Factors Associated with Disability and Mortality among Necrotizing Fasciitis Patients in Thailand, 2018

Hirunwut Praekunatham[1*], Panupong Tantirat[2]

1 Division of Occupational and Environmental Diseases, Department of Disease Control, Ministry of Public Health, Thailand

2 Division of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand

*Corresponding author, email address: phirunwut@gmail.com

Abstract

Necrotizing fasciitis (NF) is a serious skin and soft tissue infection that can lead to disabilities and mortalities. A study was carried out to describe demographic characteristics of NF patients, and determine factors associated with disability and mortality. Information on all patients who were diagnosed as NF from 1 Jan to 31 Dec 2018 were extracted from the databases of Health Data Center in Thailand. Univariate and multivariate analyses using logistic regression were performed to determine the associated factors. In 2018, of total 19,071 NF cases, 6.3% died. Median age was 59.7 years old (Q1-Q3 = 49.1-69.5 years). Most of the cases developed NF at ankle and foot (43.0%), followed by lower leg (28.2%). The amputation rate among the cases was 8.2%. Multivariable analysis showed the significant risk factor for amputation as having diabetes mellitus (adjusted OR 6.81, 95% CI 5.97-7.77). Risk factors for mortality included being elderly (OR 1.81, 95% CI 1.56-2.11), and having hypertension (OR 1.17, 95% CI 1.00-1.36), cirrhosis (OR 4.26, 95% CI 3.42-5.28) or cancer (OR 1.88, 95% CI 1.33-2.59). Morbidity and mortality among NF patients were significant in Thailand. Health workers should be trained for early diagnosis and intensive treatment for NF, especially among elderly and patients with chronic diseases in order to prevent the subsequent complications.

Keywords: necrotizing fasciitis, NF, disability, mortality, risk factor

Introduction

Necrotizing fasciitis (NF) is one of the serious skin and soft tissue infections as it can cause the death of tissues, subsequently leading to disability and mortality.[1-3] Most patients who develop NF require prompt treatment with proper antibiotics and surgical procedures in order to save lives.[2,3] In some developed countries such as Canada, Norway and the United States, the incidence of NF ranged from 0.1 to 3 per 100,000 population.[4-6] Moreover, recent studies suggested that NF usually occurred among elderly and people with chronic diseases like diabetes and hypertension, as compared to the normal population.[3,7] Complications such as limb loss, sepsis or even death can also develop. According to Khammuan et al, amputation rate among NF patients was found to be 8.4% while case fatality rate was reported to be 5.4%.[8]

In Thailand, knowledge on the nationwide situation of NF as well as factors associated with disability and mortality among NF patients remained limited. This study, thus, was carried out in order to describe demographic characteristics, and determine factors influencing amputation and death among NF patients.

Methods

Study Design

A cross-sectional analytic study using secondary data extracted from Health Data Center (HDC) of Thailand was conducted. The HDC is the database system with big data technology, developed by the Information and Communication Technology Center, Office of the Permanent Secretary, Ministry of Public Health. Basically, the HDC database consisted of 43 files; however, only 8 files named "person", "address", "diagnosis_opd", "diagnosis_ipd", "procedure_opd",

"procedure_ipd", "chronic" and "admission" , were extracted for this study.

Study population were all patients diagnosed as NF (ICD-10 code: M72.6) from 1 Jan to 31 Dec 2018. Variables selected were gender, age, occupation, nationality, diagnosis date of NF, underlying diseases (diabetes, hypertension, cirrhosis, alcoholism, cancer or HIV infection) and treatment results (cured, amputated or dead). Based on International Standard Classification of Occupations (ISCO-08), patients' occupations were classified into 10 major groups: (i) managers, (ii) professionals, (iii) technicians and associate professionals, (iv) clerical support workers, (v) services and sales workers, (vi) skilled agricultural, forestry and fishery workers, (vii) craft and related trades workers, (viii) plant and machine operators and assemblers, (ix) elementary occupations, and (x) armed forces occupations. Patients who reportedly did not have a job were categorized as "unemployed". The infection site of NF in a patient was identified by the fifth character of the ICD10 code (e.g., M72.67 for NF at ankle and foot).

Data Analysis

The data were analyzed using R software version 3.5.2 and RStudio® version 1.2.1335. In descriptive statistics, key categorical variables such as gender, nationality, occupation, and underlying diseases were described in percentage, whereas age variable was calculated as median with interquartile range (Q1-Q3). In the analytic study, univariate logistic regression was initially performed to determine prevalent odds ratio (OR) with 95% confidence interval (CI). Significant variables from the univariate analysis were then selected for multivariate logistic regression in order to calculate adjusted odds ratio (adjusted OR) with 95% CI.

Table 1. Characteristics of necrotizing fasciitis patients reported in the database of Health Data Center, Thailand, 2018

Characteristics	Number of cases (%)
Gender (n=18,725)	
Male	11,084 (59.2)
Female	7,641 (40.8)
Nationality (n=18,702)	
Thai	18,404 (98.4)
Others	298 (1.6)
Occupation (n=18,140)	
Elementary occupations	5,935 (32.7)
Skilled Agricultural, Forestry and Fishery Workers	5,816 (32.1)
Unemployed	1,566 (8.6)
Services and Sales Workers	1,215 (6.7)
Managers	250 (1.4)
Professionals	209 (1.1)
Technicians and Associate Professionals	162 (0.9)
Others	2,987 (16.5)
Underlying disease (n=19,071)	
No	7,258 (38.1)
Yes	11,813 (61.9)

Table 1. Characteristics of necrotizing fasciitis patients reported in the database of Health Data Center, Thailand, 2018 (con't)

Characteristics	Number of cases (%)
Patients with underlying diseases (n=11,813)	
Hypertension	8,525 (72.2)
Diabetes mellitus	8,073 (68.3)
Cirrhosis	963 (8.2)
Alcoholism	663 (5.6)
Cancer	445 (3.8)
HIV infection	111 (0.9)
Affected part (n=19,071)	
Ankle and foot	8,191 (43.0)
Lower leg	5,372 (28.2)
Hands	1,395 (7.3)
Forearm	669 (3.5)
Upper leg	449 (2.3)
Arm	249 (1.3)
Shoulder	25 (0.1)
Others	474 (2.5)
Unspecified	1,949 (10.2)
Multiple sites	298 (1.6)
Amputation (n=19,071)	
No	17,505 (91.8)
Yes	1,566 (8.2)

Results

Descriptive Study

In 2018, a total of 19,071 NF patients were recorded in the HDC database, with incidence rate as 31.1 per 100,000 population. Male to female ratio was 1.5:1. Median age was 59.7 years old (Q1-Q3 49.1-69.5 years). The majority of the NF cases (98.4%) were Thai. According to ISCO, most of the patients (32.7%) were classified with elementary occupations, followed by skilled agricultural, forestry and fishery workers (32.1%) and unemployed (8.6%). (Table 1)

In addition, 8,191 (43.0%) NF patients developed infection at ankle and foot, followed by lower leg (28.2%), hands (7.3%) and forearm (3.5%). We found that 1,566 patients had severe infection, and required amputation, with the amputation rate as 8.2%. Additionally, 1,209 patients died after developing NF, and case fatality rate was 6.3%. In 2018, out of 19,071 patients, 11,813 (61.9%) had underlying diseases. Hypertension (72.2%) was the most common disease, followed by diabetes mellitus (68.3%), cirrhosis (8.2%), alcoholism (5.6%), cancer (3.8%) and HIV infection (0.9%). (Table 1)

Analytic Study

Regarding to the univariate logistic regression, factors that were significantly associated with amputation were being female (OR 1.29, 95% CI 1.17-1.44); under 15 years of age (OR 0.11, 95% CI 0.04-0.27); having diabetes mellitus (OR 6.81 95% CI 5.97-

7.77), hypertension (OR 2.06, 95% CI 1.86-2.29), cirrhosis (OR 0.52, 95% CI 0.38-0.70), alcoholism (OR 0.47, 95% CI 0.31-0.67), or cancer (OR 0.60, 95% CI 0.38-0.90); and experiencing single infection site (compared with multiple infection site) (OR 1.83, 95% CI 1.11-3.29). (Table 2)

Table 2. Univariate analysis on amputation and mortality among necrotizing fasciitis patients reported in the database of Health Data Center, Thailand, 2018

Characteristics		Odds ratio for amputation (95% CI)	Odds ratio for mortality (95% CI)
Gender	Female	1.29 (1.17-1.44)*	0.97 (0.86 – 1.09)
	Male	Ref.	Ref.
Age	< 15 years old	0.11 (0.04-0.27)*	0.10 (0.02-0.31)*
	> 60 years old	1.02 (0.92-1.13)	1.66 (1.47-1.87)*
	15-60 years old	Ref.	Ref.
Occupation	Elementary	1.02 (0.84-1.25)	0.76 (0.62-0.93)*
	Skilled Agriculture	0.91 (0.71-1.17)	0.67 (0.52-0.86)*
	Others	0.97 (0.81-1.21)	0.40 (0.33-0.50)*
	Unemployed	Ref.	Ref.
Diabetes mellitus	Yes	6.81 (5.97-7.77)*	0.88 (0.78-0.99)*
	No	Ref.	Ref.
Hypertension	Yes	2.06 (1.86-2.29)*	1.24 (1.11-1.40)*
	No	Ref.	Ref.
Cirrhosis	Yes	0.52 (0.38-0.70)*	3.76 (3.15-4.46)*
	No	Ref.	Ref.
HIV infection	Yes	0.99 (0.46-1.85)	0.99 (0.42-1.99)
	No	Ref.	Ref.
Alcoholism	Yes	0.47 (0.31-0.67)*	1.44 (1.08-1.87)*
	No	Ref.	Ref.
Cancer	Yes	0.60 (0.38-0.90)*	2.52 (1.90-3.28)*
	No	Ref.	Ref.
Number of infection site	Single	1.83 (1.11-3.29)*	0.70 (0.48-1.08)
	Multiple	Ref.	Ref.

Note: ** Statistical significance at α< 0.05*

        Ref. stands for reference

However, in terms of mortality, being under 15 (OR 0.10, 95% CI 0.02-0.31) and over 60 years old (OR 1.66 95% CI 1.47-1.87), and having diabetes mellitus (OR 0.88, 95% CI 0.78-0.99), hypertension (OR 1.24, 95% CI 1.11-1.40), cirrhosis (OR 3.76, 95% CI 3.15-4.46), alcoholism (OR 1.44, 95% CI 1.08-1.87) or cancer (OR 2.52, 95% CI 1.90-3.28) were significant. Regarding to occupations, the NF patients with elementary occupations (OR 0.76, 95% CI 0.62-0.93), skilled agricultural, forestry and fishery works (OR 0.67, 95% CI 0.52-0.86), and others (OR 0.40, 95% CI 0.33-0.50) had lower risk of mortality when compared with unemployed group. (Table 2)

Statistically significant variables (*P*-value< 0.05) in the univariate analysis were included in the multivariate logistic regression model. The findings showed that patients with diabetes had greater risk of amputation (adjusted OR 6.81, 95% CI 5.97-7.77) compared to the non-diabetic patients. Nonetheless, chance of amputation among NF patients seemed to be lower among children aged under 15 years (adjusted OR< 0.001, 95% CI< 0.0001-0.0014), and

patients with cirrhosis (adjusted OR 0.64, 95% CI 0.44-0.90) or cancer (adjusted OR 0.52, 95% CI 0.30-0.84). (Table 3)

Considering mortality as an outcome, the significant risk factors included being in the elderly age group (adjusted OR 1.81, 95% CI 1.56-2.11), and having hypertension (adjusted OR 1.17, 95% CI 1.00-1.36),

cirrhosis (adjusted OR 4.26, 95% CI 3.42-5.28) or cancer (adjusted OR 1.88, 95% CI 1.33-2.59). Nevertheless, diabetic patients (adjusted OR 0.79, 95% CI 0.67-0.92) and those who worked as skilled agricultural workers (adjusted OR 0.44, 95% CI 0.35-0.55) or other occupations (adjusted OR 0.74, 95% CI 0.57-0.96) were less likely to die due to NF. (Table 3)

Table 3. Multivariate logistic regression analysis for amputation and mortality among the NF patients, Thailand, 2018

Characteristics		Adjusted odds ratio (95% CI) for amputation	Adjusted odds ratio (95% CI) for mortality
Gender	Female	1.00 (0.89-1.13)	1.04 (0.90-1.20)
	Male	Ref.	Ref.
Age	< 15 years old	<0.001 (<0.0001-0.0014)*	0.23 (0.01-1.03)
	> 60 years old	0.91 (0.80-1.03)	1.81 (1.56-2.11)*
	15-60 years old	Ref.	Ref.
Occupation	Elementary	1.04 (0.84-1.29)	0.92 (0.75-1.13)
	Skilled Agriculture	0.84 (0.69-1.04)	0.44 (0.35-0.55)*
	Others	0.80 (0.62-1.03)	0.74 (0.57-0.96)*
	Unemployed	Ref.	Ref.
Diabetes	Yes	7.27 (6.19-8.58)*	0.79 (0.67-0.92)*
	No	Ref.	Ref.
Hypertension	Yes	0.99 (0.87-1.13)	1.17 (1.00-1.36)*
	No	Ref.	Ref.
Cirrhosis	Yes	0.64 (0.44-0.90)*	4.26 (3.42-5.28)*
	No	Ref.	Ref.
Alcoholism	Yes	0.66 (0.41-1.01)	0.93 (0.67-1.28)
	No	Ref.	Ref.
Cancer	Yes	0.52 (0.30-0.84)*	1.88 (1.33-2.59)*
	No	Ref.	Ref.
Number of infection site	Single	1.53 (0.86-3.02)	0.78 (0.49-1.32)
	Multiple	Ref.	Ref.

Note: *Statistical significance at α< 0.05*

Ref. stands for reference

Discussion

This study shed light on the factors that posed a risk to disability or mortality following NF. The findings could be helpful to aid health care workers in making a rational decision on treatment and disease control of NF.

One of the strengths of this study was that all the NF (19,071) patients recorded in HDC during 2018 were included in this study. These data were reported from all provinces throughout the country, except Bangkok.

Thus, the results from this study could represent the characteristics of all NF patients nationwide.

In this study, we had determined the amputation rate among NF patients in Thailand during 2018 as 8.2%. This finding was compatible with a study by Khamnuan et al.[8], conducted in three provinces of Thailand – Chiang Rai Province, Kamphaeng Phet Province and Phayao Province. Based on the multivariate logistic regression analysis, the significant risk factor of amputation among NF patients was found to be presence of underlying

diseases such as diabetes. This finding was consistent with the previous studies by Khamnuan, Ahn and Cheng.[8-10] The possible explanation was that diabetes mellitus can lead to peripheral vascular disease, especially at lower extremities, thereby increasing risk of infections and causing a delay in wound healing.[11-16] Consequently, once diabetic patients develop NF and fail to receive early appropriate treatment, severe tissue necrosis will occur, which requires extensive surgery. Some patients would subsequently end up with amputation of limbs.

Interestingly, our study had shown that the diabetic NF patients were less likely to be dead, compared to those without diabetes. The medical doctors tend to give close attention on the NF patients with diabetes due to high risk of developing tissue necrosis as previously mentioned. Thus, the diabetic patients tend to receive early recognition and aggressive surgical treatment in order to save their lives. This might possibly be the convincing explanation as to why diabetes was found to be a significant protective factor for mortality, but a significant risk factor for amputation.

Case fatality rate among NF patients in this study was found to be 6.3%. This result was similar to a study by Awsakulsutthi which reported the case fatality rate of 5.9%.[17] In accordance to other previous research studies, we also demonstrated that the significant risk factors for mortality among NF patients were over 60 years of age, and presence of hypertension, cirrhosis or cancer.[18,19] Aging, cirrhosis and cancer can cause alterations of immunity.[20-23] Once the patients with these underlying conditions develop severe infection like NF, they are more likely to end up with septicemia which is one of the major causes of death.[24] In addition, being hypertensive is known to be strongly associated with age as well.[25,26]

In addition, results from the multivariate logistic regression demonstrated that the unemployed patients had higher risk of mortality, compared with those with an occupation. Patients engaged in elementary occupations did not show statistically difference from the unemployed group. It could be explained that unemployment is closely related to elderly, or people with some medical conditions or low socio-economic status.[27-29] These 3 groups of people are usually prone to have severe infection and death, compared to general population.[20-23,30]

There were some limitations in this study. Laboratory findings such as total white blood count, C-reactive protein or serum creatinine were not available in the HDC database. Lack of such data might affect the accuracy of diagnosis. Moreover, although there was no information on some variables, it was not substantial since even for the occupation variable with the highest missing data, proportion of missing data was merely 4.9%.

Conclusion

In conclusion, morbidity and mortality among NF patients were among the important public health concerns in Thailand. Health care workers should be trained and reminded to initiate prompt diagnosis and adequate treatment for NF patients. The service for NF should be more emphasized in high risk populations, particularly among unemployed, elderly and patients with chronic diseases such as diabetes, hypertension, cirrhosis and cancer, in order to prevent serious subsequent complications.

Suggested Citation

Praekunatham H, Tantirat P. Factors associated with disability and mortality among necrotizing fasciitis patients in Thailand, 2018. OSIR. 2020 Mar;13(1): 9-16.

References

1. Shaikh N, Khawaiter J, Al-Thani H. Necrotizing fasciitis: a surgical and medical emergency. Surgical Science. 2012; Vol.03No.11:8.

2. Puvanendran R, Huey JCM, Pasupathy S. Necrotizing fasciitis. Can Fam Physician. 2009;55(10):981-7.

3. Headley AJ. Necrotizing soft tissue infections: a primary care review. American family physician. 2003;68(2):323-8.

4. Eneli I, Davies HD. Epidemiology and outcome of necrotizing fasciitis in children: an active surveillance study of the Canadian Paediatric Surveillance Program. The Journal of pediatrics. 2007;151(1):79-84, e1.

5. Naseer U, Blystad H, Angeloff L, Nygård K, Vold L, Macdonald E. Cluster of septicaemia and necrotizing fasciitis following exposure to high seawater temperatures in southeast Norway, June to August 2018. International Journal of Infectious Diseases. 2019; 79:28.

6. Mulla ZD, Gibbs SG, Aronoff DM. Correlates of length of stay, cost of care, and mortality among patients hospitalized for necrotizing fasciitis. Epidemiol Infect. 2007;135(5):868-76.

7. Malheiro LF, Magano R, Ferreira A, Sarmento A, Santos L. Skin and soft tissue infections in the intensive care unit: a retrospective study in a tertiary care center. Rev Bras Ter Intensiva. 2017;29(2):195-205.

8. Khamnuan P, Chongruksut W, Jearwattanakanok K, Patumanond J, Tantraworasin A. Necrotizing fasciitis: epidemiology and clinical predictors for amputation. Int J Gen Med. 2015; 8:195-202.

9. Ahn J, Raspovic KM, Liu GT, Lavery LA, La Fontaine J, Nakonezny PA, et al. Lower extremity necrotizing fasciitis in diabetic and nondiabetic patients: mortality and amputation. The international journal of lower extremity wounds. 2019;18(2):114-21.

10. Cheng N-C, Tai H-C, Chang S-C, Chang C-H, Lai H-S. Necrotizing fasciitis in patients with diabetes mellitus: clinical characteristics and risk factors for mortality. BMC Infect Dis. 2015; 15:417-.

11. Huysman E, Mathieu C. Diabetes and peripheral vascular disease. Acta chirurgica Belgica. 2009;109(5):587-94.

12. Thiruvoipati T, Kielhorn CE, Armstrong EJ. Peripheral artery disease in patients with diabetes: epidemiology, mechanisms, and outcomes. World J Diabetes. 2015;6(7):961-9.

13. Carey IM, Critchley JA, DeWilde S, Harris T, Hosking FJ, Cook DG. Risk of infection in type 1 and type 2 diabetes compared with the general population: a matched cohort study. Diabetes Care. 2018;41(3):513.

14. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J Endocrinol Metab. 2012;16 Suppl 1(Suppl1): S27-S36.

15. Brem H, Tomic-Canic M. Cellular and molecular basis of wound healing in diabetes. J Clin Invest. 2007;117(5):1219-22.

16. Dangwal S, Stratmann B, Bang C, Lorenzen JM, Kumarswamy R, Fiedler J, et al. Impairment of wound healing in patients with type 2 diabetes mellitus influences circulating microRNA patterns via inflammatory cytokines. Arterioscler Thromb Vasc Biol. 2015;35(6):1480-8.

17. Awsakulsutthi S. A retrospective review of necrotizing fasciitis in Thammasat University Hospital. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2010;93 Suppl 7: S246-53.

18. Dworkin MS, Westercamp M, Park L, McIntyre A. The epidemiology of necrotizing fasciitis including factors associated with death and amputation. Epidemiol Infect. 2009; 137:1609-14.

19. Khamnuan P, Chongruksut W, Jearwattanakanok K, Patumanond J, Yodluangfun S, Tantraworasin A. Necrotizing fasciitis: risk factors of mortality. Risk Manag Healthc Policy. 2015; 8:1-7.

20. Castelo-Branco C, Soveral I. The immune system and aging: a review. Gynecological endocrinology: the official journal of the International Society of Gynecological Endocrinology. 2014;30(1):16-22.

21. Malaguarnera L, Cristaldi E, Malaguarnera M. The role of immunity in elderly cancer. Critical reviews in oncology/hematology. 2010;74(1):40-60.

22. Opal SM, Girard TD, Ely EW. The immunopathogenesis of sepsis in elderly patients. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2005;41 Suppl 7: S504-12.

23. Noor MT, Manoria P. Immune dysfunction in cirrhosis. J Clin Transl Hepatol. 2017;5(1):50-8.

24. Oud L, Watkins P. Necrotizing fasciitis among patients with liver cirrhosis in Texas, 2001 - 2010: a population-based cohort study. J Clin Med Res. 2016;8(2):90-6.

25. Buford TW. Hypertension and aging. Ageing Res Rev. 2016; 26:96-111.

26. Sun Z. Aging, arterial stiffness, and hypertension. Hypertension. 2015;65(2):252-6.

27. Axelrad H, Malul M, Luski I. Unemployment among younger and older individuals: does conventional data about unemployment tell us the whole story? J Labour Mark Res. 2018;52(1):3-.

28. Janlert U. Unemployment as a disease and diseases of the unemployed. Scandinavian Journal of Work, Environment & Health. 1997; 23:79-83.

29. Doku DT, Acacio-Claro PJ, Koivusilta L, Rimpelä A. Health and socioeconomic circumstances over three generations as predictors of youth unemployment trajectories. European Journal of Public Health. 2018;29(3):517-23.

30. de Glanville WA, Thomas LF, Cook EAJ, Bronsvoort BMdC, Wamae NC, Kariuki S, et al. Household socio-economic position and individual infectious disease risk in rural Kenya. Scientific Reports. 2019;9(1):2972.