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RESEARCH ARTICLE

Temporal and seasonal trends of hospitalization and mortality associated with necrotizing fasciitis: A retrospective study of 12 years (2002 – 2013)

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ABSTRACT

Background: Necrotizing fasciitis (NF) is a rare but aggressive infection that affects the superficial fascia and progressively destroys the tissue between the skin and underlying muscles. It is a surgical emergency with significant morbidity and mortality. This study aimed to explore the temporal and seasonal trends in NF infection in Qatar.

Methods: A total of 327 patients diagnosed with NF, aged ≥ 18 years, and admitted to the Hamad General Hospital, Qatar, in 2002 – 2013 were retrospectively reviewed. The hospitalization and mortality rates in the general population in Qatar and the case fatality rate (CFR) were calculated for each year. The patients were grouped into summer, autumn, winter, and spring admissions based on their admission dates. Seasonality was studied by comparing the characteristics, bacteriological status, and outcomes of the patients admitted in different seasons.

Results: The hospitalization rate of NF in Qatar was 2.9 per 100,000 population; in the study duration, this rate decreased from 2.8 to 1.6 per 100,000 population in 2002 and 2013, respectively. The mortality rate among NF cases increased from 1.9 to 3.6 per million population, and the CFR increased from 6.7 to 23 per 100 admissions in the same duration. No temporal trends in the hospitalization and mortality rates or CFR were evident in the study duration. Polybacterial infections were higher in autumn than in other seasons. Monobacterial Gram-positive infections were higher in spring than in other seasons, and monobacterial Gram-negative infections were higher in summer than in other seasons ($p = 0.02$). However, seasonality was not evident after further analysis in terms of species, severity,

complications, length of hospital stays, and CFR in patients with NF.
Conclusion: No clear trend or seasonality was observed in terms of outcomes; however, seasonality in NF-causing bacteria was evident, as polybacterial infections were significantly higher in autumn than in other seasons, whereas monobacterial infections were more frequent in spring and summer than in other seasons. However, the severity of infections, length of hospital stay, and mortality did not significantly vary. Further microbiological studies are needed to obtain confirmatory data regarding the temporal and seasonal trends of NF.

Keywords: necrotizing fasciitis, season, temporal trend, Qatar

INTRODUCTION

Necrotizing fasciitis (NF) is a rare but aggressive infection that affects the superficial fascia and progressively destroys the tissue between the skin and underlying muscles.[1] The hospitalization rate of patients with NF is approximately 1.3 per 100,000 population per year.[2] The mortality rate associated with NF ranges from 16% to 32%, but it may reach 100% in the absence of proper treatment.[3–9] Poor outcomes are often linked to infections caused by a combination of bacteria.[10] The common risk factors of NF include diabetes mellitus, HIV infection, malignancy, illicit drug use, and malnutrition; however, NF may occur without any provocation.[10] Poor outcomes can also be partially attributed to the lack of proper management and surgical intervention supported by antimicrobial use and supportive care.[11,12]

Previous studies revealed a change in the trend of hospitalizations and mortality associated with NF.[13,14] The mortality rate was approximately 46%, which decreased to nearly 20%.[4–7,14,15] Although a large gap in knowledge regarding the seasonality of NF infections exists in the medical literature, a UK-based study has revealed that streptococcal-related NF cases increases in spring and early summer.[16] They recommended that surgeons should focus on patients with NF between April and July. In a published study in Canada, the absolute number of admissions of patients with NF is higher between March and July when the relative temperature is the highest throughout the year and less frequent in fall and winter.[17] Therefore, understanding the patterns of hospitalizations, microbiological characteristics, and outcomes remains crucial in reducing the morbidity and mortality associated with NF. Previous studies in our institute described the clinical presentations and outcomes of NF in terms of gender, predictors of mortality, and prognostic value of scoring in predicting poor outcomes.[18–20] The present study aims to examine the temporal and seasonal trends of the hospitalization and mortality associated with NF in Qatar.

METHODS

The medical records of patients admitted to the Hamad General Hospital (HGH) in Qatar between January 1, 2002, and December 31, 2013, were retrospectively analyzed. The HGH is the only tertiary care facility that serves over 2 million populations in Qatar. The following adult patients (≥18 years) were included in the study: those who were admitted in the study duration, had operative notes clearly indicating the presence of necrosis in the fascia and subcutaneous tissues, specifically mentioned NF in the operative notes, underwent diagnosis through tissue histopathology, mentioned NF in their electronic medical records, or specified NF in their discharge summary. The demographic characteristics causes of NF, clinical presentation, comorbidities, infected body regions, severity of infection in terms of the Sequential Organ Failure Assessment (SOFA) score and the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, causative agents, complications, and outcomes were recorded. The SOFA score was calculated using the following parameters: ratio of partial pressure arterial oxygen and fraction of inspired oxygen (PaO_2/FiO_2), platelet count, bilirubin level, Glasgow coma score, mean arterial pressure, use of vasopressors, creatinine level, and urine output.[21] The LRINEC score was determined using C-reactive protein, white blood cell, hemoglobin, sodium, creatinine, and glucose levels.[22] The population data (≥18 years of age) from Qatar Statistics Authority were used to calculate the hospitalization and mortality rates in the general population each year.[23] The case fatality rate (CFR) is the proportion of the mortality among the NF cases throughout the course of the infection. Patient demographic data, clinical presentation, comorbidities, infection causing bacteria and site of infection, severity of infection in terms of SOFA and LRINEC, complications developed in the hospital, duration of hospital stay, and mortality were presented. Moreover, these variables were compared

among patients categorized in terms of season through appropriate statistical tests. A detailed background of the bacterial agents causing NF was provided. The study was approved with a waiver of informed consent by the Institutional Review Board of Hamad Medical Corporation (IRB # 14066/14). The study was compliant with the relevant ethical guidelines, and patient data anonymity was maintained.

Climate overview

Summer in Qatar occurs in May to September, which is marked by a very hot climate that can reach over 50 °C and have low rainfall. Winter falls in December to February, which is characterized by cool but still warm temperatures (average = 23°C) and occasional rainfall. Spring (March and April) and autumn (October and November) are warm and dry (Table 1).[24]

Data analysis

Data were presented as numbers, percentages, mean ± standard deviation, or medians with interquartile range as appropriate. The normality of data distribution was tested via a Shapiro–Wilk test, and skewed data were subjected to a nonparametric test as appropriate. The upper and lower limits of 95% confidence interval of a proportion were calculated using the Wilson procedure, e.g., the CFR in four seasons in Qatar.[25,26] Categorical variables were compared through Pearson chi-square (χ^2) and Fisher's exact tests as appropriate. Continuous variables, such as the length of hospital stay, were compared via Student's t-test (2 groups) or one-way ANOVA (for more than two continuous groups) with Bonferroni's post hoc test as appropriate. Trends and seasonality were examined through time-series analysis using Excel. Data with 2-tailed $p < 0.05$ was considered significant. Data were analyzed using SPSS version 21 (SPSS Inc., Chicago, Illinois).

Table 1. Air temperature and relative humidity by season in Qatar [24]

Season	Months	Mean air temperature range (°C)	Mean relative humidity range (%)
Summer	May – Sep	31.8 – 35.3	43 – 62
Autumn	Oct – Nov	24.6 – 29.5	64 – 67
Winter	Dec – Feb	17.5 – 19.6	71 – 73
Spring	Mar – Apr	21.7 – 26.4	54 – 63

RESULTS

A total of 327 patients with NF were admitted to the HGH in the 12-year period from January 1, 2002, to December 31, 2013. The demographic characteristics, causes and clinical presentation of NF, comorbidities of the patients, causative microorganisms, infected body sites, severity, complications, and outcomes are presented in Table 2.

Three out of four admissions were males. The mean age of the patients was 51 years (ranged = 19 – 95 years). Nearly one out of three patients were aged 60 years and above. Most of the patients presented with local swelling (72%) followed by pain disproportionate to the local swelling (63%) and fever (61%). The median duration of symptoms was 4 days (range = 1 – 30 days). The most commonly reported comorbidities were diabetes mellitus (51%), hypertension (35%), and kidney disease (15%). The most frequent site of infection (53%) was the lower limb, followed by the perineum (24%). Type II infection (monobacterial Gram-positive or Gram-negative infection) was present in the majority of the patients (n = 201, 66%; Table 2 and Figure 1). The mean SOFA and LRINEC scores were 10 and 6, respectively. Septic shock developed in 23% of the patients. The median ICU and hospital stays were 5.5 and 16 days, respectively. Mortality was 84 out of 327 cases (26%).

Trends of NF hospitalization and mortality

Table 3 shows the hospitalization trends of NF and mortality associated with NF over the years. The adult population in Qatar increased by twofold in the study duration. Similarly, the number of NF admissions increased; however, the number of admissions evidently varied. The hospitalization rate was 2.9 per 100,000 adult populations per year in Qatar. These rates were 2.8 in 2002 and 1.6 per 100,000 of the population in 2013. This result showed an overall decreasing trend in the NF hospitalization rate even though the number of admissions increased over time. The mortality rate among the NF cases was 6.6 per million populations per year, which corresponded to the CFR of 23.5 per 100 NF admissions. The NF mortality rates were 1.9 and 3.6 in 2002 and 2013, respectively. No trends in the NF mortality rates or CFR were observed. The mortality rate and CFR were

Table 2. Characteristics of patients with necrotizing fasciitis (NF) admitted to Hamad General Hospital between 2002 and 2013 (N = 327)]

Demographic data	
Males	245 (74.9)
Age (mean; year)	50.9 ± 15.3
Causes and presentation	
No history of injury	279 (85.3)
Trivial trauma	43 (13.1)
Swelling	235 (71.9)
Pain	207 (63.3)
Fever	200 (61.2)
Duration of symptoms (days, IQR)	4 (3 – 6)
Comorbidities	
Diabetes Mellitus	167 (51.0)
Coronary Artery Disease	45 (14.1)
Chronic Kidney Disease	49 (15.0)
Hypertension	114 (34.9)
Chronic liver Disease	21 (6.4)
Site of infection	
Lower limb	174 (53.2)
Perineum	79 (24.2)
Abdomen and groin	38 (11.6)
Severity of NF	
SOFA score	10.3 ± 3.2
SOFA > 6	299 (99.3)
LRINEC Score	6.2 ± 3.0
Causative bacteria[1]	
Polybacteria	106 (34.5)
Monobacteria	201 (65.5)
Marine bacteria	0
Bacteria and fungi[2]	30 (9.8)
Complications and Outcomes	
Septic shock	76 (23.2)
ICU LOS (IQR)	5.5 (3 – 13)
Hospital LOS (IQR)	16 (8 – 29)
Mortality	84 (25.7)

Data expressed as numbers and valid percentages in bracket, mean ± standard deviation (SD), or median with interquartile range (IQR) in bracket.
[1]Available data on bacteriology (N = 307), valid percent used;
[2]possible overlap with other bacteria.
Abbreviations: SOFA, Sequential Organ Failure Assessment; LRINEC, Laboratory Risk Indicator for Necrotizing Fasciitis; LOS, length of stay

the highest in 2010, i.e., 14.9 per million population and 47.6%, respectively.

Trends of NF hospitalization and mortality in different seasons

Table 4 shows the frequency of hospitalization and mortality in the study duration. The number of admissions and the number of deaths were the highest in summer, followed by those recorded in winter. This finding was consistent with the longer duration of summer and winter than that of the other seasons. The CFR was the highest in autumn (34%), followed by that observed in winter (26%); however, these seasonal variations in CFR were not statistically significant ($p > 0.05$). The data were not normally distributed in terms of HLOS with a mean of 23.7 (95% CI = 20.6 – 26.84).

Table 5 shows that seasonality was not evident in demographic characteristics, comorbidities, symptoms, infected body sites, severity, complications, or length of hospital stay of the patients with NF. However, the type of bacteria causing NF significantly differed in the four seasons; that is, monobacterial Gram-positive infection was predominant in all the seasons except autumn ($p = 0.02$). Chi-square analysis revealed no significant differences in NF-causing species; Gram-positive cocci, including *Staphylococcus*, *Streptococcus*, and *Enterococcus*, accounted for the majority of the infections in all the seasons. Although the proportion of Gram-negative rods, including *Escherichia coli* and *Pseudomonas aeruginosa*, was not statistically significant, it was higher in autumn than in other seasons ($p = 0.49$). The time-series analysis indicated no clear trend or seasonality in terms of outcomes.

DISCUSSION

This study showed that the hospitalization rate of the patients with NF in Qatar was 2.9 per 100,000 populations per year, and the rate decreased by 24% between 2002 and 2013. The mortality rate associated with NF was 6.6 per million population per year, which increased from 1.9 to 3.6 per million population in this duration. The CFR of the patients with NF increased. Although mortality did not significantly vary in different seasons, the CFR was higher in autumn than in other seasons. Notably, polybacterial infections were significantly higher in autumn than in other seasons. Monobacterial Gram-positive infections were higher in spring than in other seasons, and monobacterial Gram-negative infections were higher in summer than in other seasons.

The current study was based on a nationally representative sample, because the HGH is the only institution that provides care for all surgical emergencies in Qatar. In our study, the CFR peaked (48%) in 2010, but this value decreased to 23% in 2013.

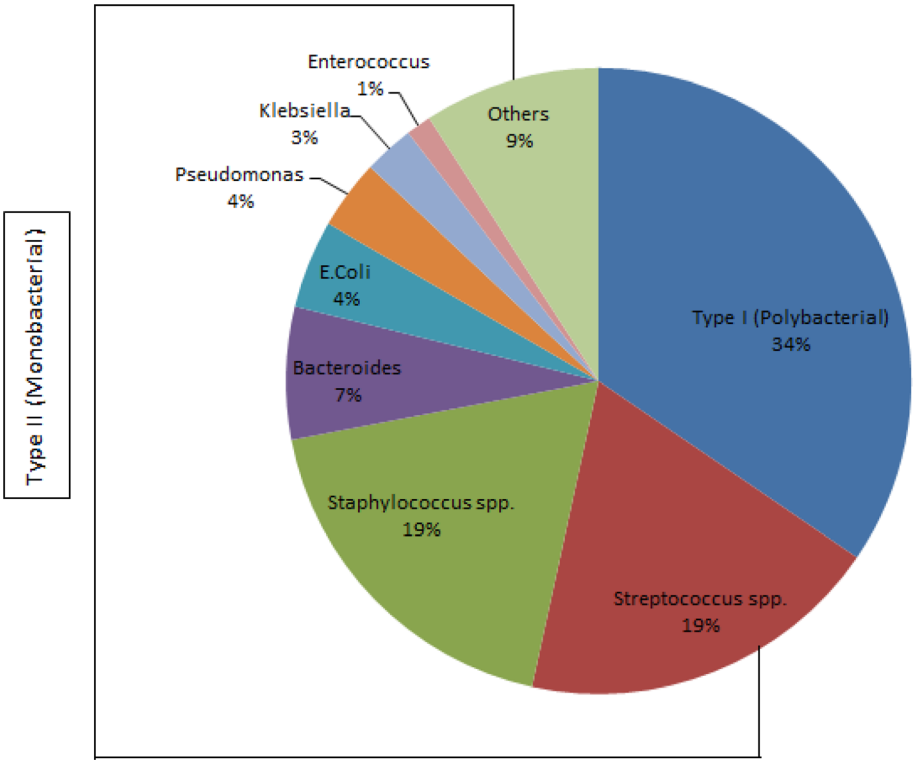

Figure 1. Bacteria causing necrotizing fasciitis among patients admitted to Hamad General Hospital, Doha, Qatar (2002 – 2013)

This decrease in mortality was consistent with previous findings in different parts of the world.[3–8,11,12] The decrease in CFR in the final years of the study reflected the improvement in the management of NF in our institution. The increase in the number of admissions and the decrease in the hospitalization rate could be attributed to the twofold increase in the Qatar population in the study duration.[23] The

Table 3. Hospitalization and mortality trends associated with necrotizing fasciitis (NF) in Qatar

Year	Number of hospital admissions for NF	Mortality	Adult population in Qatar*	Hospitalization rate per 100,000 population	Mortality rate per million population	Case fatality rate per 100 admissions
2002	15	1	527,558	2.84	1.90	6.67
2003	28	3	554,728	5.05	5.41	10.71
2004	13	2	585,364	2.22	3.42	15.38
2005	16	3	654,408	2.44	4.58	18.75
2006	25	4	743,021	3.36	5.38	16.00
2007	33	12	855,217	3.86	14.03	36.36
2008	21	5	998,965	2.10	5.01	23.81
2009	40	12	1,187,753	3.37	10.10	30.00
2010	42	20	1,343,673	3.13	14.88	47.62
2011	15	5	1,406,380	1.07	3.56	33.33
2012	53	11	1,420,828	3.73	7.74	20.75
2013	26	6	1,667,697	1.56	3.60	23.08
Total	327	84	Average	2.89	6.63	23.54

*Ministry of Development Planning and Statistics, Statistics [23]

Table 4. Hospitalization rate, mortality rate, and case fatality rates by season among patients with necrotizing fasciitis (NF)

Seasons	Number of NF hospitalizations (%) (N = 327)	Number of deaths (%) (N = 84)	Case fatality rates (%) [95% CI]
Summer	131 (40.1)	30 (35.7)	22.9 [16.2 – 31.2]
Autumn	44 (13.5)	15 (17.9)	34.1 [20.9 – 50.0]
Winter	92 (28.1)	24 (28.6)	26.1 [17.7 – 36.5]
Spring	60 (18.3)	15 (17.9)	25.0 [15.1 – 38.1]

Table 5. Patient characteristics, site of infection, bacteriology, severity, complication, and duration of hospital stay of patients with NF by season

	Summer (May – Sep) N = 131	Autumn (Oct – Nov) N = 44	Winter (Dec – Feb) N=92	Spring (Mar – Apr) N = 60	P-value
Age	50.6 ± 15.4	53.3 ± 13.1	51.3 ± 16.2	49.5 ± 15.3	0.63
Males	101 (77.1)	35 (79.5)	64 (69.6)	45 (75.0)	0.52
Comorbidities					
• Diabetes mellitus	63 (49.2)	16 (38.1)	50 (55.6)	23 (39.0)	0.13
• Coronary artery disease	19 (14.8)	10 (23.8)	10 (11.1)	6 (10.2)	0.19
• Hypertension	43 (33.6)	20 (47.6)	27 (30.0)	24 (40.7)	0.19
• Chronic kidney disease	19 (14.8)	10 (23.8)	9 (10.0)	11 (18.6)	0.18
Presentation					
• Swelling	95 (77.9)	31 (81.6)	68 (81.0)	41 (71.9)	0.58
• Pain	85 (69.7)	27 (71.1)	56 (66.7)	39 (68.4)	0.96
• Fever	85 (69.7)	23 (60.5)	57 (67.9)	35 (61.4)	0.59
Site of infection					
• Lower limb	62 (47.3)	26 (59.1)	50 (54.3)	36 (60.0)	0.31
• Perineum	33 (25.2)	8 (18.2)	23 (25.0)	15 (25.0)	0.80
• Abdomen/groin	17 (13.0)	5 (11.4)	9 (9.8)	7 (11.7)	0.91
Bacteriology					
• Polybacterial	40 (31.5)	24 (54.5)	26 (31.7)	16 (29.6)	0.02
• Monobacterial Gram +ve	55 (43.3)	12 (27.3)	45 (54.9)	27 (50.0)	
• Monobacterial Gram −ve	32 (25.2)	8 (18.2)	11 (13.4)	11 (20.4)	
NF causing Species					
• Gram + cocci	100 (67.1)	36 (65.5)	75 (72.1)	44 (65.7)	0.49
• Gram − rods	21 (14.1)	11 (20.0)	17 (16.3)	8 (11.9)	
• Anaerobes	28 (18.8)	8 (14.5)	12 (11.5)	15 (22.4)	
SOFA score	10.1 ± 3.2	10.6 ± 2.9	10.5 ± 3.5	10.2 ± 3.2	0.73
SOFA score > 6	119 (90.8)	40 (90.9)	79 (85.8)	52 (86.7)	0.18
LRINEC score	5.9 ± 3.1	7.2 ± 3.4	6.3 ± 2.8	6.1 ± 2.8	0.15
Septic Shock	27 (24.8)	12 (37.5)	21 (27.6)	15 (28.3)	0.57
ICU LOS	5 IQR (3-13)	9.5 IQR (3-14)	5 IQR (3-13)	5.5 IQR (3-13)	0.32
Hospital LOS	18 IQR (8-29)	26 IQR (9-31)	18 IQR (8-29)	19.5 QR (8-29)	0.51

• Data expressed as numbers and valid percentages in bracket, mean ± standard deviation (SD), or median with interquartile range (IQR) in bracket.
• NF: necrotizing fasciitis; Gram +ve cocci, *Staphylococcus aureus, Streptococcus pyogenes*, and enterococci; Gram −ve rods, *Escherichia coli* and *Pseudomonas aeruginosa*; Anaerobes: *Bacteroides* and *Clostridium* species.

hospitalization rate in our study was less than that reported in Texas (6.9 per 100,000 person-years) but was higher than that in Florida (1·3 per 100,000 population).[8,27] These two states had a population that is tenfold that of Qatar in the study duration. However, the Texas population-based study reported a 2.7% increase in the hospitalization rate of NF per year, which was in contrast to our findings.[27] A New Zealand-based study conducted between 1990 and 2006 also showed that the annual NF incidence significantly increased from 0.18 to 1.69 and from 0 to 0.3 per 100,000 person-years, respectively,[28] and its CFR was 21%, which was very close to the overall CFR in our series (24%). A study in Canada revealed that the incidence of necrotizing soft tissue infections is 1.4 cases per 100,000 inhabitants per year.[17]

Factors such as bacterial virulence and antimicrobial resistance influence the hospitalization rates and mortality of patients with NF.[9,29,30] *Staphylococcus* and *Streptococcus* infections can occur simultaneously, thereby increasing the risk of mortality.[1,3] In our study, the majority of polybacterial infections were simultaneous *Staphylococcus* and *Streptococcus* infections and might have increased the severity of infections (measured by SOFA or LRINEC scores). Consequently, poor outcomes, including increased duration of ICU and hospital stays and mortality, were observed. *Streptococcus* accounted for 55% of the polybacterial infections that occurred simultaneously with *Staphylococcus* or other bacteria. Conversely, 46% of the polybacterial infections were caused by *Staphylococcus* and *Streptococcus* or other bacteria. Therefore, *Streptococcus* or *Staphylococcus* was part of the infection in most of polybacterial infections.

In our study, polybacterial infections might have resulted in severe infections, especially among the patients admitted in autumn. Microorganisms produce and release toxins into the systemic circulation, possibly causing systemic inflammatory response syndrome that progresses into septic shock, multiple organ dysfunction syndrome, and death.[31] Notably, the prevalence of septic shock was high among the patients admitted in autumn, but this value was not statistically significant. Monobacterial streptococcal infections might have resulted in less severe infections than other monobacterial or polybacterial infections. Khamnuan et al.[7] observed that streptococcal infections are more frequent in the nonamputation NF group than in the amputation group, whereas *E. coli* infections are dominant in the amputation group.

In a UK-based study, seasonal variations in the incidence of streptococcal NF are observed, and they increase in spring and early summer.[16] Several studies have also revealed a seasonal variation in *Staphylococcus aureus* and peak occurrences in summer or autumn.[30] A review of these studies provided evidence supporting the seasonality of *S. aureus*, particularly in the case of skin and soft tissue infections.

In a published study in Canada, the hospitalization rate of patients with NF also has seasonal variations;[17] furthermore, the incidence rates per 100,000 persons are significantly correlated with the increased monthly temperatures, and the absolute number of hospitalization is higher in March and July than in other months. However, the incidence rate is not correlated with humidity. Infections caused by *Clostridium* species are associated with the highest mean weekly temperatures, followed by those caused by *Streptococcus*.[17] In our study, 40% of the admissions following NF were detected in summer. Although the absolute number of hospitalization and the number of deaths were the highest in summer, the severity of NF in terms of CFR was the highest in autumn (34%), followed by those in winter (26%), spring (25%), and summer (23%;Table 4). Our study also found variations in the types of bacteria causing NF in terms of season; that is, polybacterial infections increased in autumn, whereas monobacterial Gram-negative infections increased in summer.

In addition to bacterial virulence, antimicrobial resistance plays an important role in seasonal variations in bacterial infections. A US-based study has reported the peak incidence of skin and soft tissue infections caused by community-acquired methicillin-resistant *S. aureus* (CA-MRSA) between May and December; however, these infections vary geographically.[32] A Japanese study has demonstrated that the prevalence of MRSA colonization in summer is higher than that in other seasons.[33]

However, seasonal variations in NF could not be explained solely on the basis of factors such as atmospheric conditions, prevalence or virulence of the causative agents, mode of transmission, or host's behavior. They are the essential elements of a traditional model of infectious disease causation, and it consists of an external agent, a host, and an environment. Several confounding factors, including population growth, population density, human movement, and environmental changes, are associ-

ated with seasonality. Cyclic changes in weather patterns are possibly linked to dermatological conditions, making the skin more susceptible to bacterial infections.

The main limitation of this study was its retrospective design, so some areas, such as microbiological characteristics, remain understudied. Although the information about the genus of causative agents was provided, the information about the species was inadequate, thereby limiting the interpretation of seasonal variations. In addition, poor outcomes such as limb amputation or severe disability were not explored.[18 – 20]

CONCLUSION

No clear trend or seasonality was observed in terms of outcomes; however, seasonality in NF-causing bacteria was evident, as polybacterial infections were significantly higher in autumn than in other seasons, whereas monobacterial infections were more frequent in spring and summer than in other seasons. However, the severity of infections, length of hospital stay, and mortality did not significantly vary. Further microbiological studies are needed to obtain confirmatory data regarding the temporal and seasonal trends of NF.

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