World J Surg (2018) 42:2314–2320
https://doi.org/10.1007/s00268-018-4515-z

ORIGINAL SCIENTIFIC REPORT

Necrotizing Soft Tissue Infections at a Tertiary Referral Hospital in Rwanda: Epidemiology and Risk Factors for Mortality

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Published online: 7 February 2018

Abstract

Background Necrotizing soft tissue infections (NSTI) are emergency surgical conditions with severe physiologic and metabolic derangement. These infections are associated with increased rates of mortality and morbidity worldwide, particularly in developing countries if not diagnosed and treated early.

Methods This prospective, observational cohort study includes all patients aged 12 and above who presented at Department of Surgery, University Teaching Hospital of Kigali from April 2016 to January 2017 with NSTI. We describe epidemiology, operative management, and outcomes of care. We determined risk factors for mortality using multivariate logistic regression.

Results We identified 175 patients with confirmed diagnosis of NSTI. The majority of patients (53%) were male, and the mean age was 44 years. The median duration of symptoms was 8 days [interquartile range (IQR) 5–14]. The median length of hospital stay was 23 days (IQR 8–41). The overall mortality was 26%. Multivariate regression analysis revealed four independent predictors of mortality: presence of shock at admission [odds ratio (OR) 14.15, 95% confidence interval (CI) 0.96–208.01, $p = 0.050$], renal failure (OR 8.92, 95% CI 1.55–51.29, $p = 0.014$), infection located on the trunk (OR 5.60, 95% CI 0.99–31.62, $p = 0.050$), and presence of skin gangrene (OR 4.04, 95% CI 1.18–13.76, $p = 0.026$).

Conclusion In Rwanda, NSTI mortality is high and associated with advanced disease. It is imperative that efforts are focused on early consultation, diagnosis, and surgical management to prevent adverse outcomes.

Introduction

Necrotizing soft tissue infections (NSTIs) are severe infections of any layer of soft tissue compartment including superficial and deep soft tissues [1, 2]. NSTIs were first recognized and described by Hippocrates in 500 B.C. as a complication of erysipelas [3]. In 1871, Jones reported 2642 cases of what he termed "hospital gangrene" with a mortality rate of 46% [4]. NSTIs are commonly polymicrobial infections characterized by a rapid spread, clinical deterioration, and increased mortality and morbidity [5–7]. For many patients, there is a history of trauma or surgery with wound contamination. NSTIs can occur in any area of the body with extremities being the most commonly involved part [2].

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The incidence of this condition varies from site to site with national and regional variation in both etiology and microbiology [8].The worldwide incidence of NSTIs is estimated at 0.4 cases per 100,000. In USA, there were more than 13,000 cases in 2007, with an annual incidence of 4.5 per 100,000 population [9]. In the South Pacific, the incidence is estimated at 6.1 per 100,000 population [7]. In Africa and Asia, no true incidence is known, but the estimate is more than 1 case per 100,000 population per year [5, 9–11]. Mortality in patients with NSTIs is high, ranging from 14 to 42% [6, 10, 12–14].

Early diagnosis and treatment are essential for survival. Treatment consists of broad-spectrum antibiotics, wide surgical debridement, and supportive care [2, 8, 15]. Antibiotic treatment is initially broad spectrum and then tailored to antimicrobial susceptibilities of isolated organisms [2, 16, 17]. Patients may require multiple debridements or amputations to ensure adequate source control [6, 12].

Rwanda is a densely populated, low-income country in East Africa [18]. University Teaching Hospital of Kigali (Centre Hopitalier Universitaire de Kigali, CHUK) is a referral hospital in Kigali, Rwanda, that serves as referral hospital for 44 district hospitals and over 6 million people [19]. The hospital has a capacity of 513 beds with a 7-bed intensive care unit (ICU). The department of surgery accounts for 146 hospital beds and 6 main operating rooms. Emergency surgical conditions account for 70% of general surgery operations with soft tissue infections accounting for a significant proportion of these cases [20]. No data are available in Rwanda on the clinical characteristics and outcomes of care for patients with NSTI. The aim of this study was to describe the epidemiology, management, and outcomes of patients with NSTI at tertiary referral hospital in Rwanda and determine admission factors associated with mortality.

Methods

This was a prospective study of all patients aged 12 and above with a diagnosis of NSTI managed by the Department of Surgery at CHUK over a 10-month period (April 2016–January 2017). NSTI was defined as any patient with severe skin and soft tissue infection confirmed by the treating surgeon intra-operatively.

Data were collected on demographics, comorbidities, clinical presentation, precipitating event, operative management, complications, and duration of hospital stay. Cardiac disease included hypertension and congestive heart disease. Renal disease included both chronic and acute renal failure. This included patients with a prior history of renal disease or those who had creatinine of >88.4 μmol/L on admission. Pulmonary disease included patients with asthma, chronic obstructive pulmonary disease, and history of tuberculosis. We defined shock as any clinical status of persistent hypotension (systolic blood pressure less than 90 mmHg) despite adequate intravenous fluid resuscitation. Tachycardia was defined as a heart rate greater than 110 beats per minute. Leukocytosis was defined as a white blood cell counts greater than 10,000 μmol/L. Anemia was defined as hemoglobin less than 10 g/dL. Complications included pneumonia, unplanned intubation, prolonged ventilator duration, cardiac arrhythmia, cardiopulmonary arrest, acute kidney injury, surgical site infection, septic shock, and death. All outcomes were measured in-hospital. Patients were followed until death or hospital discharge.

NSTI was classified as superficial necrotizing infection (any soft tissue infection not reaching the fascia), necrotizing fasciitis (deep infection involving the fascia), pyomyositis, Fournier's gangrene (necrotizing infection of the perineum and genitalia), and wet gangrene of extremities based on intra-operative findings [17].

Data were collected using a pretested questionnaire during recruitment and follow-up of the patients. A database was created using Excel, and STATA 13.0 software was used for statistical analysis. We used frequencies and percentages for categorical data, and median and interquartile range (IQR) for continuous data. The association between variables was assessed using Chi-square test. The relationship between risk factors and mortality was studied using a multivariate logistic regression analysis. Variables with a p value <0.1 on bivariate analysis were incorporated in a multivariate logistic model analysis. A p value <0.05 on multivariate analysis was considered statistically significant.

The institutional review boards of the University of Rwanda College of Medicine and Health Sciences and CHUK Ethics Committee approved this study.

Results

Over a 10-month period (April 2016–January 2017), 198 patients at CHUK had suspected NSTI, with 175 diagnoses confirmed by intra-operative assessment (Fig. 1). Ninety-two (52.6%) patients were male and 83 (47.4%) patients were female (Table 1). The mean age was 43.8 years (range 12 and 92 years). The majority of patients were from Kigali City (43%) and Eastern Province (32%). Eighty-six (49%) patients presented with comorbidities with the most common being cardiac disease ($n = 29$, 17%), diabetes mellitus ($n = 28$, 16%), smoking ($n = 23$, 13%), and human immunodeficiency virus (HIV) infection ($n = 20$, 11%).

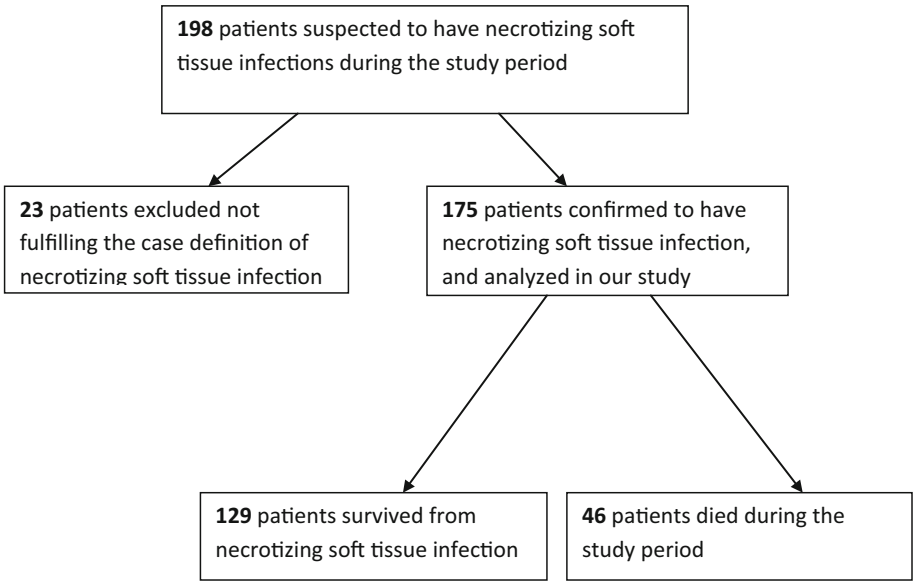

Fig. 1 Patients' flowchart during the study period

Table 1 Baseline characteristics of patients with necrotizing soft tissue infections presenting at University Teaching Hospital of Kigali ($N = 175$)

	N (%)	Survivors *N* (%) $N = 129$	Non-survivors *N* (%) $N = 46$	*p* value, survivors versus non-survivors
Sex				
Male	92(53)	71(77)	21(23)	0.305
Female	83(47)	58(70)	25(30)	
Age				
12–35 years	73(42)	53(73)	20(27)	0.975
36–50 years	41(23)	31(76)	10(24)	
>50 years	61(35)	45(74)	16(26)	
Referral province				
Kigali city	75(43)	54(72)	21(28)	0.973
East	56(32)	41(73)	15(27)	
South	17(10)	13(76)	4(24)	
North	15(8)	11(73)	4(27)	
West	12(7)	10(83)	2(17)	
Comorbidities	86(49)	65(76)	21(24)	0.610
Cardiac disease	29(17)	22(76)	7(24)	1.000
Diabetes mellitus	28(16)	22(79)	6(21)	0.643
Smoking	23(13)	17(74)	6(26)	1.000
Human immunodeficiency virus	20(11)	17(75)	3(15)	0.287
Renal disease	8(5)	3(38)	5(62)	0.030
Pulmonary disease	6(3)	4(67)	2(33)	0.656
Paraplegia	5(3)	4(80)	1(20)	1.000
Liver disease	3(2)	1(33)	2(67)	0.169
Other	15(9)	8(67)	4(33)	0.313

Eighty-nine patients (51%) had a precipitating event with the most common being postoperative infection in 43 (25%) patients and trauma in 37 (21%) patients. Eighty-six patients (49%) had no precipitating event (Table 2). The most common presenting symptoms included pus discharge ($n = 153$, 87%), edema ($n = 149$, 85%), pain ($n = 119$,

Table 2 Clinical presentation and physiologic parameters of patients with necrotizing soft tissue infections at a tertiary referral hospital in Rwanda ($n = 175$)

	N (%)	Survivors *N* (%) *N* = 129	Non-survivors *N* (%) *N* = 46	*p* value, survivors versus non-survivors
Precipitating event				
Postoperative infection	43(25)	23(53)	20(47)	0.001
Trauma	37(21)	31(81)	6(19)	0.175
Burns	5(3)	5(100)	0(0)	0.213
Idiopathic	86(49)	66(77)	20(23)	0.235
Signs and symptoms at admission				
Pus discharge	153(87)	110(72)	43(28)	0.198
Edema beyond erythema	149(85)	111(74)	38(26)	0.631
Pain disproportionate to findings on examination	119(68)	90(76)	29(24)	0.462
Skin necrosis	118(67)	81(69)	37(31)	0.029
Presence of skin blisters	93(53)	61(66)	32(34)	0.010
History of fever	81(46)	56(69)	25(31)	0.230
Skin anesthesia	62(35)	46(74)	16(26)	1.000
Crepitations	16(9)	9(56)	7(44)	0.133
Admission vital signs				
Temperature ≥38 °C	69 (39)	49 (71)	20 (29)	0.599
Tachycardia (pulse >110 beats per minute)	93 (53)	63 (68)	30 (32)	0.061
Shock on admission (SBP <90 mmHg)	20 (11)	6 (30)	14 (70)	<0.001
Laboratory investigations				
Leukocytosis (white blood cells >10,000 μmol/L)	102(58)	71(70)	31(30)	0.166
Anemia (hemoglobin <10 g/dL)	68(39)	49(72)	19(28)	0.727
Increased creatinine (>88.4 μmol/L)	46(26)	23(50)	23(50)	<0.001
Site of infection[a]				
Lower extremity	94(54)	77(82)	17(18)	0.010
Trunk	44(25)	22(50)	22(50)	<0.001
Perineum	35(20)	23(66)	12(34)	0.283
Upper extremity	13(7)	13(100)	0(0)	0.022
Other	1(1)	1(100)	0(0)	1.000
Involved tissue plane				
Subcutaneous tissues	139(79)	105(76)	34(24)	0.293
Fascia	154(88)	109(71)	45(29)	0.016
Muscle	68(39)	55(81)	13(19)	0.113
Diagnostic type				
Necrotizing fasciitis	74(42)	48(65)	26(35)	0.206
Wet gangrene of extremities	50(29)	41(82)	9(18)	
Fournier's gangrene	25(14)	15(60)	10(40)	
Superficial necrotizing infection	16(9)	15(94)	1(6)	
Pyomyositis	10(6)	10(100)	0(0)	

[a]Possible to have more than one involved body site

68%), and skin necrosis ($n = 118$, 67%). The median length of symptoms was 8 days (IQR 5–14).

The most common types of NSTI were necrotizing fasciitis ($n = 74$, 42%) followed by gangrene of extremities ($n = 50$, 29%), Fournier's gangrene ($n = 25$, 14%), superficial necrotizing infections ($n = 16$, 9%), and pyomyositis ($n = 10$, 6%). The most commonly involved tissue planes were the deep fascia ($n = 154$, 88%) and subcutaneous tissues ($n = 139$, 79%). The most commonly involved body parts were lower extremities ($n = 94$, 54%) and trunk ($n = 44$, 25%).

The time patients spent in hospital from the presumptive diagnosis to operation varied between 30 min and 240 h with a median of 18 h. We defined delayed operative time as time from admission to surgery more than 12 h, and there was no difference in patients taken to surgery within 12 h or after ($p = 0.11$). All patients ($N = 175$) underwent operation, with the most common initial operations debridement ($n = 90$, 51%) and amputation or disarticulation ($n = 52$, 30%). A second operation was performed in 24 patients with the most common second operations being skin graft ($n = 12$, 50%) and amputation or disarticulation ($n = 5$, 21%) (Table 3). In total, 57 (33%) patients underwent amputation or disarticulation.

Postoperative complications were noted in 89 patients (51%). The most common complications were septic shock ($n = 50$, 29%) and pneumonia ($n = 29$, 17%). Eight patients (5%) were admitted in ICU with a median ICU duration of 3 days (IQR 1.5–4). The overall mortality was 46 (26%). The median length of hospital stay for survivors was 29 days (IQR 15–48).

Factors associated with mortality on multivariate analysis included: presence of shock at admission [odds ratio (OR) 14.15, 95% confidence interval (CI) 0.96–208.01, $p = 0.050$], renal failure (OR 8.92, 95% CI 1.55–51.29, $p = 0.014$), infection located to the trunk (OR 5.60, 95% CI 0.99–31.62, $p = 0.050$), and presence of skin gangrene (OR 4.04, 95% CI 1.18–13.76, $p = 0.026$) (Table 4).

Table 3 Operative management and outcomes for patients with necrotizing soft tissue infections ($n = 175$)

	N	%
Operative management		
First operation		
Debridement	90	51
Amputation/disarticulation	52	30
Incision and drainage	10	6
Laparotomy and debridement	23	13
Second operation		
Debridement	3	13
Amputation/disarticulation	5	21
Skin graft	12	50
Diverting stoma	4	17
Admitted to intensive care unit	8	5
Complications, in-hospital	89	51
Septic shock	50	29
Cardiopulmonary arrest	46	26
Pneumonia	29	17
Acute kidney injury	16	9
Ventilator use	14	8
Cardiac arrhythmia	13	7
Surgical site infection	13	7
Unplanned intubation	4	2
Other	25	14
Mortality, in-hospital	46	26

Discussion

Overall, the epidemiology and clinical presentation of NSTIs in this study were similar to other studies [6, 12]. This study found a lower mean age, which may be associated with an overall lower mean population age in Rwanda compared with high-income countries [21]. Only 6.7% of Rwandan population is 55 years or older [18, 21]. Most patients were referred from Kigali or the Eastern Province, which is similar to the overall surgical referral pattern for this hospital [20]. The incidence of comorbidities was lower in this study compared with other studies, which may be related to the lower patient age [12]. The most common presentation was pus discharge, edema beyond erythema, pain, focal skin gangrene, and skin blistering, consistent with clinical presentation described elsewhere [1, 13]. Postoperative infection and trauma as precipitating event were similar to other studies [5, 13]. Lower extremities were the most affected body part, with a high incidence of truncal involvement which may be associated with the high incidence of Fournier's in this study [5, 13, 22].

The mean symptom duration prior to presentation was 8 days. There are many potential reasons for this long symptom duration, which were not assessed in this study. There may be a delay in patient recognition, delay in health care presentation, or transfer delays. In addition, patients with shorter duration of symptoms may have had more aggressive disease and potentially died prior to transfer to the referral hospital. Furthermore, the fact that patients were delayed (average symptom duration of 8 days) could be linked to nonsignificant difference in mortality in regards to when patient was taken to theater. However, some authors reported significant difference between mortality and time to intervention from symptom onset or hospital admission [23]. More studies related to health-seeking behavior and pre-hospital challenges in systems of care would help to better understand and determine modifiable factors to improve the mortality and morbidity.

Most patients underwent a single debridement, which is lower than other studies [6, 12]. There are two potential reasons for the lower debridement rate. One possibility is that the decreased number of second relook is due to surgical delivery system issues such as lack of operating room time. Another possibility is that patients had their infection controlled with the initial operation and did not need re-debridement. The amputation rate was 33%, which is

Table 4 Multivariate analysis

	Adjusted odds ratio	95% confidence interval	*p* value
Tachycardia (pulse >110 beats per minute)	1.24	0.47–3.26	0.653
Fascia involvement	2.75	0.22–34.21	0.431
Postoperative infection	1.88	0.45–7.95	0.390
Presence of skin blisters	1.72	0.68–4.30	0.246
Lower extremity	0.41	0.10–1.65	0.213
Skin gangrene	4.04	1.18–13.76	0.026
Shock at admission	14.15	0.96–208.01	0.050
Infection located to the trunk	5.60	0.99–31.62	0.050
Renal disease	8.92	1.55–51.29	0.014

higher than other studies [6, 12]. Other studies have noted an association limb amputation and delayed presentation [7, 15, 24]. Amputation may be viewed as an efficient form of source control in this setting. In addition, flap reconstruction is more challenging in this environment limiting the limb salvage rate.

The overall mortality in our study was 26% similar to other studies [2, 6, 9, 22, 25, 26]. However, some centers have lower mortality rates [11, 13]. As suggested in other studies, differences in mortality may be due to differences in practice patterns, microbiology, or epidemiology [6, 12]. Delayed operative management has been associated with increased mortality rate [7, 10, 13]. In our study, similar to Kao et al. [6], delayed operative management was not associated with increased mortality. In contrast to other studies, factors like advanced age, immunosuppression by human immunodeficiency virus infection, and elevated white blood count were not significantly associated with mortality in our study [13, 22, 26, 27]. This is likely due to different population demographics with a lower mean age and lower incidence of comorbidities.

Multiple regression analysis revealed four independent predictors of mortality: shock on admission, renal failure, truncal involvement, and skin gangrene. Many of these predicting factors correlate with other published studies [8, 26, 28]. Shock and renal failure indicate patients with critical illness and organ failure. Due to resource limitations, other measures of organ failure are more difficult to assess. This hospital does not routinely have access to laboratory studies such as bilirubin, coagulation factors, lactate, or arterial blood gas. Therefore, the incidence of organ failure is likely underestimated in this patient population.

Patients with NSTI often have severe physiologic and metabolic derangements that predispose the patient to develop organ failure, with many patients requiring ICU admission [1]. In our study, only 5% of patients were admitted in ICU for aggressive resuscitation and supportive care. This low rate of ICU admission may be due to several factors. One reason may be due to the shortage of ICU space (only 7 ICU beds shared by the entire hospital), which could be improved by increasing the infrastructure and equipment to accommodate patients at an early stage of postoperative management. Another possibility for the low ICU admission rate may be that patients with septic shock on admission died prior to ICU admission.

There are limitations to be considered while interpreting the results. These data are from a single hospital in Rwanda which functions as a tertiary referral hospital for 44 district hospitals. The hospital catchment area represents 60% of the Rwandan population. However, there are likely patients that die before reaching this tertiary level hospital. There were no data collected on management prior to hospital admission, and we did not collect data on illness severity scores used in other studies. The degree of source control at time of operation was not assessed limiting some analysis. All outcomes were in-hospital, and we did not collect data on long-term functional outcomes. The long-term complications would help to characterize the disease sequelae and identify the factors related to favorable and unfavorable NSTI long-term functional outcome.

Conclusion

Our study showed that patients with NSTI in Rwanda have a high morbidity and mortality, and most admission predictors of mortality can be prevented by the adequate understanding and knowledge of this condition for a proper diagnosis, management, and timely transfer.

Acknowledgements We acknowledge the contributions of residents in surgery rotating at CHUK during the study period, laboratory technicians, emergency, theater, and surgical ward nurses for data collection.

Author contributions CM led study design, protocol development, literature search, led data collection and analysis with support from JR, abstract and manuscript development, interpretation and dissemination of results. JR, CF, and FN supported study design, protocol development, literature search, results interpretation, and dissemination of results. All authors critically reviewed the manuscript and approved the final version for publication.

Compliance with ethical standards

Conflict of interest Authors have no conflicts of interest to report.

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