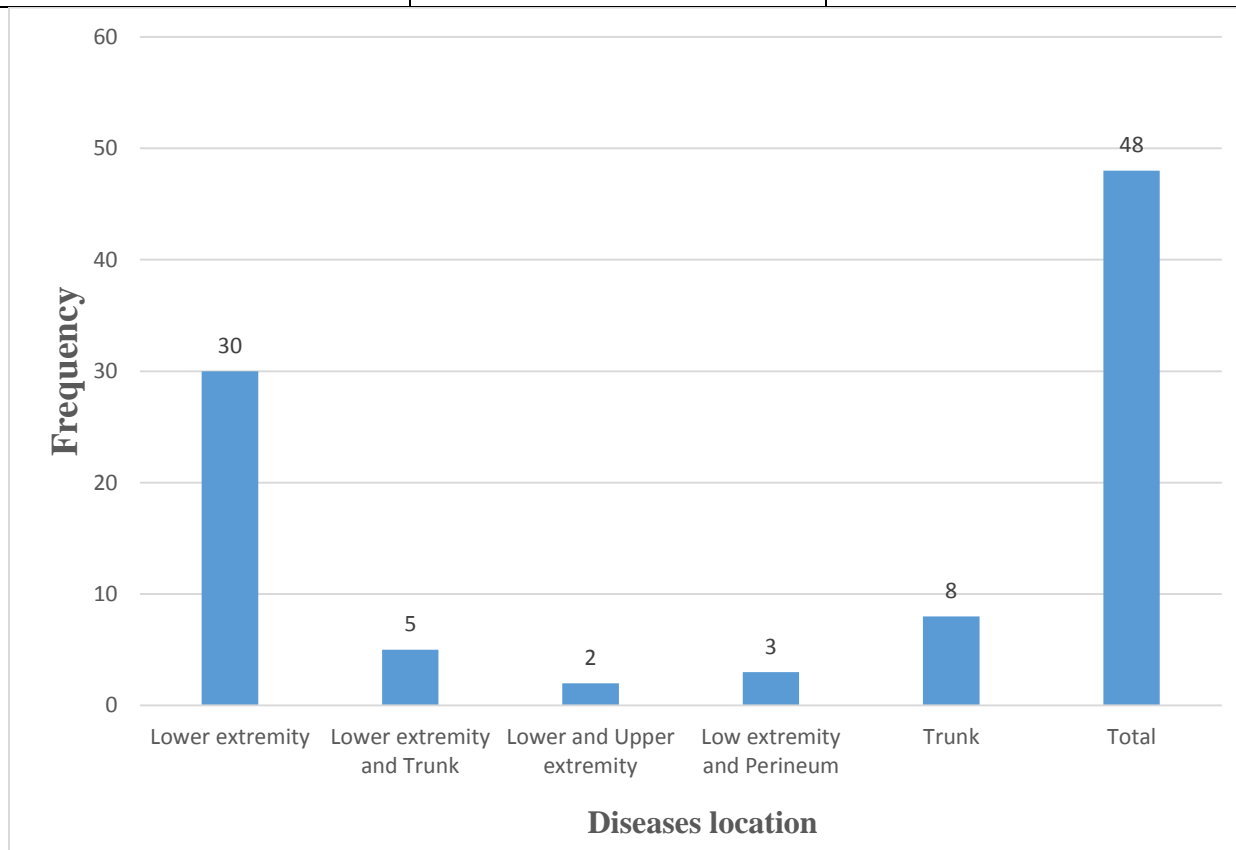
more affected. Among seven patients with comorbid conditions four patients were died, three diabetic patients, one patient with COVID-19. All of the patients who were presented in shock (eight in number) were died. The study shows significant association between hypotension on presentation and risk of mortality. Delay on presentation also has significant association with mortality

**Figure 1: Pie chart showing sex distribution of patients diagnosed with necrotizing fasciitis in JMC in 2021.**

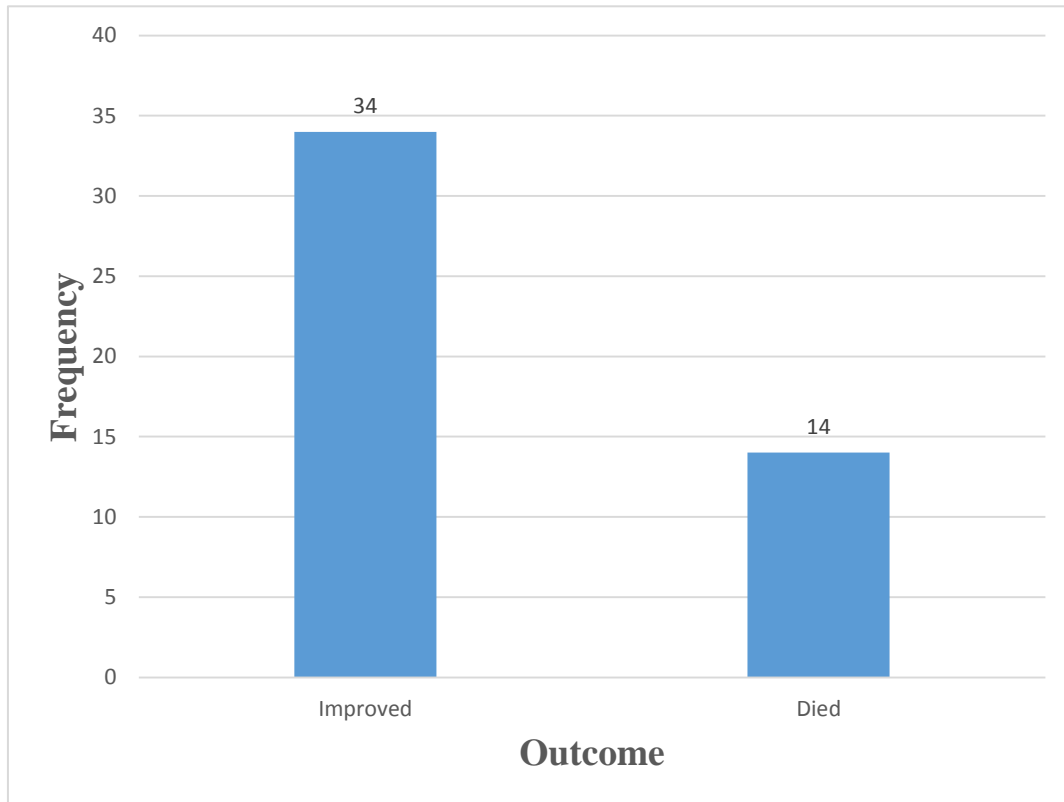


**Table 1 Anatomic location of the diseases**

| Diseases location          | Frequency | Percent    |
|----------------------------|-----------|------------|
| Lower extremity            | 30        | 62.5       |
| Lower extremity and Trunk  | 5         | 10.4       |
| Lower and Upper extremity  | 2         | 4.2        |
| Low extremity and Perineum | 3         | 6.3        |
| Trunk                      | 8         | 16.7       |
| <b>Total</b>               | <b>48</b> | <b>100</b> |

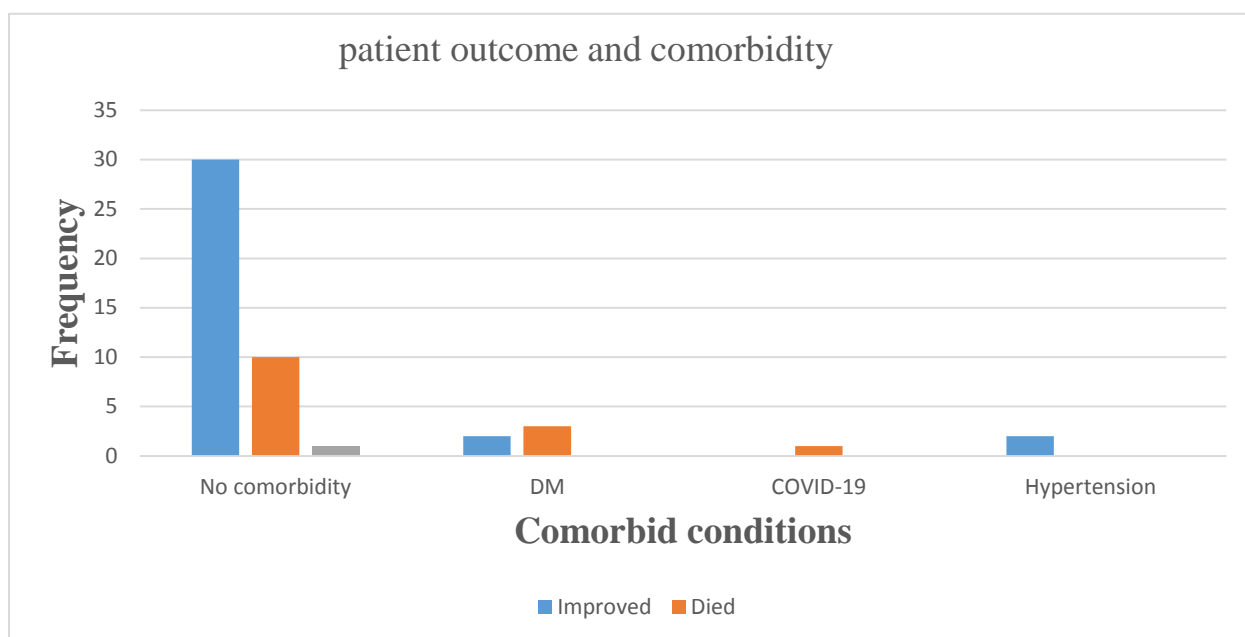


**Figure 2: Final outcome of patients after treated for Necrotizing fasciitis in JMC 2021 GC**





**Figure 3;**Bar graph showing patient outcome in relation to comorbidities



**Table 2;**Table showing antibiotic sensitivity test result;

|                  | <b>Ceftraxone</b> | <b>Ceftazidime</b> | <b>Vancomycin</b> | <b>Gentamycin</b> |
|------------------|-------------------|--------------------|-------------------|-------------------|
| <b>Sensitive</b> | 58.3              | 70.6               | 47.05             | 54.55             |
| <b>Resistant</b> | 41.7              | 29.3               | 52.95             | 45.45             |

## CHAPTER SIX:DISCUSSION

The aim of this study was to investigate factors determining mortality and outcome of patients with necrotizing fasciitis. According to this study, Among forty eight patients who were assessed fourteen patients died with a mortality rate of 29.16% .This figure is in the range of most of the worldwide reports but when compared to the study done in JU hospital ten years back mortality is increased by 10%. Factors significantly associated with mortality are, early age, late presentation to a hospital, shock on presentation, and presence or absence of comorbid conditions.

Multivariate logistic regression analysis (<https://pubmed.ncbi.nlm.nih.gov/>), showed that more than 1 comorbidity, thrombocytopenia, anemia, more than 24 h delay from onset of symptoms to surgery and age greater than 60 were independently associated with mortality. This study found that *K. pneumoniae* was the most common cause of necrotizing fasciitis while in our study *S. aureus* is the commonly identified microorganism. Early operative debridement was independently associated with lower mortality.

Up on sensitivity test the identified organisms are sensitive to ceftraxone (9.7%), ceftazidime (16.2), vancomycin (25.8%), gentamycin (38.7%), and clindamycin (38.7%) of the cases. The commonly identified microorganism *S. aureus* is highly sensitive to gentamycin (90%), ciprofloxacin and moderately sensitive to vancomycin. In case of our patients under study the most commonly given antibiotics are ceftaxone and metronidazole. It indicates our options of antibiotics for necrotizing fasciitis has to be revised.

## **LIMITATIONS**

Difficulty of accessing patients chart because of poor keeping in record room is the main limitation during this study.

## **RECOMMENDATIONS**

Antibiotics administration has to be according to sensitivity test result and it has to be documented.

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