Declaration

I Shingirirai Christopher Meki hereby certify that this dissertation is the product of my own work and in submitting it for my Masters of Medicine in Urological Surgery, further attest that it has not been submitted in part or in whole to another university or general publication.

Signature........................................... Date...........................................

MR. T. I MANGWIRO

having supervised and read this dissertation, am satisfied that this is the original work of the author whose name it is being presented. I confirm that the work has been completed satisfactorily and is ready for presentation to the examiners.

Signatures:

Supervisor........................................... Date...........................................

Chairman........................................... Date...........................................
Abstract
Background: Fournier’s gangrene is a potentially life threatening, infective necrotizing fasciitis of the external genitalia and perineum. The average world mortality rate is between 20 – 30%. The factors associated with mortality are not universally accepted and have not been described in our environment.

Main objective: To determine the disease related mortality rate and factors associated with mortality among patients admitted with a clinical diagnosis of Fournier’s gangrene at 3 tertiary hospitals in Harare, Zimbabwe.

Study Design: A prospective observational descriptive study on 51 consecutive patients with a clinical diagnosis of Fournier’s gangrene managed at 3 tertiary hospitals in Harare, Zimbabwe over a 2 year period.

Materials and Methods: The study was done after approval by the relevant regulatory boards and after obtaining informed consent from the patients. Data on demographics, clinical history and physical examination, vital signs and laboratory values on admission were recorded on a designed data collection sheet. All patients received intravenous broad spectrum antibiotics and fluid resuscitation and surgical debridement. The number and time to first surgical debridement and any additional surgical procedures performed were recorded. The patients were followed up from admission till discharge from hospital or death. The patients were stratified according to outcome, whether dead or alive and comparison between survivors and non survivors was done to determine factors associated with mortality using chi squared or Fischer exact test for categorical variables and student t test for comparison of the means. Binary multiple regression analysis was performed to determine independent factors associated with mortality.

Results: The disease related hospital mortality rate was 27% (14/51). The median hospital stay was 15 days. The median age of the 51 patients was 43 years. The patients that did not survive were significantly older than those that survived (58.36 ± 21.04 vs 42.76 ± 14.40 years)(p=0.021). The presence of at least one comorbity was associated with an increased mortality (p=0.007). HIV was the commonest risk factor accounting for 36% of the cases. Neither the presence of HIV nor diabetes mellitus was associated with mortality. Renal failure at presentation was significantly associated with mortality, with a rate of 70% among patients.(p=0.001). The urogenital tract source of infection was associated with increased mortality (p=0.01) while a cutaneous source was associated with survival. (p=0.003). E coli and staphylococcus aures were the commonest pathogens isolated. A delay in first surgical debridement beyond 24 hours from time of admission was significantly associated with an increased mortality (p=0.04). The number of debridement did not differ significantly between survivors and non survivors. A body surface area involvement of > 5% and abdominal involvement was also significantly associated with higher mortality. The admitting clinical and biochemical parameters significantly associated with non survivors were a high respiratory rate, low haemoglobin, hyperkalemia, elevated blood urea nitrogen and elevated creatinine. There was no factor that was independently associated with mortality after multiple logistic regression analysis.

Conclusion: Fournier’s gangrene remains a potentially fatal condition in our enviroment with a mortality rate of 27%. On univariate analysis an older age, presence of renal failure on admission, a urogenital source of infection, severe sepsis, abdominal involvement, anemia, hyperkalemia and delay in surgical debridement is associated with mortality in our enviroment. The presence of HIV and diabetes mellitus and number of surgical debridement does not seem to affect mortality in our enviroment.
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Table of Contents

Abstract ...........................................................................................................................................(i)
Acknowledgments ............................................................................................................................(ii)
Table of contents ............................................................................................................................(iii)
List of tables .....................................................................................................................................(iv)
List of figures .....................................................................................................................................(v)
Abbreviations ....................................................................................................................................(vi)

Chapter 1: Introduction and Literature Review .............................................................................. 1
1.1 Introduction ................................................................................................................................1
1.2 Epidemiology ..............................................................................................................................2
1.3 Etiology and Predisposing factors ............................................................................................2
1.4 Microbiology and Pathogenesis ...............................................................................................3
1.5 Anatomical consideration and spread of infection .................................................................7
1.6 Clinical presentation ..................................................................................................................9
1.7 Investigations ..........................................................................................................................10
1.8 Management ..........................................................................................................................12
1.9 Outcome and Prognosis ..........................................................................................................19

Chapter 2: Background and Objectives of study ........................................................................... 23
2.1 Statement of problem and Justification .................................................................................23
2.2 Research Question and Hypothesis .......................................................................................25
2.3 Objectives ................................................................................................................................26

Chapter 3: Study design and Methodology .................................................................................. 27
3.1 Study design ..........................................................................................................................27
3.2 Material and Methods ............................................................................................................28

Chapter 4: Results .........................................................................................................................31

Chapter 5: Discussion, Conclusion and Recommendations ..................................................................48
5.1 Discussion .............................................................................................................................48
5.2 Conclusion .............................................................................................................................59
5.3 Recommendations ..................................................................................................................60

Limitations of study .........................................................................................................................61

References .........................................................................................................................................62

Appendices .......................................................................................................................................71
Appendix 1: Data collection tool ..................................................................................................72
Appendix 2: Consent forms .............................................................................................................75
Appendix 3: Body surface area nomogram ....................................................................................80
Appendix 4: Laboratory reference ranges .....................................................................................82
Appendix 5: Severe sepsis criteria ................................................................................................84
### List of tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1.1 : Bacterial Culture results in patients with Fournier’s gangrene</td>
<td>4</td>
</tr>
<tr>
<td>Table 4.1 : Comorbidities and risk factors of Fournier’s gangrene</td>
<td>36</td>
</tr>
<tr>
<td>Table 4.2 : Summary of admitting clinical and laboratory parameters</td>
<td>41</td>
</tr>
<tr>
<td>Table 4.3 : Comparison of survivors and no survivors on different variables.</td>
<td>45</td>
</tr>
<tr>
<td>Table 4.4 : Clinical and biochemical differences between survivors and non survivors</td>
<td>46</td>
</tr>
<tr>
<td>Table 5.1: Mortality rates from different countries worldwide</td>
<td>49</td>
</tr>
<tr>
<td>Figure</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>Figure 1.1: Anatomy of the fascia of the abdomen and pelvis</td>
<td>8</td>
</tr>
<tr>
<td>Figure 4.1: Box plot of age distribution of patients with Fournier’s gangrene</td>
<td>31</td>
</tr>
<tr>
<td>Figure 4.2: Histogram of age distribution of patients with Fournier’s gangrene</td>
<td>32</td>
</tr>
<tr>
<td>Figure 4.3: Box plot of age comparison between survivors and non survivors</td>
<td>33</td>
</tr>
<tr>
<td>Figure 4.4: Distribution of patients by area of origin</td>
<td>34</td>
</tr>
<tr>
<td>Figure 4.5: Distribution of origin of infection of Fournier’s gangrene.</td>
<td>35</td>
</tr>
<tr>
<td>Figure 4.6: Comparison of survivors and non survivors by origin of infection</td>
<td>36</td>
</tr>
<tr>
<td>Figure 4.7: Degree of dissemination of disease by region involved</td>
<td>39</td>
</tr>
<tr>
<td>Figure 4.8: Distribution of disease according to severity of involvement and outcome</td>
<td>40</td>
</tr>
</tbody>
</table>
**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>ATP</td>
<td>Adenosine Triphosphate</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>FGSI</td>
<td>Fournier’s Gangrene Severity Index</td>
</tr>
<tr>
<td>UFGSI</td>
<td>Ululag Fournier’s Gangrene Severity Index</td>
</tr>
<tr>
<td>APACHE</td>
<td>Acute Physiology and Chronic Evaluation Scale</td>
</tr>
<tr>
<td>CT</td>
<td>Computer Tomography</td>
</tr>
<tr>
<td>HBO</td>
<td>Hyperbaric Oxygen therapy</td>
</tr>
<tr>
<td>VAC</td>
<td>Vacuum Assisted Closure</td>
</tr>
<tr>
<td>BUN</td>
<td>Blood Urea Nitrogen</td>
</tr>
<tr>
<td>JREC</td>
<td>Joint Research Ethics Committee</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for Social Scientist</td>
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</tbody>
</table>
1.1 Introduction

Fournier’s gangrene is a potentially fatal, fulminant infective necrotizing fasciitis of the genitalia, perineum and peri-anal regions\(^1\). It is characterized by an obliterative endarteritis of small blood vessels of the subcutaneous tissue secondary to a polymicrobial infection acting synergistically to allow rapid invasion and tissue necrosis.\(^{1,15}\)

The disease definition has evolved over time, initially from that of an idiopathic disease process in a healthy male to one in which there is an identifiable cause commonly associated with an underlying risk factor. Sir Alfred Fournier (1832-1914) a Parisian dermatologist with an interest in venereal disease and whom the disease is named after, described this condition in 1883 amongst five otherwise healthy young males with unusual cases of idiopathic perineal gangrene.\(^2\) The disease had been described earlier on by Baurienne in 1764 according to Ong and Ho.\(^3\) Avicenna (980-1037) a Persian physician had also described a similar condition in his book The Canon of Medicine.\(^3\) According to Hirschmann who presented on the writing of Flavius Josephus it is believed that King Herod of Judea (BC 73-BC 4) succumbed to genital gangrene with underlying chronic kidney disease and diabetes.\(^7\)

Aggressive fluid resuscitation, early surgical debridement and broad spectrum antibiotic therapy are critical and fundamental in the management of this debilitating disease. The worldwide mortality rate has remained high with an average of 20 -30% despite an advance in treatment over the years.\(^4,5\) The various factors associated with mortality have been described but not universally accepted.
Literature Review

1.2 Epidemiology of Fournier’s gangrene

The true incidence of this disease is not known but some studies have suggested an incidence of 1 per 7500 - 750 000.\(^5\) Fournier’s gangrene tends to affect males more than females in a ratio of 10:1 according to a review of 1726 cases by Eke.\(^5\) The observation of the disease in females is not universally accepted.\(^9\) The disease can occur at any age with cases of children having been described.\(^5\) The peak age of Fournier’s gangrene is in the 5\(^{th}\) and 6\(^{th}\) decade as described in the developed world.\(^10,11,15,21,34,40\) In the developing world the disease tends to affect younger patients in the 4\(^{th}\) decade of life.\(^12,69,70,71\) The disease tends to affect people of low socioeconomic status though it has been described among affluent people.\(^1,5,40\) The disease may be rising in the western world due to an increasing aging population.\(^72\)

1.3 Etiology and predisposing factors.

In about 90% of the cases an etiological factor can be found after a diligent search, far from an idiopathic etiology as described early on by Sir Alfred Fournier (1883).\(^1,2,3\) The source of infection can be from the urogenital tract (45%), anorectal source (33%) or cutaneous/skin (21%).\(^11\) Urethral stricture disease accounts for the majority of the cases arising from the urogenital tract.\(^1,6,43\) The other genitourinary causes include prolonged or neglected urinary catheters, instrumentation, penile implant insertion, prostate biopsy, epididymitis and hydrocele aspiration.\(^1,10,11,22\) The anorectal causes include perianal abscess, anorectal fistula, rectal malignancies, appendicitis, colonic perforation and hemorrhoidectomy.\(^11,15,22,33\)
The cutaneous sources include skin furuncle, perineal, hernia and pelvic surgery. Some cases of Fournier’s gangrene are attributed to poor scrotal hygiene.

An underlying systemic disorder causing a depressed immunity or vascular disease is commonly identified. The common underlying conditions associated with Fournier’s gangrene include diabetes mellitus, alcoholism, chronic use of steroids, malignancy, malnutrition and HIV infection. Diabetes mellitus is the commonest underlying systemic disease associated with Fournier’s gangrene seen in the western world accounting for 60% of patients. Hyperglycemia depresses cellular immunity and reduces phagocytic function of neutrophils and macrophages. There is also reduced neutrophil adhesion, chemotaxis and wound healing associated with hyperglycaemia. Additionally diabetic patients suffer from a microvascular disease which further predisposes them to Fournier’s gangrene. Alcoholism is seen in about 25-50% of cases. Alcoholism is associated with poor hygiene, malnutrition and immunosuppression. The number of cases of Fournier’s gangrene in Africa due to underlying human immunodeficiency virus (HIV) has been on the rise. A recent study by Ngugi et al revealed that the prevalence of HIV among patients with Fournier’s gangrene was around 16.4%. HIV positive patients tend to be younger with a wide spectrum of microbiology.

1.4 Pathogenesis and microbiology

Fournier’s gangrene is characteristically a poly microbial infection. The pathogenesis of Fournier’s gangrene is that of an endarteritis obliterans causing vascular thrombosis and necrosis of subcutaneous tissue and overlying skin. The infection can originate from the urogenital tract, ano-rectum or from the skin.
There is invasion of the local defense by multiple infective organisms which act in synergy, to allow the rapid progression of necrosis along fascial planes.\textsuperscript{1,6,14,15,22} The infection represents an interaction between the host immunity and the virulence of the causative organism. The host compromised immune system commonly encountered may allow the rapid spread and progression of disease especially in patients with HIV, malnutrition, diabetes mellitus, malignancies and chronic steroid therapy.\textsuperscript{6,9,11,33,23}

The organisms are mainly perineal and genital organ commensals or normal flora of the gastrointestinal tract that become virulent in the setting of immunosuppression.\textsuperscript{13,14} The organisms isolated are a combination of aerobes and anaerobes with occasional yeasts.\textsuperscript{6,12,13,14}

The following table 1.1 illustrates a breakdown of the organism commonly isolated and their relative frequency from various studies as presented by Vick and Carson (1999).\textsuperscript{16}

\textbf{Table 1.1: Spectrum of bacteria isolated on culture: Results in 236 patients with Fournier’s gangrene from data presented by Vick & Carson.}

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Number</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Escherichia coli</td>
<td>128</td>
<td>54</td>
</tr>
<tr>
<td>Bacteroides</td>
<td>97</td>
<td>50</td>
</tr>
<tr>
<td>Staphylococci</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Proteus</td>
<td>54</td>
<td>23</td>
</tr>
<tr>
<td>Streptococci</td>
<td>54</td>
<td>23</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>48</td>
<td>20</td>
</tr>
<tr>
<td>Enterococcus fecalis</td>
<td>43</td>
<td>18</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>38</td>
<td>16</td>
</tr>
<tr>
<td>Peptostreptococci</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Clostridia</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Corynebacteria</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Provinenca</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Citrobacter</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

\textit{Adapted from Vick R & Carson C, Fourniers’s disease; Urologic Clinics of North America, 26;4:1999}
The average number of organisms cultured from different series ranges from 1.3 to 3.9.\textsuperscript{6,11,24,41,50,68}

The contributing organisms include gram positive bacteria like *Streptococcus species*, *Staphylococcus*, and *Enterococcus fecalis*.\textsuperscript{16,72} The gram negative bacteria isolated, mainly rods include *Escherichia coli*, *Pseudomonas*, *Klebsiella pneumonias*, *Proteus species*, *Acinetobacter* species and *Citrobacter* species.\textsuperscript{16} *Bacteroides* is the commonest anaerobe encountered.\textsuperscript{11,24,46} The other anaerobes encountered include gram positive *Peptostreptococcus*, *Corynebacterium*, *Clostridium species* and gram negative *Fusobacterium*.\textsuperscript{16,76} The most commonly isolated organism is E coli in about 60% of the positive cultures.\textsuperscript{6,11,15,16}

Crepitus which is commonly encountered is suggestive of the presence of anaerobes which produce insoluble nitrogen and hydrogen.\textsuperscript{16} Clostridia which is commonly associated with gas formation is rarely isolated and its presence is commonly associated with myonecrosis.\textsuperscript{16,46}

The aerobic bacterial organisms invading the subcutaneous tissue of the external genitalia and perineum secrete a variety of enzymes which fixes complement and platelet aggregation resulting in coagulation and thrombosis of vessels.\textsuperscript{14,16} This results in a fall in tissue oxygen tension and formation of oxygen radicals (superoxide anions, hydroxyl ions, hydrogen peroxide) which damage cell membranes. The reduced ATP production as a result of the hypoxic environment results in tissue ischemia and necrosis of subcutaneous tissue. This hypoxic environment allows facultative anaerobes to thrive and grow.\textsuperscript{14,15,40}

*Streptococci* and *Staphylococcus* species secrete hyaluronidases which destroys connective tissue aiding in fascial digestion and progression of disease.\textsuperscript{6} Additionally *Streptococci* secretes
streptokinase and streptodornase which damages cell DNA by depolymerization.\textsuperscript{14,15,16}

*Staphylococcus* additionally produces coagulase that clots plasma resulting in bacteria being coated with fibrin altering phagocytosis by macrophages\textsuperscript{6,14,15}. The gram negative rods release lipopolysaccharide a powerful endotoxin which also causes vascular thrombosis.\textsuperscript{15,16} The lipopolysaccharide antigen can enter into the systemic circulation and activate complement by the alternate pathway to elaborate pro inflammatory markers like IL-1 and TNF that results in profound septic shock and multi organ failure.\textsuperscript{6,15,16} *Escherichia coli* additionally secretes protease, Hemolysin Hly A, a toxin and an acid polysaccharide capsule that inhibits activation of complement and protect bacteria from phagocytosis.\textsuperscript{16}

*Bacteriodes* an anaerobe produces other enzymes like collagenase, lecithinases, hyaluronidase and DNAse which digest fascia allowing further invasion by aerobes.\textsuperscript{6,15,16} Additionally it also secretes heparinase which causes thrombosis of vessels to maintain a hypoxic enviroment.\textsuperscript{16} *Bacteriodes* is capable of inhibiting phagocytosis to allow the growth and proliferation of aerobes.\textsuperscript{16} *Enterococcus fecalis* is an facultative anaerobe, its virulence is due to secretion of lytic enzymes, a hemolysin (cytolysin) which creates pores on cell membranes.\textsuperscript{16}

The rate of fascia destruction can be as rapid as 2-3cm/hr.\textsuperscript{15,16} The extension of infection and necrosis into deeper layers beyond the fascia leading to myonecrosis is rare and if present may indicate presence of clostridium pefringens.\textsuperscript{16}
1.5 Anatomic Considerations and spread of infection

The anatomical attachments of the external genitalia, perineum and abdomen determines the spread of Fournier’s gangrene.\textsuperscript{1,15,22} The perineum has two triangles, an anterior urogenital triangle and a posterior anorectal triangle. The urogenital focus of infection tends to primarily involve the anterior triangle while the anorectal source of infection involves the posterior triangle.\textsuperscript{6,33} The perineal body between the triangles limits the spread of infection from the anterior urogenital region to the posterior anorectal triangle although infection can easily spreads from the posterior anorectal triangle to involve the anterior urogenital triangle.\textsuperscript{1,15}

The Colles’ fascia in the perineum is attached and fixed laterally to the pubic rami and the fascia lata of the thigh. On its posterior attachment the Colles’ fascia is fixed to the inferior fascia of the urogenital diaphragm which then forms the perineal body. It is these lateral and posterior attachments that limits and confines the lateral and posterior spread of the disease\textsuperscript{1,11,15}. The Colles’ fascia becomes the dartos fascia that surrounds the scrotum and penis as shown on figure 1.1 below. The Colles’ fascia becomes Scarpa’s fascia/membranous layer above the inguinal ligament. The Camper’s fascia, a fat layer of varying thickness superficial to the Scarpa’s fascia invests the blood vessels that supply the skin of the anterior abdominal wall which are involved in the disease process to cause necrosis. The Scarpa’s fascia anteriorly extends superiorly to fuse with Campers’ fascia at the clavicles thereby limiting spread of infection beyond this region. The infection spreads via a path of least resistance from the perineum to the pelvis, anterior abdominal wall, chest wall up to the clavicles following these anatomical fascial planes.\textsuperscript{1,11,15,22}
The following diagram, figure 1.1 shows the anatomy of the fascial planes of the lower abdomen and perineum.

![Figure 1.1: Anatomy of the fascial planes of the lower abdomen and pelvis. (adapted from Eke, 2000)](image)

The perineal fascia is continuous with the retroperitoneal fascia via the internal and external spermatic fascia of the spermatic cord. This anatomical relation is a potential path for the spread of infection into the retroperitoneum and vice versa.\(^{15}\) A psoas abscess or perinephric abscess may track along the inguinal canal and spermatic cord fascia to involve the Colles’ fascia in the perineum. If there is no easily identifiable cause of Fournier’s gangrene the retroperitoneum should be suspected as the source of infection.\(^{23}\)
1.6 Clinical Presentation

The disease presentation is variable, it may take an insidious onset or take a fulminant course that is preceded by a prodromal phase of fever, prostration and perineal discomfort over a period of about 2-9 days. Early recognition is critical for prompt management of this debilitating condition which is an “embarrassment to the patient and enigmatic to the physician.”

The mode of presentation will depend on the source of infection. If the origin of infection is from the urogenital tract the patient may have a history of lower urinary tract symptoms. An anorectal source of infection may be indicated by symptoms of anal pain, history of fissures or hemorrhoids. As the disease progresses they are features of swelling, erythema and pain at the site of entry which is commonly accompanied by fever. The commonest presentation according to Ferreira is scrotal swelling, fever and pain. In another case series by Ersay, they noted that perianal/scrotal pain and tachycardia was common (78.6%) and (61.4%) respectively in association with scrotal or perineal purulent discharge. The clinical signs such as pyrexia, tachypnea and septic shock may not be consistently found in severely immunosuppressed patients. Crepitus associated with swelling of the involved area is present in 50-60% of cases.

The overlying skin may appear normal or shiny in the initial stages of the disease while the underlying subcutaneous tissues and fascia are necrotic. The patient may have profound systemic symptoms out of proportion to the degree of involved skin. The patches of skin eventually appear necrotic with progression of the subcutaneous inflammation due to the
thrombosis of its blood supply in the subcutaneous fascia.\textsuperscript{22} The testis become shamefully exposed as the dartos fascia and skin fall away.

The extent of body involvement can be confined to the genitalia and perineum or extend to involve the pelvis, abdomen and chest up to the clavicles. The patient is obviously unwell and may have comorbidities, like renal failure, diabetes mellitus, HIV, and malignancy.\textsuperscript{5,72} There should be an effort to identify these comorbidities as they are crucial in management and prognosis of this disease.\textsuperscript{11,15,22,24} The patient may present or progress to septic shock with single or multi-organ failure which is a leading cause of death.\textsuperscript{22,23}

1.7 Investigations

The following investigations are necessary to assess the hemodynamic instability, severity of metabolic derangements associated with this condition.\textsuperscript{24}

1. A full blood count and differential.

2. Blood urea, electrolytes and creatinine. Renal failure may present as part of multi organ failure or as part of an underlying disorder. Blood sugar levels should be done as hyperglycemia or hypoglycemia is common.


4. Urine and blood cultures including pus swabs and tissue for culture.

5. Coagulation studies if there is evidence of severe sepsis.

The anemia commonly found in patients with Fournier’s gangrene is due to lack of functioning red blood cells due to endarteritis obliterans and sepsis.
The white cell count is mostly elevated but may be blunted in immunosuppressed patients such as HIV infected and patients on chronic steroid therapy. The electrolytes abnormalities may include hyponatremia, hypernatremia and hypokalemia. Some patients with kidney injury present with hyperkalemia and raised blood urea nitrogen and creatinine. Some patients have hypocalcemia due to release of free fatty acids by bacterial lipases that chelates ionized calcium. Blood cultures and wound swabs are of great importance as they guide antibiotic therapy. The HIV status of the patients should be investigated as this may be the presenting sign of this disease.

There are differences between survivors and non survivors in the various laboratory parameters on admission. A high serum creatinine, lactate, calcium, or low bicarbonate has been noted amongst non survivors. A low magnesium has been found to be associated with poor prognosis in very ill patients therefore monitoring serum magnesium levels in these patients is essential. The calcium levels may be increased due to renal failure, bacteremia or use of parenteral nutrition. The change in magnesium levels is due to reduced absorption from the gut, with an increased loss in urine.

The diagnosis of Fournier’s gangrene is mainly clinical due to its characteristic presentation, however imaging may be helpful in early diagnosis especially during the prodromal phase of the disease or when diagnosis is doubtful. On conventional radiography, gas accumulation in the tissues is found in about 90% of the patients. The tissue pnuematosis seen on radiography is due to gas forming organisms and can be seen extending from the scrotum and perineum. The absence of gas on radiography does not exclude a diagnosis of Fournier’s gangrene.
Ultrasound scanning of the scrotal tissue may show a thickened scrotal wall, containing hyper echoic foci that show reverberation artifacts representing gas in the wall. Ultrasound is able to differentiate Fournier’s gangrene from an incaserated inguinal hernia by locating the gas within the bowel wall. Computer tomography (CT) scanning will show fluid collection, fat stranding, and an asymmetrical thickening of the tissues as well as the subcutaneous gas collection. CT scan may aid in the diagnosis of an underlying cause such as a fistulous tract, perianal abscess or a retroperitoneal source of infection.

Fournier’s gangrene should be differentiated from other infective conditions of the external genitalia like scrotal cellulitis, scrotal abscess, strangulated hernia which may present with similar symptoms of pain, erythema and swelling. The difference between Fournier’s gangrene and these other conditions is there presence of necrosis of the subcutaneous tissue in patients with Fournier’s gangrene.

1.8 Management

Fournier’s gangrene is potentially life threatening, early diagnosis and surgical treatment is of paramount importance with implications on outcome. The major goals of treatment are aggressive fluid resuscitation along with correction of electrolyte abnormalities, intravenous broad spectrum antibiotics and early surgical debridement with wound care and future reconstructive surgery.

Fluid resuscitation is important to optimize the hemodynamic status of these patients as they are usually volume depleted due to sepsis. Vasopressors may be additionally useful in patients presenting with shock.
The onset of confusion with hypotension and oliguria with lactic acidosis may herald the onset of septic shock with such patients requiring invasive monitoring and admission into an intensive care unit for cardiopulmonary support.\textsuperscript{48}

Blood transfusion may be necessary in patients with severe anemia to maintain hemoglobin above levels above 10g/dl, critical for optimal oxygen delivery to the tissues.\textsuperscript{48} Any coagulopathy should be recognized and treated appropriately with platelets and fresh frozen plasma before surgical debridement. It is imperative to maintain the blood glucose level of 4-6 mmol/l as this optimizes cellular immunity and wound healing.\textsuperscript{48}

\textbf{Antibiotic therapy}

Empiric broad spectrum antibiotic therapy is essential and should be given immediately upon admission until blood and tissue culture sensitivity results are available.\textsuperscript{22} The broad spectrum antibiotic therapy should cover both aerobes and anaerobes.\textsuperscript{6,15,40} The antibiotic triple therapy is commonly a combination of a penicillin that is effective against \textit{Streptococcus} and \textit{Enterococci}, a third or fourth generation cephalosporin or aminoglycosides that is effective against gram negative rods like \textit{E coli} and metronidazole effective against anaerobes like \textit{Bacteriodes}.\textsuperscript{23,31} Clindamycin may be used in place of metronidazole to cover for anaerobes. It has been shown to suppress bacterial toxin and increased modulation of cytokines.\textsuperscript{40} Aminoglycosides should be avoided in patients in renal failure due to their nephrotoxicity. The use of carbapenems like imipenem, meropenem, ertapenem or beta lactams uredopenicillins like piperrazilline-tazobactam has been advocated for in recent literature due to their ability to have a broader spectrum as monotherapy with less renal toxicity.\textsuperscript{32}
This may be the future choice of therapy to replace the traditional triple therapy as they are easy to administer as once daily dosing though expensive and not easily available.\textsuperscript{32}

**Surgical Debridement**

Surgical debridement remains the most successful mode of treatment since being introduced by Meleney in the 1920’s.\textsuperscript{33} The main goal of surgical debridement is to remove all non-viable necrotic tissue and eliminating the source of infection. It is important that the time to first surgical debridement be kept to the minimum as it is key to survival with significant reduction in morbidity.\textsuperscript{34;35,45} It may be difficult to judge the full extent of the disease involvement from skin appearance as it may be less involved than the subcutaneous disease. Multiple surgical debridement is the rule with an average of 3.5 procedures per patient.\textsuperscript{36}

The debridement which starts with a skin incision in the scrotum or midline of the perineum should extend radially into the subcutaneous fascia with the anatomy of the fascia planes in mind. The overlying skin that is necrotic should be excised; viable skin should be dissected and undermined to expose the underlying necrotic subcutaneous fascia.\textsuperscript{72} This reduces wound size leaving more skin for future reconstruction. The demarcation between necrotic and viable tissue can be easily recognized by failure to easily separate the affected fascia from the deep fascia and muscle during blunt dissection.\textsuperscript{1,49,72}

The wounds should be inspected daily and if any necrotic areas are identified repeat debridement should be done. The wound surprisingly heal well by secondary intention and if defects are large, reconstruction can be done once the wound is free of infection.
The type of reconstruction depends on the size of the wound and available tissues for reconstruction. Various methods are used for reconstruction ranging from mobilization of the remaining adjacent scrotal skin to split thickness graft which is commonly used\textsuperscript{15} and myocutaneous flaps.

Suprapubic or transurethral catheterization may be required to prevent wound contamination or be used as a form treatment for patients with urethral stricture disease or urethral abscess.\textsuperscript{22,47} Catheterization aids in monitoring urine output during fluid resuscitation.\textsuperscript{72}

A colostomy may be required in patients who have ano-rectal source of infection with involvement of the anal sphincter, patients with rectal or colonic perforation and patients with extensive posterior perineal triangle involvement.\textsuperscript{15} These patients may continuously contaminate the wound with fecal matter due to anal incontinence thereby delaying wound healing as they is reinfection. The colostomy may aid early oral intake thus optimizing wound healing by provision of adequate nutrition and reduced wound contamination.\textsuperscript{15,22,47}

Depending on the series about 15\% of the patients will have a colostomy.\textsuperscript{15} A study by Corcoran et al and some series have shown a higher mortality associated with a colostomy.\textsuperscript{25,26} Diverting colostomy does not seem to reduce the number of debridement required.\textsuperscript{26} Bronder et al\textsuperscript{44} advocates colostomy to be done on second look debridement when patient is stable and well resuscitated. He noted most patients who are acutely and severely ill have an ileus in the first 48 hours upon admission.\textsuperscript{44}
The testes are rarely affected in the disease process due to their direct blood supply from the abdominal aorta.\textsuperscript{22,23} If the testis are involved it is due to a preexisting epididymo-orchitis or scrotal abscess or a retroperitoneal source of infection. The rate of orchidectomy for a necrotic testis has been documented to be between 10 - 21\%.\textsuperscript{6,15,25,31} If the testis are exposed after debridement they may be temporarily buried in the lateral thigh pouch or in a subcutaneous pouch created in the lower abdomen. If the testis are buried in the lateral thigh pouch they should be placed at different levels to avoid the testis from rubbing against each other when the patient is walking.\textsuperscript{22} The testis can then be removed from the pouches at the time of skin reconstruction.

**Wound dressing and topical therapy**

The goals of wound care should be to allow additional chemical debridement, avoiding reinfection and promoting natural healing with good granulation. Various solutions have been described that aid wound debridement and useful as dressing agents. The chemicals used for cleaning and dressing wounds include hydrogen peroxide, Eusol (Edinburgh University solution), povodine iodine, 0.025% sodium hypochlorite, (Dakin solution) and glycerine and ischmmol.\textsuperscript{15,40} Simple irrigation of the wound with normal saline keeps the dressing moist and is effective in large open wounds.

Hydrogen peroxides aids in the separation of slough and granulation of the wound, but should be used with caution in closed tissues as liberation of oxygen in closed tissues may cause tissue damage.\textsuperscript{1,39,41} Heggers et al has shown that irrigation of the wound with 0,025% sodium hypochlorite is safe, nontoxic to healthy tissue, bactericidal and effective in Fournier’s
gangrene.\textsuperscript{43,44} Lyophilized collagenase application has been found useful in the enzymatic debridement of necrotic tissue.\textsuperscript{47}

Topical therapy in the form of pure unprocessed honey to aid wound healing has been described.\textsuperscript{40} Honey has an antibacterial effect due to its low \textit{ph} of 3.6, high osmolarity and phenolic effect which makes it good at desloughing off necrotic tissues.\textsuperscript{41} It increases the local tissue oxygen levels with a good aid in wound healing. Its effect can be seen in a week of its application.\textsuperscript{40} They are no randomized controlled trials to assess its efficacy compared to other types of dressing. Dressings with 5\% acetic acid is effective against \textit{Psuedomonas} infection which is easily recognizable by its distinct odor and green appearance on the dressing.

Hyperbaric oxygen (HBO) therapy has been used as an adjunct to treatment of Fournier’s gangrene.\textsuperscript{54,55} The presence of crepitus mistakenly attributed to clostridial infections made some authors to advocate for the use of HBO in every case of Fournier’s gangrene.\textsuperscript{54,55,72} However hyperbaric oxygen has been found to be effective even in non clostridial infections.\textsuperscript{3,15} HBO therapy involves putting a patient in a high ambient pressurized environment (2-2.5 absolute atmosphere) while breathing 100\% oxygen.\textsuperscript{54,55,72} HBO therapy achieves its effect by enhancing arterial oxygenation of the tissues with release of oxygen free radicals which are directly toxic to bacteria.\textsuperscript{53,72} The improved tissue oxygenation allows maximum neutrophil phagocytic function, improved fibroblast proliferation and angiogenesis\textsuperscript{42,54,55}. It also reduces the tissue edema by causing vasoconstriction and allows maximum antibiotic transportation.\textsuperscript{54,55,72}
Hyperbaric oxygen therapy may reduce the function of other antibiotics like ciprofloxacin and vancomycin by increasing tissue oxygen content while it enhances function of aminoglycosides which depend on an oxygen dependent pump to cross the cell membrane.\textsuperscript{53,72} HBO therapy is expensive, logistically cumbersome and mostly unavailable in low resource countries.\textsuperscript{40,45} It is potentially dangerous as it can cause central nervous system toxicity and barotrauma to the middle ear if used in closed air spaces.\textsuperscript{42,54,55} In diabetics it exacerbates hypoglycemia.\textsuperscript{42}

The application and use of HBO therapy among patients with Fournier’s gangrene is still a matter of continuous debate.\textsuperscript{72} They are no prospective randomized trials on the use of HBO therapy on patients with Fournier’s gangrene though small retrospective studies have supported its use in these patients.\textsuperscript{34,40,42} They are studies that have shown a survival advantage with the use of HBO therapy\textsuperscript{52,54}. Mehli\textsuperscript{52} et al showed improved survival (11.7%) with use of hyperbaric oxygen therapy and surgical debridement compared to surgical debridement alone (37.5%).\textsuperscript{52} However Shupak and colleagues\textsuperscript{55} found an increased mortality rate (36%) with the use of hyperbaric oxygen therapy compared to non-use of hyperbaric oxygen therapy among these patients (25%).\textsuperscript{55}

Vacuum assisted closure (VAC) of wounds minimizes skin defects and speeds wound healing.\textsuperscript{56} The wound is exposed to sub atmospheric pressure for an extended period which aids debridement and healing.\textsuperscript{56} It reduces the number of dressing changes, with better patient comfort and reduced duration of hospital stay. The placement of VAC device in the scrotal region poses a significant challenge.\textsuperscript{56}
1.9 Outcome and Prognosis

Fournier’s’ gangrene is a potentially fatal condition with significant morbidity.\textsuperscript{1,15} The mortality rate varies from 3 – 45\% across the world with an average of 20 -30\%.\textsuperscript{5,43} In the early days the mortality was as high as 80\%.\textsuperscript{43} Mortality has remained high despite availability of broader spectrum antibiotics, early and timely surgical debridement.\textsuperscript{5} The major causes of death in patients with Fournier’s gangrene is severe sepsis, coagulopathy, acute kidney injury and multiple organ failure.\textsuperscript{23}

Renal failure, hepatic dysfunction, and increasing age, delay in treatment, extensive disease involvement, severe sepsis or septic shock at presentation and immunosuppression have been found to be associated with increased mortality.\textsuperscript{22,24,45,27} In a population based review of 1641 cases of Fournier’s gangrene by Sorensen et al,\textsuperscript{22} a higher mortality was associated with an advanced age and four comorbidities namely renal failure, heart failure, hypertension and coagulopathy.\textsuperscript{22} The presence of diabetes mellitus as noted by some authors may have an adverse outcome.\textsuperscript{6,15,27} The data available seem to suggest that HIV does not affect survival as long as treatment is initiated early enough.\textsuperscript{12} However this study by Elem et al\textsuperscript{12} had a small series of 8 patients and did not account for the effect of degree of immunosuppression as they was no measure of the CD4 count.\textsuperscript{12}

Additional procedures required during admission namely, colostomy, penectomy, mechanical ventilation and dialysis were associated with a greater mortality in some series.\textsuperscript{22} Each surgical operation the patient needed increased the unadjusted odds of death by 27\% as noted by Laucks.\textsuperscript{22} The ano-rectal source of infection has a higher mortality compared to other sources of
infection (urogenital and cutaneous) as the region is awash with a wide spectrum of virulent pathogenic bacteria.\textsuperscript{44,45} It remains uncertain whether the number of surgical procedures and extent of disease may have an adverse effect on the outcome of this disease.\textsuperscript{11,15} The role of extent of body involvement on remains debatable with some authors suggesting that a body surface area involvement of greater than 5% is associated with a high mortality.\textsuperscript{27,57} However Clayton et al\textsuperscript{11} disputes this as their results showed that mortality is not related to the extent of body surface area involved.\textsuperscript{11}

The altered homeostasis as seen in changes in heart rate, respiratory rate, temperature as well as abnormalities in serum electrolytes and blood count variables seem to be associated with poor outcome.\textsuperscript{24} Laor et al\textsuperscript{24} described and published a Fournier’s gangrene severity index (FGSI) score based on nine prognostic parameters associated with poor prognosis.\textsuperscript{24} The nine parameters used to calculate the score are heart rate, temperature, respiratory rate, serum sodium, serum potassium, serum bicarbonate levels, serum creatinine, hematocrit and leucocyte count with a grading of zero to four based on the deviation from the normal. The FGSI score is the total of the nine parameters added together. Laor et al\textsuperscript{24} demonstrated that an FGSI score of greater than 9 was associated with a 75% probability of death while a score of less than or equal to 9 is associated with a 78% chance of survival.\textsuperscript{24} The time to presentation and time to surgical debridement were not found to significantly affect survival.\textsuperscript{24}

The FGSI index has been further validated by Yeniyol and Tuncer.\textsuperscript{58,59} Yilmazlar et al modified the FGSI score by adding age and extent of involvement to the parameters as they were found to affect survival.\textsuperscript{27}
The use of the FGSI index as a predictor of mortality has not been universally accepted with some authors disputing its usefulness in predicting mortality.\textsuperscript{60,61} In a series of 70 cases published by Jenane et al\textsuperscript{60} they showed that the FGSI index was not predictive of mortality but rather the extent of body involvement and metabolic abnormalities were significant predictors of survival.\textsuperscript{60}

Fournier’s gangrene is a condition associated with significant morbidity.\textsuperscript{58,62} The morbidity associated with the disease can be as short as 2 days and as long as 278 days depending on the extent of the disease.\textsuperscript{58} The patient very often requires multiple surgical debridement with future reconstruction.\textsuperscript{31} The greater the aggressive debridement, the greater the defect for reconstruction and the longer the hospital stay.\textsuperscript{31} The patients managed with minimal debridement may have a shorter hospital stay with similar outcome as compared to those with wide debridement.\textsuperscript{39} The mean hospital stay of patients managed with minimal debridement (45 ± 10 days) was significantly less compared to extensive surgical debridement (62 ± 12 days) according to a study by Frezza.\textsuperscript{39}

Reconstructive surgery is done when the wound is clean and free from any sepsis.\textsuperscript{63} The type of wound closure depends on size of the defect and its location. The types of reconstruction described include use of secondary delayed closure by skin mobilization and suturing, split or full thickness grafting and use of vascularized myocutaneous flaps.\textsuperscript{63} Split thickness grafting is commonly used with good and acceptable results even with large wound defects.\textsuperscript{50,63}

The grafting can be done on a single or multiple setting with sites of harvest of skin from the buttocks, arms and trunk.\textsuperscript{63}
The penis should be primarily skin grafted with unexpanded skin grafts to prevent scar healing which has future implications on erectile function. Myocutaneous vascularized flaps should be used when there is not enough skin to cover the defect or if the defect is deep with exposure of tendons. The gracilis myocutaneous flap commonly utilized yields the best results due to its close proximity to the perineum, good mobility and hidden donor site scars. A report series of 43 cases over a period of eleven years published by Parkash and Gajendran showed that disease confined to the scrotum and penis could be covered by mobilizing remnant of skin to cover the defect. The inner aspect of the prepuce was used to cover the defect on the shaft of the penis. The defects beyond the scrotum and penis were supplemented with split skin grafts. Meshed unexpanded split thickness skin grafts have been used to cover penile skin loss with good uptake and good functional outcome.

They are late complications associated with this disease which include chordee, painful erections and erectile dysfunction when the penile shaft is involved and healing with strictures. Infertility may result from burying the testis in the thigh pouches due to high temperatures though it is rare.
CHAPTER 2: Background and Objectives

2.1 Statement of problem and justification of study

Fournier’s gangrene remains a highly fatal condition worldwide with mortality rates averaging 20-30% worldwide in spite of advances in technology and medical practice.\(^5\) The factors associated with mortality are not universally accepted and remain controversial.\(^6\) Many of the studies on Fournier’s gangrene are of small series, mainly retrospective and done over a long period of time.

Masanzu (2004) in a local retrospective review of 80 cases of Fournier’s gangrene managed at 2 tertiary hospitals in Harare, Zimbabwe between 1999 and 2004 showed an average mortality of about 25%. The factors or prognostic variables associated with mortality are not known in our setting and have not been studied.

The study serves to establish the factors associated with mortality among patients with Fournier’s gangrene, namely age, extent of tissue involvement or body surface area involvement, extent of immunosuppression (HIV, diabetes mellitus), clinical and biochemical parameters on admission.

The role of HIV infection is not clearly defined in literature due to small number of cases. This study may identify any association of HIV with higher mortality. Zimbabwe has a high prevalence of HIV currently at 15% as compared to the western world at 0.2% as of 2014 UNAIDS report.\(^7,8\) Diabetes mellitus is the commonest identifiable factor in about 65% of cases in Europe and North America.\(^1,11,15,34\)
The prevalence and outcome of patients with diabetes mellitus amongst our patients with Fournier’s gangrene is not known and has not been investigated. This study will help in improved care and better management of patients with Fournier’s gangrene in our environment by identifying patients that are at higher risk of death.
2.2 Research question and hypothesis

This study will seek to answer the following question:

What is the disease related mortality rate and factors associated with death amongst patients admitted with a clinical diagnosis of Fournier’s gangrene at three tertiary referral hospitals in Harare, Zimbabwe?

Hypothesis

1. The disease related mortality rate in our hospital settings is comparable to other institutions in the world.

2. The following factors will be associated with poor outcome (death):
   - An older age
   - Delay in presentation
   - Extent of disease at presentation
   - Anorectal source of infection
   - HIV, Diabetes mellitus
   - Renal failure on admission
   - Laboratory parameters on admission (white cell count, hemoglobin level, serum sodium, serum potassium, blood urea nitrogen and serum creatinine)
   - Severe sepsis
   - Delay in surgical debridement
   - Number of surgical debridement
2.3 OBJECTIVES OF THE STUDY

2.3.1 Main objective: To determine the disease related mortality, morbidity and factors associated with mortality amongst patients with a clinical diagnosis of Fournier’s gangrene at 3 tertiary hospitals in Harare, Zimbabwe.

2.3.2 Specific Objectives

1) To describe the demographics and clinical features of patients admitted with a clinical diagnosis of Fournier’s gangrene.

2) To determine the mortality rate and morbidity (hospital stay) of patients admitted with a clinical diagnosis of Fournier’s gangrene.

3) To determine the association between patient’s age, time to presentation, comorbidity and degree of dissemination of disease and non-survival among patients with a clinical diagnosis of Fournier’s gangrene.

4) To determine the admitting clinical and biochemical parameters associated with non-survival amongst patients with a clinical diagnosis Fournier’s gangrene.

5) To determine the association between HIV infection and non-survival among patients with a clinical diagnosis of Fournier’s gangrene.

6) To determine the association between time to first surgical debridement, number of surgical debridement and non-survival among patients with Fournier’s gangrene patients.
CHAPTER 3: Study design and Methodology

3.1 Study design

This study is a prospective observational study of patients admitted with a clinical diagnosis of Fournier’s gangrene admitted and managed at three tertiary hospitals in Harare Zimbabwe over a 2 year period.

3.2 Setting

The study was conducted at 3 tertiary hospitals in Harare, Zimbabwe namely:

- Parirenyatwa Group of Hospitals
- Harare Central Hospital
- Chitungwiza Central Hospital

3.3 Study Population

The study was on 51 patients with a clinical diagnosis of Fournier’s gangrene admitted and managed at 3 tertiary institutions in Harare.

Case definition
Fournier’s gangrene defined as evidence of an infective necrotizing fasciitis of the external genitalia, perineum and perianal region

Inclusion Criteria
All patients of any age group with a clinical diagnosis of Fournier’s gangrene admitted and managed at 3 tertiary hospitals in Harare Zimbabwe.

Exclusion criteria
1. Patients with perianal or peri urethral abscess with no soft tissue involvement.
2. Scrotal cellulitis and scrotal abscess with no evidence of soft tissue necrosis
3.4 Sample Size Calculation

The sample size was calculated to be 51 using the Dobson’s sample size formula as shown below:

\[ N = \frac{P(100\% - P)}{SE^2} \]

\( P = \) proportion of patients who are likely to die from Fournier’s gangrene in hospital being 25% from a previous local study, (Masanzu 2004)

\( SE = \) standard Error = 6.1 (Z=1.64 and CI =90%)

The precision with which we decided the proportion of patients who are likely to die during hospital admission must be within \( \pm 10\% \) of the true value. It was assumed that the mortality rate is around 25% with a range between 15% and 35%.

3.2 Materials and Methods

This study was conducted after approval by the Department of Surgery of the University of Zimbabwe, the Joint Research and Ethics Committee (JREC) and the institutional hospital approval boards. The study was a prospective observational study on 51 consecutive patients admitted and managed at 3 tertiary hospitals in Harare, Zimbabwe with a clinical diagnosis of Fournier’s gangrene over a 2 year period.

The patients were enrolled into the study prospectively after obtaining an informed consent. The diagnosis of Fournier’s gangrene was made from the medical history and physical examination of the patients at presentation to the hospital. The data on demographics, clinical and biochemical parameters were carefully examined from patient records on admission and
recorded on a designed data sheet. The origin of disease whether urogenital, anorectal, cutaneous source as well as underlying causes of disease was extensively looked for and recorded. The presence and number of comorbidities was noted and recorded. This included the patient’s HIV status, presence of diabetes mellitus and renal dysfunction. The extent of disease involvement on each patient was calculated as a percentage using a modified body surface area nomogram used routinely to assess the extent of burn injuries as modified by Palmer et al (appendix 3). The penis, scrotum, and perineum each accounts for 1% of the body surface area while each ischio rectal fossa accounts for 2.5%. The disease severity was classified according to being minor if its less than 3%, moderate if between 3% and 5% and severe if greater than 5%. The presence of severe sepsis based on the surviving sepsis global campaign of 2012 was noted and recorded (see appendix 5).

All patients received intravenous fluids, immediate surgical debridement and broad spectrum intravenous antibiotics consisting of a penicillin, gentamicin and metronidazole on admission. Ceftriaxone was used in place of gentamicin among patients with renal failure. The patients would have periodical wound inspection, surgical debridement would be repeated according to the progression of soft tissue necrosis. Wound dressing was done using glycerine and ischmmol after daily salt sitz bath as well as chemical debridement with hydrogen peroxide and wound irrigation with normal saline. Necrotic tissue and pus swab were sent for culture and empirical antibiotics were replaced by specific antibiotics according to culture sensitivity reports. The patients were followed up from admission till death or discharge from hospital.
The treatment information on surgical debridement, antibiotics, intravenous fluids and intensive care admission was recorded. The time to first surgical debridement, number and type of surgical debridement of these patients were recorded on a designed data sheet. The type of urinary diversion, orchidectomy or any colostomy fashioned were noted and recorded. The duration of hospital stay of the patients and type of reconstruction procedures done were recorded. The data was stratified by outcome whether the patient survived or died. Mortality was defined as disease related death during hospital admission.

Statistical package for social scientists (SPSS) was used for data analysis. Descriptive statistics were used to report measures of central tendencies for quantitative variables. The data was analyzed for statistical differences between survivors and non survivors using the Chi squared/Fisher exact test for categorical variables. A 2-sided tailed student t test was used to compare the difference of the means between survivors and non survivors. The statistical significance level was set at a p value of less than 0.05. Multivariate regression analysis was additionally performed to determine independent variables associated with mortality.
CHAPTER 4: Results

The total number of patients observed in this study over the two year period was 51. They were three study sites namely, Parirenyatwa hospital, Harare hospital and Chitungwiza hospital. Parirenyatwa hospital and Harare hospital managed an equal number of cases each with 22/51 (43%) cases while Chitungwiza hospital managed a total of 7/51 (14%) cases during the study period.

4.2 Patient Characteristics

The median age of the study participants was 43 years (mean age - 47 ± 18.3; range 19 – 94 years), as shown on figure 4.1 box plot of the age distribution of the 51 patients. All patients were of male.

The following figure 4.1 shows a box plot of the age distribution of the 51 patients in this study.
The following figure 4.2 below is a histogram showing the distribution and frequency of different age groups of the 51 patients seen in this study.

![Figure 4.2: Histogram of age distribution](image)

The modal age group range was between 40.1 – 50 years of age as shown on figure 4.2 above. They were 40/50 patients (78%) below the age of 60 years while 12% of the patients were above the age of 60 years. They were no children observed during the study period.

The overall mortality rate during hospital admission among the three tertiary hospitals due to Fournier’s gangrene was 27% (14/51). The median hospital stay of the 51 patients was 15 days with a range of 1 – 90 days.
The following figure 4.3 is a box whisker plot showing the age comparison between survivors and non survivors. (N=51)

The patients that did not survive were significantly older than those that survived, 58.36 ± 21.04 years vs 42.76 ± 14.40 years respectively (p=0.021), as depicted in figure 4.3 box whisker plot of age comparisons of survivors and non survivors above.

The mortality of patients above the age of 60 years (56%) was significantly higher compared to patients of an age below 60 years (20%), p value = 0.03.

They were more patients from rural areas 30/51 (59%) compared to patients coming from the urban area 21/51 (41%) as depicted by the following bar chart on figure 4.4.
The following figure 4.4 shows the distribution of origin and outcome of the 51 patients seen in this study.

They were 6/21 (28.6%) deaths of patients from an urban setting compared to 8/30 (26.7%) deaths of patients from the rural areas as shown from figure 4.4 above. This difference was not statistically significant between these two groups. (p=0.563).

4.3 Clinical features

The median duration of symptoms before presentation in the entire cohort of the 51 patients was 6 days, mean 7.34 ±5.17 days and a range of 2-30 days. The patients that died in this study had a mean duration of symptoms of 8.69 ± 5.23 days compared to survivors with a mean duration of symptoms of 6.86 ± 5.13 days.
Although the patients that died had a longer duration of symptoms suggestive of delay in presentation compared to survivors this difference was not statistically significant. (p=0.29).

The majority of the infection originated from the urogenital tract in 22/51 (40%) while the anorectal source accounted for 32% (15/21) of the cases in the study as depicted in figure 4.5 below. The source of infection that originated from the skin (cutaneous) was observed in 12/51 (24%) patients.

The following figure 4.5 shows the distribution of patients according to the origin of infection.

The commonest cause of genitourinary source of infection was urethral strictures disease 9/22 (41%) followed by neglected catheters with 5/22 (23%) of the cases.
The commonest cause of anorectal source of infection in this study was ischiorectal abscess.

The source of infection could not be ascertained on two patients (idiopathic) in this study.

Fournier’s gangrene developed on two patients after voluntary adult male circumcision. One of the patients had no underlying risk factor to the development of the disease while the other patients had a history of heavy smoking. There was no mortality observed on both patients however there was significant morbidity as a result of total penile skin loss. Reconstruction was done in form of unmeshed non expanded partial thickness skin grafting.

The following figure 4.6 shows the comparison between survivors and non survivors by origin of infection amongst the 51 patients seen in this study.

![Figure 4.6: Comparison of survivors and non survivors by origin of infection (N=51)](chart.png)

The cutaneous source of infection had no deaths as shown by figure 4.6 above while the most deaths were of patients with a urogenital source of infection 10/22 (45%).
The anorectal source of infection had 3/12 death representing a mortality of 25% in this study.

The urogenital source of infection was significantly associated with mortality in this study compared to the anorectal source of infection and skin source. (p=0.01). The cutaneous source of infection was significantly associated with a better outcome compared to the urogenital and anorectal sources (p=0.003).

They were 37/51 (73%) patients with at least one comorbidity or underlying risk factor to Fournier’s gangrene. The presence of at least one comorbidity was significantly associated with non survival (36.1%) compared to no deaths (0%) amongst patients with no comorbidity (p=0.007). The commonest underlying risk factor to Fournier’s gangrene was human immunodeficiency virus (HIV) infection accounting for 36% (18/51) followed by renal failure with 25% (13/51) as shown in table 4.1 below.

The following table 4.1 shows the frequencies of the comorbidities and underlying risks factors of patients with Fournier’s gangrene seen in this study.

**Table 4.1: Comorbidities and underlying risk factors on 51 patients seen in the study.**

<table>
<thead>
<tr>
<th>Comorbidity/ Risk factor</th>
<th>Frequency (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Immunodeficiency virus</td>
<td>18</td>
</tr>
<tr>
<td>Renal failure</td>
<td>13</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>5</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4</td>
</tr>
<tr>
<td>Heavy Smoking</td>
<td>2</td>
</tr>
<tr>
<td>Steriod therapy</td>
<td>1</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>2</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1</td>
</tr>
<tr>
<td>Quadriplegia</td>
<td>1</td>
</tr>
</tbody>
</table>
They were 57% of the patients with renal failure had a urogenital source of infection while 29% had an anorectal source of infection.

The mean age of patients with HIV infection was 38.8 ± 9.2, (range 25 – 64 years). The mean CD4 count of patients with HIV infection was 189cell/ul, (median 191cell/ul) with a range of 16 – 389cell/ul. They were only 5/18 (28%) patients with HIV infection on highly active antiretroviral therapy (HAART). They were more deaths 6 /18 (33.3%) amongst HIV positive patients compared to 7/32 deaths (21.9%) amongst HIV negative patients. However this difference was not statistically significant (p=0.29). The mean CD4 count of survivors was not significantly different from non survivors, 212 ± 104 and 154 ± 139 respectively (p=0.40).

Diabetes mellitus accounted for about 10% (5/51) of the cases. Diabetes mellitus was not significantly associated with mortality (p=0.61). There was only one death amongst the five patients with diabetes mellitus.

One patient developed Fournier’s gangrene after being on prolonged steroid therapy for nephrotic syndrome. They were four patients with malignancies; two of them had advanced prostate carcinoma while the other two had rectal carcinoma.

Renal failure at presentation was significantly associated with mortality in this study (p=0.001), 57% of these patients had a urogenital source of infection. The mortality rate amongst patients with renal failure was 70%.

4.4 Extent of body involvement with Fournier’s gangrene.

The majority of the patients (73%) had disease confined to the external genitalia and or perineum while 10 % (5/51) of the patients had disease extending beyond the pelvis to involve
the abdomen and or thighs as shown by figure 4.6 below with 17.6% of the patients having disease confined to the pelvis. There were no patients with disease extension to the chest wall.

The following figure 4.7 shows a pie chart of the distribution and frequency according to the degree of dissemination.

![Figure 4.7: Degree of dissemination of disease by region](image)

The extent of disease beyond the pelvis was significantly associated with mortality (p=0.02).

The mortality rate of patients with disease beyond the pelvis was 80% (4/5) in this study.

The severity of disease involvement as measured by a percentage of total body surface area nomogram (see appendix3) showed that majority of the patients, 33/51 (64.7%) had a minor degree of involvement i.e less than 3%. They were 12/51 (23.5%) patients with a severe degree of disease involvement that is greater than 5% as shown by figure 4.8 above.
The following figure 4.8 shows the bar chart of the severity of disease involvement and comparison of survivors and non survivors according to percentage of the total body surface area involved by Fournier’s gangrene.

The mean body surface area involvement among the non survivors was significantly higher (5.29 ± 3.14 %) than the patients that survived (2.34 ± 1.81%) (p=0.004). They were significantly more deaths 7/12 (58.3%) patients with severe disease involvement compared to patients with a body surface area involvement of less than 5% (p=0.03) as shown by figure 4.8 above.

4.5 Clinical and biochemical parameters on admission

On admission 11/50 patients (22%) had an elevated axillary temperature above 38°C while two patients had hypothermia with an axillary temperature of less than 35°C. They were 9 patients with hypotension defined as systolic blood pressure of less than 90mmHg at admission.
Tachycardia (heart rate > 90 beats per minute) was noted in 33/50 patients (64.7%). The median respiratory rate was 21 with a range of 15 to 35.

The following table 4.2 illustrates the summary of laboratory and clinical parameters on admission of the patients observed in this cohort. (see appendix 4 for laboratory reference ranges)

<table>
<thead>
<tr>
<th>Clinical and laboratory variables on admission</th>
<th>N</th>
<th>Mean ± SD</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature – °C</td>
<td>50</td>
<td>36.98 ± 1.20</td>
<td>37 (33.10 – 40 C)</td>
</tr>
<tr>
<td>Heart rate – beats per minute</td>
<td>50</td>
<td>100.46 ± 18.51</td>
<td>97.5 (64 – 157)</td>
</tr>
<tr>
<td>Systolic blood pressure – mmHg</td>
<td>50</td>
<td>111.1 ± 20.10</td>
<td>110 (70 – 152)</td>
</tr>
<tr>
<td>Diastolic blood pressure – mmHg</td>
<td>50</td>
<td>66.2 ± 14.04</td>
<td>69 (39 – 90)</td>
</tr>
<tr>
<td>Respiratory rate - breath per minute</td>
<td>50</td>
<td>21.86 ± 4.00</td>
<td>21 (15 – 35)</td>
</tr>
<tr>
<td>Random blood sugar – mmol/l</td>
<td>50</td>
<td>8.09 ± 5.73</td>
<td>6.55 (2.4 – 33)</td>
</tr>
<tr>
<td>White Cell count x 10^9 cell/ l-</td>
<td>49</td>
<td>15.57 ± 11.97</td>
<td>13.4 (3.32 – 61.89)</td>
</tr>
<tr>
<td>Hemoglobin – g/dl</td>
<td>49</td>
<td>10.6 ± 3.08</td>
<td>10.9 (3.8 – 17.8)</td>
</tr>
<tr>
<td>Platelet Count x 10^9/l</td>
<td>49</td>
<td>279 ± 183</td>
<td>269 (7 – 797)</td>
</tr>
<tr>
<td>Sodium – mmol/l</td>
<td>49</td>
<td>135 ± 5.18</td>
<td>135 (128 – 147)</td>
</tr>
<tr>
<td>Potassium – mmol/l</td>
<td>49</td>
<td>4.44 ± 1.11</td>
<td>4.1 (2.3 – 8.3)</td>
</tr>
<tr>
<td>Urea – mmol/l</td>
<td>49</td>
<td>15.72 ± 21.7</td>
<td>7.1 (2.1 – 104)</td>
</tr>
<tr>
<td>Creatinine – umol/l</td>
<td>49</td>
<td>236 ± 315.99</td>
<td>113 (59 – 1439)</td>
</tr>
<tr>
<td>Bicarbonate – mmol/l</td>
<td>13</td>
<td>20.00 ± 7.4</td>
<td>20 (1.32 – 32)</td>
</tr>
<tr>
<td>Albumin g/L</td>
<td>29</td>
<td>22.37 ± 8.22</td>
<td>22 (5 – 35)</td>
</tr>
<tr>
<td>Calcium. – mmol/l</td>
<td>25</td>
<td>2.18 ± 0.30</td>
<td>2.21 (1.65 – 2.95)</td>
</tr>
<tr>
<td>Magnesium - mmol/l</td>
<td>25</td>
<td>0.9 ± 0.26</td>
<td>0.84 (0.57 – 1.54)</td>
</tr>
<tr>
<td>Phosphate – mmol/l</td>
<td>25</td>
<td>1.26 ± 0.43</td>
<td>1.13 (0.64 – 2.73)</td>
</tr>
</tbody>
</table>

Severe sepsis according to surviving sepsis global campaign of 2012 criteria (see appendix 5), was observed in 20/50 patients (40%). The mortality was significantly higher among patients with severe sepsis (83.3%) compared to patients without severe sepsis (p=0.001). The respiratory rate among non survivors was significantly higher compared to survivors, (24.85 ±
6.2) vs (20.81 ± 2.15) respectively (p=0.04). They were no significant differences between survivors and non survivors on heart rate, blood pressure and random blood sugar on admission.

The laboratory investigations on admission showed a median white cell count of $13.4 \times 10^9$ cells/L on 49 of the patients. They were 29/50 (58%) patients with an elevated white cell count above $12 \times 10^9$ cells/dl (see appendix 4). The mean hemoglobin level amongst the patients at presentation was 10.6 g/dl, range (3.8 – 17.8 g/dl). They were 62.7% (32/49) of patients presenting with hemoglobin of level of less than 12g/dl. They were 6/49 (11.8%) patients with a platelet count below $100 \times 10^9$/L. They were no significant difference on white cell count and platelet count between survivors and non survivors. The mean hemoglobin concentration was significantly lower amongst non survivors compared to survivors, $(7.84 \pm 2.35\text{g/dl})$ vs $(11.5 \pm 2.76\text{g/dl})$, respectively (p value=0.0002).

On electrolyte abnormalities, 51% of the patients (25/49) had hyponatremia. The potassium levels were abnormal among 14/49 (28.5%) patients, seven of the patients had either hypokalemia while the other seven had hyperkalemia. The patients with hyperkalemia had a significantly higher mortality (71%) compared to patients with normal potassium levels (11%), (p=0.002). The sodium level between survivors and non survivors was not statistically different.

They were 26/49 (53%) patients with an abnormally elevated blood urea nitrogen level (see appendix 4 on laboratory reference range). The creatinine level was elevated amongst 16/49 (33%) of patients. The patients that did not survive had a significantly elevated urea levels compared to the survivors, $38.52 \pm 33.14 \text{mmol/l}$ vs $8.32 \pm 5.69 \text{mmol/l}$ respectively (p=0.0091).
Similarly the creatinine levels of non survivors was found to be significantly higher than that of non survivors, $544.83 \pm 515.23$ umol/l vs $136.48 \pm 100$ umol/l, (p=0.02)

They were 8/25 (32%) patients with hypocalcemia with hypercalcemia being noted on one patient. The abnormalities of magnesium was noted amongst 9/25 (36%) patients, with an elevated magnesium level being found in 6 out of the total 25 patients while three of the patients had a low magnesium level. The serum phosphate level was abnormal on 6 out of the 25 patients with five of the patients having hyperphosphatemia while one patient had a low phosphate level (see appendix 4 for laboratory reference ranges). The mean albumin level was $22.37 \pm 8.22$g/dl with range from 5 – 35g/dL.

The abnormalities in calcium, magnesium, phosphate levels were not statistically different between survivors and non survivors. The albumin level was also not statistically different between the patients that survived and those that did not survive.

4.6 Management, operative characteristics and outcome

All the 51 patients received fluid resuscitation and broad spectrum antibiotic cover. The commonest antibiotic combination consisted of benzylpenicillin, gentamicin and metronidazole on 32 out of the 51 patients. Ceftriaxone was used in place of gentamicin in 13 patients found to have renal failure. Wound culture results were available on 19.6% (10/51) patients. The positive culture rate was 80% and 62.5% of the cultures isolated more than one organism. *Staphylococcus and Escherichia coli* were the commonest bacteria isolated accounting for 63% and 50% respectively.
All the 51 patients underwent surgical debridement of necrotic tissue. They were 42/50 (84%) patients that had debridement done within 24 hours from admission while 8/50 (16%) patients had debridement done after 24 hours from admission. A delay in first surgical debridement after 24 hours from admission was significantly associated with mortality 62.5 % versus 19.1%, (p=0.04). The median number of debridement in this cohort of patients was three with a range of 1 – 9. The number of surgical debridement did not differ significantly between survivors and non survivors.

They were no patients that had orchidectomy procedure, neither a colostomy. They were 40/51(78.4%) patients that had urinary catheterization, of which 57.5% was suprapubic catheterization while the remainder had transurethral catheterization. They were 9 patients that received blood transfusion accounting for a transfusion rate of 18%.There was only one patient that had admission into the intensive care unit for inotropic support. The patient died 15 days from the day of admission into the intensive care due to septic shock and multi organ failure.

Reconstruction procedures were done in the form of delayed primary closure or skin grafting. Delayed primary closure was done on 25 out the 37 patients (68%) that survived. The remaining skin was mobilized as flaps and sutured to close scrotal defects after the wound was clean. Split thickness skin grafting was done on the remaining 8 patients. They were no myocutaneous flaps procedures done.
4.6 Outcome and factors associated with mortality.

The following table 4.3 summarizes the differences between survivors and non survivors.

**Table 4.3 Comparison of survivor and on survivors (significance level p<0.05)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non Survivors (mean ± sd)</th>
<th>Survivors (mean ± sd)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/years</td>
<td>58.36 ± 21.04</td>
<td>42.76 ± 14.40</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of Symptoms/days</td>
<td>8.69 ± 5.23 days</td>
<td>6.86 ± 5.13 days</td>
<td>0.29</td>
</tr>
<tr>
<td>Origin of infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>10 (45.45%)</td>
<td>12 (54.55 %)</td>
<td>0.01</td>
</tr>
<tr>
<td>Anorectal</td>
<td>3 (25%)</td>
<td>9 (75.00%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>0 (0%)</td>
<td>15 (100%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Dissemination of disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confined to the pelvis</td>
<td>10 (21.74%)</td>
<td>36 (78.26%)</td>
<td>0.017</td>
</tr>
<tr>
<td>Beyond pelvis (Abdomen, thighs)</td>
<td>4 (80.00%)</td>
<td>1 (20.00%)</td>
<td></td>
</tr>
<tr>
<td>Body surface Area involvement (%)</td>
<td>5.29 ± 3.14</td>
<td>2.34 ± 1.81</td>
<td>0.004</td>
</tr>
<tr>
<td>Severe Total Body Surface Area (&gt;5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>7 (58.33%)</td>
<td>5 (41.67%)</td>
<td>0.03</td>
</tr>
<tr>
<td>NO</td>
<td>7 (13.73%)</td>
<td>32 (79.07%)</td>
<td></td>
</tr>
<tr>
<td>Presence of at least one comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>13 (36.11%)</td>
<td>23 (63.89%)</td>
<td>0.007</td>
</tr>
<tr>
<td>NO</td>
<td>0 (0.00%)</td>
<td>14 (100%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>1 (20.00%)</td>
<td>4 (80.00%)</td>
<td>0.61</td>
</tr>
<tr>
<td>NO</td>
<td>12 (26.67%)</td>
<td>33 (73.33%)</td>
<td></td>
</tr>
<tr>
<td>Human Immunodeficiency Virus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>6 (33.33%)</td>
<td>12 (66.67%)</td>
<td>0.29</td>
</tr>
<tr>
<td>NO</td>
<td>7 (21.88%)</td>
<td>25 (78.13%)</td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>7 (70%)</td>
<td>3 (30%)</td>
<td>0.001</td>
</tr>
<tr>
<td>NO</td>
<td>6 (15%)</td>
<td>34 (85%)</td>
<td></td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>10 (83.33%)</td>
<td>2 (16.67%)</td>
<td>0.001</td>
</tr>
<tr>
<td>NO</td>
<td>10 (27.03%)</td>
<td>27 (72.97%)</td>
<td></td>
</tr>
<tr>
<td>Time to surgical Debridement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 24 hours from admission</td>
<td>8 (19.05%)</td>
<td>34 (80.95%)</td>
<td>0.04</td>
</tr>
<tr>
<td>&gt; 24 hours from admission</td>
<td>5 (62.5%)</td>
<td>3 (4.00%)</td>
<td></td>
</tr>
<tr>
<td>Number surgical debridement</td>
<td>2.23 ± 1.30</td>
<td>2.72 ± 1.69</td>
<td>0.28</td>
</tr>
</tbody>
</table>
The number of patients that died in this cohort of patients was 14 out 51 patients representing a mortality rate of 27%. They were 37 survivors in this cohort. The median hospital stay was 15 days with a range 1 – 90 days. They were 81% of the survivors that had a hospital stay of for more than 10 days.

The following table 4.4 summarizes the admitting clinical and biochemical differences between survivors and non survivors.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Non survivors (mean ± sd)</th>
<th>Survivors (mean ± sd)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate (breath/min)</td>
<td>50</td>
<td>24.85 ± 6.20</td>
<td>20.81 ± 2.15</td>
<td>0.04</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>50</td>
<td>36.27 ± 1.34</td>
<td>37.23 ± 1.05</td>
<td>0.03</td>
</tr>
<tr>
<td>Heart rate (beats per min)</td>
<td>50</td>
<td>103.46 ± 14.48</td>
<td>99.41 ± 19.82</td>
<td>0.44</td>
</tr>
<tr>
<td>White cell count (x 10⁹ cell/l)</td>
<td>49</td>
<td>23.17 ± 19.75</td>
<td>13.10 ± 6.79</td>
<td>0.11</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>49</td>
<td>7.84 ± 2.35</td>
<td>11.50 ± 2.76</td>
<td>0.0002</td>
</tr>
<tr>
<td>Platelet count (x 10⁹/l)</td>
<td>49</td>
<td>220 ± 205.64</td>
<td>298 ± 173.27</td>
<td>0.25</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>49</td>
<td>134.42 ± 5.88</td>
<td>136.11 ± 4.95</td>
<td>0.38</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>49</td>
<td>5.11 ± 1.72</td>
<td>4 (11.4%)</td>
<td>0.10</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
<td>31 (88.6%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>49</td>
<td>38.52 ± 33.14</td>
<td>8.32 ± 5.69</td>
<td>0.01</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>49</td>
<td>544.83 ± 515.23</td>
<td>136.48 ± 100</td>
<td>0.02</td>
</tr>
<tr>
<td>Random Blood sugar (mmol/L)</td>
<td>50</td>
<td>6.87 ± 2.93</td>
<td>8.51 ± 6.42</td>
<td>0.22</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>29</td>
<td>18.42 ± 8.48</td>
<td>23.19 ± 8.10</td>
<td>0.29</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>25</td>
<td>2.11 ± 0.28 (1.71 – 2.35)</td>
<td>2.20 ± 0.31 (1.65 – 2.95)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Significant levels: p value <0.05
They were differences between the survivors and non survivors on clinical and laboratory indices on admission. The factors found to be associated with mortality as shown on table 4.3 above were an older age, a urogenital source of infection, severe body surface area involvement of >5%, extension of disease beyond the pelvis, presence of at least one comorbidity, renal failure, severe sepsis and delay in first surgical debridement beyond 24 hours from time of admission.

HIV infection, diabetes mellitus, and delay in presentation, transfusion and the number of surgical debridement were not significantly associated with increased mortality.

The admitting clinical and biochemical parameters that were significantly found to be associated with non survival were, an increased respiratory rate, a low hemoglobin concentration, an elevated serum potassium, blood urea nitrogen and creatinine levels.

Multiple logistic regression analysis done did not show any individual parameter to be independently associated with mortality.
CHAPTER 5: Discussion, Conclusion and Recommendation

5.1 Discussion

Fournier’s gangrene is a poly-microbial infective necrotizing fasciitis of the external genitalia and perineum.\textsuperscript{1} The disease is potentially life threatening and is associated with a high mortality and significant morbidity.\textsuperscript{1,6,15,22,24} The mortality due to Fournier’s gangrene varies worldwide with a range of 3% to 45%.\textsuperscript{1,5} The mortality has remained high despite advancement of medical care and availability of intensive care and monitoring.\textsuperscript{1,5,43} The major causes of death are severe sepsis, coagulopathy, renal failure and multi organ dysfunction.

In this prospective study of 51 patients the mortality rate during hospital admission due to Fournier’s gangrene was found to be 27%. This mortality rate is similar to an unpublished 5 year retrospective review of 81 cases from a similar population by Masanzu (2004) that established an overall mortality rate of 25%. Our mortality is still high but compares to reports from some developed countries like Turkey and Croatia, as shown in table 5.1 below although higher compared to studies from North America with mortality of 7.5%. The mortality rates from studies done in African countries range from 3.6% to 24% as depicted in table 5.1 below. They are studies that have recorded zero mortality from Fournier’s gangrene.\textsuperscript{78} A 3 year review study by Katib et al on 20 male patients of a mean age of 56 years had a 0% mortality rate.\textsuperscript{78} They attributed this excellent outcome from the moderate severity of the cases and urgent radical surgical debridement.\textsuperscript{78}
However, on this study by Katib et al.\textsuperscript{78} there was significant morbidity amongst their patients, 15\% of the cases (3/20) undergoing penile amputation while 30\% of the patients had orchidectomy. The length of hospital stay of their patients averaged 22.3 days.\textsuperscript{78}

The following table 5.1 summarizes the mortality rates as noted from different countries around the world.

<table>
<thead>
<tr>
<th>Author of study</th>
<th>Country</th>
<th>Duration of study (Years)</th>
<th>Number of cases</th>
<th>Mean Age (years)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altarac et al\textsuperscript{81} (2012)</td>
<td>Croatia</td>
<td>15</td>
<td>41</td>
<td>62</td>
<td>36.6</td>
</tr>
<tr>
<td>Eke\textsuperscript{5} (2000)</td>
<td>Worldwide</td>
<td>49</td>
<td>1726</td>
<td>N/A*</td>
<td>16</td>
</tr>
<tr>
<td>Ugwumba\textsuperscript{69} (2012)</td>
<td>Nigeria</td>
<td>13</td>
<td>28</td>
<td>48.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Sorensen et al\textsuperscript{21} (2009)</td>
<td>USA</td>
<td>4</td>
<td>1680</td>
<td>50.9</td>
<td>7.5</td>
</tr>
<tr>
<td>Tuncel et al\textsuperscript{59} (2006)</td>
<td>Turkey</td>
<td>7</td>
<td>20</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Ngugu et al\textsuperscript{70} (2014)</td>
<td>Kenya</td>
<td>9</td>
<td>146</td>
<td>38.6</td>
<td>20.5</td>
</tr>
<tr>
<td>Malik et al\textsuperscript{83} (2010)</td>
<td>Pakistan</td>
<td>8</td>
<td>73</td>
<td>57.3</td>
<td>17.8</td>
</tr>
<tr>
<td>Aliyu et al\textsuperscript{77} (2013)</td>
<td>Nigeria</td>
<td>5</td>
<td>38</td>
<td>37.8</td>
<td>15.8</td>
</tr>
<tr>
<td>Elem et al\textsuperscript{12} (1995)</td>
<td>Zambia</td>
<td>1.5</td>
<td>10</td>
<td>32</td>
<td>20</td>
</tr>
<tr>
<td>Bjurlin et al\textsuperscript{85} (2013)</td>
<td>USA</td>
<td>7</td>
<td>122</td>
<td>49</td>
<td>4.9</td>
</tr>
<tr>
<td>Benjelloun et al\textsuperscript{69} (2013)</td>
<td>Morocco</td>
<td>6</td>
<td>50</td>
<td>54</td>
<td>24</td>
</tr>
<tr>
<td>Roghmann\textsuperscript{84} (2012)</td>
<td>Germany</td>
<td>10</td>
<td>44</td>
<td>59</td>
<td>30</td>
</tr>
<tr>
<td>Kabay\textsuperscript{84} (2008)</td>
<td>Turkey</td>
<td>12</td>
<td>72</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>Chen et al\textsuperscript{83} (2011)</td>
<td>Taiwan</td>
<td>8</td>
<td>50</td>
<td>53.6</td>
<td>12</td>
</tr>
<tr>
<td>Mehl et al\textsuperscript{12} (2010)</td>
<td>Brazil</td>
<td>8</td>
<td>40</td>
<td>47.2</td>
<td>20</td>
</tr>
<tr>
<td>Macro et al\textsuperscript{66} (2010)</td>
<td>Spain</td>
<td>12</td>
<td>51</td>
<td>63</td>
<td>16</td>
</tr>
<tr>
<td>Ersoz et al\textsuperscript{82} (2012)</td>
<td>Turkey</td>
<td>3</td>
<td>52</td>
<td>55</td>
<td>23.8</td>
</tr>
<tr>
<td>Yilmazlar et al\textsuperscript{21} (2015)</td>
<td>Turkey</td>
<td>10</td>
<td>80</td>
<td>57</td>
<td>21</td>
</tr>
<tr>
<td>Katib et al (2013)</td>
<td>Saudi Arabia</td>
<td>3</td>
<td>20</td>
<td>55.95</td>
<td>0</td>
</tr>
<tr>
<td>Tang et al (2015)</td>
<td>USA</td>
<td>4</td>
<td>2656</td>
<td>51.8</td>
<td>11.1</td>
</tr>
</tbody>
</table>

* N/A – not available
Fournier’s gangrene was initially thought to affect otherwise healthy young men with no apparent identifiable cause as described early on by Sir Albert Fournier in 1883. However the disease spectrum has evolved over time to include both males and females of any age group with commonly a predisposing factor. In this study series of 51 patients, all patients admitted with a clinical diagnosis of Fournier’s gangrene were of male sex with a median age of 43 years (mean 47 years, range 19 -94 years.) This represents a population of significantly younger patients compared to most studies from Europe and North America as shown from table 5.1 above. The mean age of the patients from most western studies is between 55.8 years and 63.5 years. Our population median age of 43 years is consistent with most studies from Nigeria, Kenya and Zambia which noted a much younger group of patients with an average age between 36 years to 48 years. A review 1726 cases of Fournier’s gangrene cases by Eke noted that about 10% of the patients are female. This study did not record any female patients. They were no cases of Fournier’s gangrene amongst children in this series although cases have been described in literature.

In this study the patients that did not survive were significantly older than those that survived, 58.36 years vs 42.76 years respectively (p=0.02). This is similar to studies by Laor et al, Clayton et al and Benjoullan et al who found out that the patients that did not survive were significantly older than the survivors. This has been confirmed by other various studies. Sorensen et al in a population based study of 1641 cases, showed that age was a strong predictor of mortality (OR 4- 15, P<0.0001). However Tuncel et al and Corcocan et al did not find any significant age differences between survivors and non survivors.
The cause or origin of infection in Fournier’s gangrene is almost identifiable in more than 90% of the cases.\(^1\) This is in contrast to earlier descriptions of an idiopathic disease process amongst healthy man by Sir Alfred Fournier whom the disease is named after.\(^2\) The cause of Fournier’s gangrene can be from the urogenital tract, anorectal source or cutaneous source. In this study the source of infection was identifiable in 96% of the patients (49/51) with only two idiopathic cases. The two cases in our study that were considered idiopathic did not undergo any imaging to rule out the retroperitoneum as the source of infection which may be difficult to identify clinically.

The urogenital source accounted for most (40%) of the cases of Fournier’s gangrene in this study while the anorectal and cutaneous/skin sources accounted for 32% and 21% of the infections respectively. This is similar to findings by Clayton and co workers\(^{11}\) who showed that the urogenital (45%) is the commonest source of infection. The anorectal foci accounted for 33% of the cases while the cutaneous source accounted for 21% of the cases in their study.\(^{11}\) In a Spanish study by Marco et al,\(^{66}\) 40% of the cases were of idiopathic origin, they acknowledged that the source of infection might have been overlooked in the process.\(^{66}\) The common urogenital causes include urethral strictures and indwelling catheter.\(^{1,6,43}\) In this series of patients with urogenital source of infection, urethral stricture disease was seen in 40% of urogenital cases while indwelling catheters were seen in 23% of the cases. Majority of cases of Fournier’s gangrene caused by indwelling catheters in this study were due to poor catheter care.
They were two cases of Fournier’s gangrene that developed as a result of complication of adult male circumcision. There is an increase in the number of adult male circumcision in Zimbabwe with a cumulative number of about 180,000 men having been circumcised since 2012 when the voluntary medical male circumcision program was launched at a national level in an effort to reduce HIV transmission. Galukande et al reported two cases of Fournier’s gangrene in Uganda after voluntary adult male circumcision. None of these patients died from the disease but there was significant morbidity with severe loss of penile skin that required split thickness grafting similar to cases recorded in this study. The cases of Fournier’s gangrene resulting as a complication of adult male circumcision in our environment may rise in the future as the VAMC continues to expand to reach its intended target of 1.2 million circumcised male by 2017.79

They are studies to suggest that the anorectal source of infection is associated with higher mortality compared to the urogenital and cutaneous source. The reason suggested in the studies is that the ano-rectum is awash with a greater diversity of enteric pathogenic bacteria. However in this study the urogenital source of infection was significantly associated with a higher mortality (45%) compared to the anorectal source of infection with (25%) of deaths (p=0.01). Renal failure was noted to be present on 57% of the patients with a urogenital source of infection compared to 29% of in anorectal source of infection. Renal failure at presentation was associated with 70% mortality rate. The cutaneous source had no deaths; patients with a cutaneous source of infection are associated with a better chance of survival compared to the urogenital or anorectal source of infection. This is similar to studies done in Nigeria which showed that the least mortality is associated with a cutaneous source of infection. This low mortality has been linked to low virulence bacteria from the skin.
The majority of patients with Fournier’s gangrene have an underlying risk factor which predispose them to the development of the disease.\textsuperscript{1} Diabetes mellitus has been considered the commonest underlying risk as reported in most literature, accounting for about 60% of the cases.\textsuperscript{6,11,50,66,71} However in this study diabetes mellitus accounted for only 10% of the cases while human immunodeficiency virus infection (HIV) was the commonest risk factor seen in 36% of the 51 cases. The prevalence of HIV in Zimbabwe is still high, at 15% compared to Europe at about 0.2% as of 2014 UNAIDS report.\textsuperscript{80} A study by Ngugi et al\textsuperscript{70} from Kenya noted that HIV had overtaken diabetes mellitus as the leading predisposing factor to Fournier’s gangrene in their enviroment.\textsuperscript{70} They found that 16.4% of the patients had HIV disease while 11% of the patients had diabetes mellitus\textsuperscript{70}. This is different from a study by Ayumba et al\textsuperscript{71} on the same population ten years earlier, that had 60% of patients having diabetes mellitus while only 4% the of patients had HIV disease.\textsuperscript{70,71} Aliyu et al\textsuperscript{77} in a study from Nigeria recorded a prevalence of HIV infection of 21% amongst their patients with Fournier’s gangrene. The HIV epidemic potentially opens a population at risk of developing Fournier’s gangrene in sub Saharan Africa.

The association of diabetes mellitus with mortality has remained controversial over time. There are studies that suggests an association between the presence of diabetes mellitus and higher mortality.\textsuperscript{6,15,52,62} However this study did not find any significant difference between survivors and non survivors amongst patients with diabetes mellitus, similar to findings of studies by Yeniyol et al\textsuperscript{58} and Marco et al.\textsuperscript{66}
The presence of HIV infection in this study was not found to be significantly associated with mortality although 33% (6/18) of HIV positive patients died compared to 22% (7/32) of HIV negative patients (p=0.29). This is similar to findings of a report by Elem and colleagues\textsuperscript{12} from Zambia that showed that the presences of HIV was not a factor associated with higher mortality as long as the management is initiated early enough.\textsuperscript{12} Elem and colleagues did not report if there the degree of immunosuppression was associated with mortality. In this study the mean CD4 count of survivors was not significantly different from that of non survivors, $212 \pm 104$ versus $154 \pm 139$ respectively (p=0.40). Thus the degree of immunosuppression in HIV positive patients was not associated with increased mortality.

Renal failure at presentation was significantly associated with a high mortality (70%) in this study (p=0.001). Sorensen et al\textsuperscript{21} showed that four specific comorbidity factors namely, renal failure, congestive cardiac failure, hypertension and coagulopathy were associated with increased mortality.\textsuperscript{21} The increased mortality associated with presence of renal failure has been confirmed by other studies as well.\textsuperscript{11,65}

The average time to presentation of Fournier’s gangrene varies in literature ranging from 2 – 9 days.\textsuperscript{15,76} Some studies have shown that a delay in presentation is significantly associated with higher mortality among patients with Fournier’s gangrene.\textsuperscript{58,67} In this study the median time to presentation of the patients with Fournier’s gangrene was 6 days with a range of 2 – 30 days. Although the average time to presentation amongst non survivors was longer than those that survived, it was not statistically significant. Similarly Corcoran et al\textsuperscript{61} and Marco et al\textsuperscript{66} did not find any significant association between delay in presentation and mortality in their studies.\textsuperscript{61,66}
There is no consensus as to whether the extent of body surface area involvement is associated with a non survival among patients with Fournier’s gangrene. They are studies that have showed that a greater body surface area of involvement is significantly associated with increased mortality. This study also revealed that non survivors had a significantly larger body surface area involvement compared with survivors and that a body surface area of greater than 5% was significantly associated with poor outcome (p=0.004) This is similar to studies by Palmer et al and Spinark et al which showed that patients with a body surface area involvement of greater that 5% have a higher mortality. They noted that survival is not directly proportional to body surface area involvement. The extent of body involvement would indicate severity of disease hence its association with mortality. This issue remains debatable as some authors dispute the association of body surface area involvement with poor outcome.

The patients that had abdominal involvement in this study series had a significantly higher mortality compared to patients that had disease limited to the external genitalia and perineum (p=0.017). Yilmazalar et al found out that dissemination of disease beyond the pelvis was significantly associated with mortality and added a dissemination score to the Fournier’s gangrene severity index (FGSI) to come with a modified FGSI score (UFGSI). Similar reports by other authors have confirmed that abdominal involvement is directly associated with increased mortality.

The diagnosis of Fournier’s gangrene is mainly clinical however laboratory investigations done will reveal the metabolic derangements associated with condition. These metabolic parameters
may predict mortality.\textsuperscript{24,61} Some studies have reported that a low serum albumin, low hematocrit and a raised blood urea nitrogen and creatinine as well as a raised alkaline phosphatase are significantly associated with mortality.\textsuperscript{24,58,59,61} This study revealed that patients that did not survive had a significantly lower hemoglobin level at admission than the patients survived (p=0.0002). Similarly to studies by Laor et al\textsuperscript{24} and Yeniyol et al,\textsuperscript{58} an elevated potassium, blood urea and creatinine are strongly associated with non survival in this study. Clayton et al\textsuperscript{11} noted that only blood urea nitrogen of >50mg/dl was associated with mortality.

Laor et al\textsuperscript{24} in their study noted that biochemical laboratory results taken individually did not appear to have any practical clinical application. They devised a Fournier’s gangrene severity index (FGSI) scoring system along the lines of the Acute Physiology and Chronic evaluation score (APACHE II).\textsuperscript{24} The FGSI score is calculated as a sum of the score of nine parameters that includes patient’s vital signs and metabolic parameters. These parameters are patient’s heart rate, temperature, respiratory rate, sodium level, potassium level, serum bicarbonate, serum creatinine, hematocrit and white cell count with any deviation from the normal having a score of 0 to 4. Laor et al\textsuperscript{24} showed a 75% probability of death amongst patients with an FGSI score of > 9 while those with a score of ≤ 9 had a 78% probability of survival.\textsuperscript{24} The FSGI score has been found to be a useful as a predictor of mortality in some studies.\textsuperscript{58,59} However its accuracy has remained controversial and its usefulness is disputed by other authors.\textsuperscript{60} This study did not measure the FGSI score among patients because some patients had incomplete metabolic values.
The management of Fournier’s gangrene warrants a multimodal approach of aggressive fluid resuscitation, initiation of broad spectrum antibiotics, and surgical debridement.¹ This study showed a significant association between delay in first surgical debridement beyond 24 hours and mortality (p=0.04) similar to studies by Spinark et al⁵⁰ and Tuncel et al⁵⁹. Kabay et al³⁴ and Korkut et al³⁵ noted that the interval between admission and surgical debridement should be as short as possible.³⁴,³⁵ Therefore surgical debridement should be initiated early to reduce mortality. Katib et al⁷⁸ in their Saudi Arabian experience attributed their excellent results of zero mortality to immediate surgical debridement done within 24 hours of admission.

Surgical debridement involves removal of all tissue that is necrotic and of doubtful viability with multiple debridement being the norm.¹,³⁶ The median number of surgical debridement was there in this study with a range of one to nine debridement sessions per patient. This is consistent with a report by Chawla et al³⁶ on repeated debridement which recorded an average debridement rate of about 3.5 sessions per patient.³⁶ Spinark et al⁵⁰ attributed a high mortality due to a higher number of surgical debridement which is influenced by body surface area involvement.⁵⁰ However this study did not find any significant differences on the number of surgical debridement amongst those that died and those that survived. This is consistent with findings by other authors that the number of surgical debridement does not influence outcome.²⁴,³⁶ Palmer and colleagues⁴⁷ further showed that multiple debridement even if performed in the first 24 hours of admission does not increase mortality.⁴⁷

In this series of 51 cases of Fournier’s gangrene no patients had orchidectomy. The rate of orchidectomy has been observed in literature to be about 21 %.⁴⁰ The testis are rarely involved
in the disease process due to their independent blood supply directly from the aorta. Therefore involvement of the testis has been considered as sign of a retroperitoneal source of infection or complicating epididymorchitis.\textsuperscript{40}

Multivariate regression analysis performed on our patients did not reveal any independent factors to be associated with mortality. The sample size in this study may not be powered enough to detect any independent factors associated with mortality. Most studies have reported variables that are significantly associated with mortality on univariate analysis only with one series suggesting that the extent of body surface area and immunosuppression to be the only independent factors associated with mortality.
5.2 Conclusion

1. Fournier’s gangrene remains a highly lethal disease amongst our patients with a mortality rate of 27%. The disease has considerable morbidity with a median hospital stay of 15 days.

2. The patients with Fournier’s gangrene are younger compared to Europe and North America with a median age of 43 years. The median duration of symptoms in our patients is 6 days. The genitourinary tract is the commonest source of infection amongst our patients with urethral stricture disease and poor catheter care accounting for most cases. HIV infection is the commonest underlying risk factor accounting for 36% of cases amongst our patients with Fournier’s gangrene. Other underlying risk factors include diabetes mellitus, renal failure, malignancy, alcoholism and steroid therapy.

3. On univariate analysis the factors that are associated with mortality in this study are an older age, a genitourinary source of infection, presence of at least one comorbid factor, presence of renal failure on admission, a body surface area involvement greater than 5%, abdominal involvement, severe sepsis, delay in surgical debridement, an elevated serum potassium, blood urea nitrogen and creatinine and a low hemoglobin at presentation.

4. HIV infection, diabetes mellitus, and delay in presentation, transfusion, and number of surgical debridement are not associated with mortality.

5. There was no factor that is independently associated with mortality in our patients with Fournier’s gangrene after multiple logistic regression analysis.
5.3 Recommendations

1. The time to first surgical debridement should be kept to a minimum as it significantly affect outcome.

2. The patients with body surface area extent greater than 5% are at higher risk of death therefore aggressive treatment and care should be carried amongst this group of patients.

3. The number of patients with Fournier’s gangrene as a result of poor catheter care is high. There should be resources channeled to teaching patients on importance of self-catheter care.

4. There should be further studies to investigate the role of the FGSI score amongst our patients.

5. Long term studies to assess functional outcomes of reconstructive surgical techniques on patients with Fournier’s gangrene in our environment.

6. They should be education about Fournier’s gangrene as a complication of adult male circumcision with significant morbidity in our environment as the voluntary medical adult male circumcision programme expands in Zimbabwe.
Limitations of the study

This study is not without its own limitations.

1. The number of patients in this study is small to detect some minor differences on other factors associated with mortality.

2. There is potential for selection bias of patients as the investigator in this study was involved in the management of the patients.

3. Some patients’ results on admitting laboratory parameter were not available and incomplete making it difficult to analyze the association of venous bicarbonate as a measure of metabolic acidosis on the mortality due to Fournier’s gangrene.

4. The blood cultures were not being done on all patients upon admission due to limited resources in the hospital. The presence of bacteremia was not investigated as a factor associated with outcome in this study.

5. In the majority of the patients the wound cultures were done days after patients have been admitted and having received antibiotics making most culture results insignificant and potentially misleading and hence a high negative culture rate.

6. They were some patients that received initial treatment outside the three tertiary hospitals before admission which could be a confounding factor on outcome.
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APPENDICES
APPENDIX 1

DATA COLLECTION SHEET
1) **Demographics**

1.1 Age: ______years

1.2 Sex: Male [ ] Female [ ]

1.3 Urban [ ] Rural [ ]

Date of admission: _____/____/____ Date of discharge/death: _____/____/____

1.4 Number of days of hospital stay: _____days

2) **Clinical Presentation**

2.1 Origin of infection

1) Genitourinary [ ] 2) Ano-rectal: [ ] 3) Cutaneous [ ] 4) Idiopathic [ ]

Cause______________________________________________________________

2.2 Duration of symptoms before presentation: _____days

2.3 Total Body surface Area of involvement: _____%

2.4 Dissemination: 1) confined to the external genitalia only [ ]

2) extension to the pelvic region only [ ]

3) extension beyond pelvis(Abdomen, chest, thigh region [ ]

2.5 Presence of a risk factors or comorbidity or preexisting conditions: YES [ ] NO [ ]

Diabetes Mellitus: YES [ ] NO [ ] Renal failure YES [ ] O [ ]

HIV infection: YES [ ] NO [ ] CD4 count _____cell/ul if Yes

Malignancies: YES [ ] NO [ ] Steroid therapy YES [ ] NO [ ]

Alcoholism: YES [ ] NO [ ] Other specify:____________________________

3) **Clinical parameters on admission.**

Temperature: _____C. Blood pressure: Sysbp_____ Diabp_____ Heart rate ___bpm

Respiratory Rate :_____ breaths per min. Random blood sugar:______mmol/l
4) **Laboratory Results at admission**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White cell count (x10^9 cells/L)</td>
<td>______</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>______</td>
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<tr>
<td>Hematocrit.</td>
<td>______</td>
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<tr>
<td>Platelet count</td>
<td>______</td>
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<tr>
<td>Sodium</td>
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<td>______</td>
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<tr>
<td>Creatinine</td>
<td>______</td>
</tr>
<tr>
<td>Bicarbonate (venous)</td>
<td>______</td>
</tr>
<tr>
<td>Albumin</td>
<td>______</td>
</tr>
<tr>
<td>Total protein</td>
<td>______</td>
</tr>
<tr>
<td>Magnesium</td>
<td>______</td>
</tr>
<tr>
<td>Phosphate</td>
<td>______</td>
</tr>
</tbody>
</table>

5) **Treatment**

5.1 **Organisms cultured:** 1) number isolated: ______ 2) Types isolated:_____________________

5.2 **Time to first surgical debridement on admission:** < 24hrs [ ] 24-48hrs [ ] > 48hrs [ ]

5.3 **No of surgical debridement during admission period:** _____

5.4 **IV fluid resuscitation** Yes [ ] No [ ]

5.5 **IV broad spectrum antibiotics** Yes[ ] No [ ] IF yes specify:______________________________

5.6 **Blood Transfusion:** Yes [ ] No [ ] Total packs/units given:________

5.7 **ICU admission** Yes [ ] No [ ]

5.8 **Urinary diversion** Yes [ ] No [ ] if yes, Transurethral [ ] Suprapubic [ ]

5.9 **Colostomy** Yes [ ] No [ ]

5.10 **Orchidectomy** Yes [ ] No [ ]

6) **Reconstruction**

Delayed primary closure [ ] Skin Grafting [ ] Myocutaneous flap procedures [ ]

7) **Outcome/Mortality**

Dead [ ] Alive [ ]
APPENDIX 2

CONSENT FORMS
SUBJECT INFORMED CONSENT - ENGLISH

PROTOCOL TITLE: FOURNIER’S GANGRENE: OUTCOME ANALYSIS AT 3 TERTIARY INSTITUTIONS IN HARARE, ZIMBABWE

PRINCIPAL INVESTIGATOR: Dr S C MEKI (MBChB-UZ) (Cell No. 0772125986)

SUPERVISOR: MR T I MANGWIRO (MMED UROLOGY UZ)

PROJECT DESCRIPTION

You are being asked to volunteer to participate in a research study conducted by an M.Med student in Urology at the University of Zimbabwe. The study involves collecting data on patients who are admitted with a diagnosis of Fournier’s gangrene at 3 major referral hospitals, namely Parirenyatwa hospital, Harare hospital and Chitungwiza hospital.

YOUR RIGHTS

Before you decide whether or not to participate in this study, you need to understand the purpose of the study. This is explained below.

PURPOSE OF RESEARCH STUDY

The purpose of the study is to determine which patients and how many die of this disease and what may be associated with death in this condition. This will help us to improve the management and care of these patients in the future.

PROCEDURES INVOLVED IN THE STUDY

Data on personal information, presentation, duration and extent of your illness upon admission will be recorded. Data of the results of the blood tests including HIV test, treatment done on you during your hospital stay will be collected and entered on a data collection sheet. The standard routine care in the management of this condition will given to you as per protocol plan of the team of doctors treating you. There is no intervention to be done on you for experimental purposes.

DISCOMFORTS AND RISKS

There is no additional risk or discomfort associated with this study other than the natural course of this disease.

POTENTIAL BENEFITS

The potential benefit is that this study will improve the care and management of this condition in future patients who are likely to die due to this disease. We cannot and do not guarantee or promise that you will receive any benefits from this study.
STUDY WITHDRAWAL

You may choose not to enter the study or withdraw from the study at any time without loss of benefits entitled to you. If you decide to withdraw or do not give consent the staff will not treat you any differently.

CONFIDENTIALITY OF RECORDS

No information identifying you will be published without your permission. Every effort will be made to protect your privacy and confidentiality to the greatest extent possible. Any information collected about you during the study or as a result of the study will be kept safely and locked in the department of Surgery for up to 5 years. This study has been approved by the College of Health Sciences of the University of Zimbabwe, and by the Medical Research Council.

PROBLEMS OR QUESTIONS

You can ask questions about this research study or consent now or at any time in the future. Please do not hesitate to ask. Contact details for the investigator are given above and for Medical Research Council below.

AUTHORIZATION

I have read this paper about the study or it was read to me and I have understood the possible risks and benefits of my participation. I know being in this study is voluntary and I choose to be part of the study. I know I can pull out of the study and I will not lose any benefits and medical care entitled to me. I will get a copy this consent form.

Client Signature:______________________________ Date: _______________________

Client Name: ___________________________________
(Printed)

Researcher Signature: _________________________ Date:_______________________

Witness Signature: _____________________________ Date:_______________________
PROTOCOL TITLE: FOURNIER’S GANGRENE: AN OUTCOME ANALYSIS OF MINIMAL BEDSIDE DEBRIDEMENT IN LOW RESORCE SETTING.

PRINCIPAL INVESTIGATOR: DR S C MEKI (MBChB - UZ) (Cell No: 0772125986)

SUPERVISOR: DR T I MANGWIRO (MMED UROLOGY – UZ)

ZVINOENDERANA NECHIRONGWA
Munokumbirawo kuti mupinde muchirongwa chirikuitwa nemudzidzi wepa University yeZimbabwe ari kuita Masters yeUrology, zvinoita kuti awane gwaro iri. Chirongwa ichi chinezvekuita neavo vanechirwere chinonzi Fournier’s Gangrene chinobata nhengo dzekunze dzekuberekesa..

KODZERO DZENYU
Musati mapa sarudzo yekuti mopinda muchirongwa here kana kuti kwete, tinoda kukutsanangurirai chinangwa chechirongwa kuti munzwisise nezvavo.

CHINANGWA CHECHIRONGWA
Donzo rechirongwa nderekuona kuti vane chirwere ichi, vanofa vangani uye vanofa nekuda kwechii uye zvaita sei. Izvi zvichabatsira kuwedzera ruzivo rwekurapa chirwere ichi paneramangwana.

ZVICHAITWA MUCHIRONGWA
Imi kana munechirewere ichi kubva pamunopinda muchipatara pachanyorwa pasi maerererano nekurwara kwenyu zvichisanganasira nzvichabuda muropa nemamwe matests amuchaitwa muri muchipatara kusvika maendeswa kumba kana kupora, Izvi zvichatorwa mumagwaro enyu ekurapwa. Marapiro amuchaitwa ndeagara achiitwa nana chiremba venyu vachakubatsirai mukurapwa kwechirwere ichi. Umbowo uhuwuri huchashandisiwa mutsvagiridzo yechirongwa ichi.

NJODZI YAMUNGASANGANA NAYO
Hatitarisire kuti pangave nenjodzi yamungasa ngane nayo kusiya kwemarwadzo anowanikwa mukurapwa kwechirwere ichi.

ZVAMUNGAWANA KUBVA MUCHIRONGWA
Chinagwana chedu ndechekubatsira kura fara kwechirwere ichi ramangwana. Hapana chamunogona kuwana chingakubatsirai kubva muchirongwa ichi kusiya kwezviri pamusoro
SARUDZO YOKUBUDA MUCHIRONGWA


KUCHENGETEDZEKA KWEKODZERO DZENYU

Hapana pachanyorwa nezvenhoroondo yenyu musina kukumbirwa mvumo. Zvose zvamuchataura nezvichaitika zvicha chengetedzwa pakahwanda. Ichirongwa chakapiwa mvumo yekuenderera mberi neMedical research council neUniversity ye Zimbabwe

MIBVUNZO KANA ZVICHEMO


KUBVUMA KUPINDA MUCHIRONGWA;


Runyoro rwenyu _________________________               Zuva ranhasi ________________
Zita renyu (rakanyorwa) ________________________________
Zita rearikuitisa chirongwa ___________________________    Zuva ranhasi____________________
Runyoro rwemufakazi________________________         Zuva ranhasi______________________
                          initials_________
APPENDIX 3

BODY SURFACE AREA NOMOGRAM
Body surface involvement using a modified body surface area Nomogram

Percentage allocation of perineal surface area

Adapted from Palmer LS et al (1995)
APPENDIX 4

LABORATORY REFERENCE RANGES
## Laboratory reference ranges

### Blood count

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White cell count</td>
<td>$4 - 10 \times 10^3/uL$</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>$12.0 - 16 \text{ g/dl}$</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>$36 - 48 %$</td>
</tr>
<tr>
<td>Platelet count</td>
<td>$150 - 400 \times 10^3/uL$</td>
</tr>
</tbody>
</table>

### Serum Electrolytes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>$133 - 146 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Potassium</td>
<td>$3.5 - 5.4 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Venous bicarbonate</td>
<td>$18 - 24 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Urea</td>
<td>$2.0 - 6.7 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Creatinine</td>
<td>$48 - 131 \text{ umol/L}$</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>$3.9 - 5.9 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Calcium level (corrected)</td>
<td>$2.05 - 2.55 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Magnesium levels</td>
<td>$0.6 - 1.1 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Phosphate levels</td>
<td>$0.6 - 1.7 \text{ mmol/L}$</td>
</tr>
</tbody>
</table>

### Liver Function Test

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bilirubin</td>
<td>$3 - 29 \text{ mmol/L}$</td>
</tr>
<tr>
<td>Alkaline Phosphate</td>
<td>$34 - 140 \text{ iU/L}$</td>
</tr>
<tr>
<td>Albumin levels</td>
<td>$28 - 53 \text{ g/L}$</td>
</tr>
<tr>
<td>Total protein</td>
<td>$50 - 86 \text{ g/L}$</td>
</tr>
</tbody>
</table>
APPENDIX 5

SEVERE SEPSIS CRITERIA
Severe sepsis criteria according to Surviving sepsis global campaign 2012

Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)

- Sepsis-induced hypotension
- Lactate above upper limits laboratory normal
- Urine output \( \leq 0.5 \text{ mL kg}^{-1} \text{ h}^{-1} \) for more than 2 h despite adequate fluid resuscitation
- Acute lung injury with \( \text{PaO}_2/\text{FiO}_2 \leq 250 \) in the absence of pneumonia as infection source
- Acute lung injury with \( \text{PaO}_2/\text{FiO}_2 \leq 200 \) in the presence of pneumonia as infection source
- Creatinine \( \geq 2.0 \text{ mg/dL} (176.8 \text{ lmol/L}) \)
- Bilirubin \( \geq 2 \text{ mg/dL} (34.2 \text{ lmol/L}) \)
- Platelet count \( \leq 100,000 \text{ IL} \)
- Coagulopathy (international normalized ratio \( \geq 1.5 \))

Adapted from Dellinger R P et al (2013)