

Effects of seasonal changes in temperature and humidity on incidence of necrotizing soft tissue infections in Halifax, Canada, 2001-2015

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ABSTRACT

الأهداف: من المحتمل أن تكون الإلتهابات النخرية للأنسجة (NSTI) خطرة ومميتة. اختلفت نتائج الدراسات المنشورة مسبقا بما يخص التغيرات المناخية و نسبة حدوث NSTI. تستعرض هذه الدراسة مدى تأثير التغيرات المناخية الموسمية (الحرارة والرطوبة) على حدوث NSTI في مدينة هاليفاكس بكندا.

الطريقة: دراسة مرجعية لحالات ال NSTI من عام 2001م إلى عام 2015م. تم الحصول على بيانات درجة الحرارة والرطوبة الإقليمية من وكالة البيئة في كندا (Environment Canada Agency). تم استخدام مربع كاي وتحليل الارتباط للبيانات الفئوية والمستمرة، على التوالي. تم إجراء الانحدار اللوجستي لتحليل معدل الوفيات.

النتائج: تم استعراض 170 حالة NSTI. أكثر الحالات حدثت ما بين شهر مارس وشهر يوليو سنويا، خاصة عندما كانت درجة الحرارة >10 درجة مئوية. ارتبطت نسبة حدوث حالات NSTI شهريا لكل 100,000 شخص مع ارتفاع درجات الحرارة الشهرية ($p<0.01$). كانت نسبة حدوث NSTI الشهرية مرتبطة عكسيا بالرطوبة ($p=0.005$). ارتبط نوع الجرثومة المسببة للمرض بمتوسط درجة الحرارة الأسبوعية ($p<0.01$) ولكن ليس بمعدل الرطوبة ($p=0.66$). ارتبط انخفاض معدل كتلة الجسم، وارتفاع درجة تقييم الجمعية الأمريكية لأطباء التخدير (ASA)، والإقامة الأطول بوحدة الرعاية المركزة، والإقامة الأقصر بالمستشفى مع معدل الوفيات. لم يتم إيجاد أي ارتباط ما بين درجة الحرارة والرطوبة مع معدل الوفيات.

الخاتمة: توضح هذه الدراسة وجود قابلية لزيادة الإصابة بالإلتهابات النخرية للأنسجة في حالات الطقس الأكثر دفئا والأقل رطوبة. مع عدم التأثير على معدل الخطورة أو التسبب في الوفاة من المرض.

Objectives: To explore weather seasonal variation in Necrotizing soft tissue infections (NSTI) in Halifax, Nova Scotia, Canada could be attributed to changes in environmental factors of temperature and humidity specifically.

Methods: A retrospective chart review of NSTIs between 2001 and 2015. Regional temperature and humidity

data were obtained from the Environment Canada Agency, Halifax, Canada. Chi-square was used for categorical variables and continuous data was used for correlation analyses. Logistic regression was performed to analyze mortality.

Results: Of 170 NSTI patients identified, more presented from March to July, especially when the temperature was $>10^{\circ}\text{C}$. Higher incidence per 100,000 persons correlated with increased monthly temperatures ($p<0.01$). Monthly NSTI incidence was inversely related to mean humidity ($p=0.005$). Causative organism was associated with mean weekly temperature ($p<0.01$) but not humidity ($p=0.66$). Low body mass index, higher American Society of Anesthesiologists class, long intensive care unit stay, and shorter overall hospital stay were associated with mortality. No correlation was identified between temperature and humidity and mortality.

Conclusion: This study demonstrates a tendency toward more frequent cases of NSTI with warmer, but less humid weather, without effect on severity or mortality.

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Necrotizing soft tissue infections (NSTI) including necrotizing fasciitis are rapidly progressing and potentially fatal bacterial infections that affect between 0.4 to 1.3 per 100,000 persons in North America.^{1,2} It is characterized by extensive necrosis of the subcutaneous tissue and fascia, which is usually accompanied by severe systemic toxicity.³ Early diagnosis can be difficult, as these infections occur beneath the skin, and visible manifestations can be mistaken for less serious conditions such as cellulitis or abscesses. Early surgical debridement of necrotic tissue, initiation of broad-spectrum antibiotics, and hemodynamic stabilization is critical to NSTI treatment. Delays in diagnosis are associated with increased length-of-stay and mortality.⁴ Multiple classifications systems have been described, including those based on anatomical location, depth of tissue involvement, and bacterial etiology.⁵ The most useful is based on bacterial etiology, as it can alter presentation and treatment adjuncts.⁴ Guiliano et al⁶ described the first classification system, which has been modified to fit additional pathogens. Type I infections account for 70-80% of cases, and consists of synergistic infections of enteric-derived anaerobic species and *Enterobacteriaceae* in addition to non-group A facultative anaerobic *Streptococci*. Type II infections represent 20-30% of cases and are monomicrobial, with the most frequent isolates being skin- or pharyngeal-derived group A *Streptococcus* (GAS) species, and less frequently can *Staphylococcus aureus*. Type III are Gram-negative, marine-associated organisms, including *Vibrio* species. Type IV are caused by fungi, and often seen in immunocompromised and trauma patients.⁴⁻⁷

Our institution is in Halifax, Nova Scotia on the Atlantic coast of Canada. The climate of Nova Scotia is more temperate than other Canadian provinces owing to its proximity to ocean water, which, due to its higher heat capacity, moderates temperature, and humidity. To this end, despite being in a more northern latitude, Nova Scotia experiences less extreme weather patterns and a narrower range of temperature variation.⁸ Previous studies have demonstrated seasonal variations in NSTI incidence, but have conflicted regarding the season NSTIs are more likely to occur.^{9,10} These previous studies did not examine specific environmental factors,

such as temperature or humidity. At our institution, we observed that more cases seem to present during the summer months. Given previous reports and our own observations, we aimed to examine whether seasonal variations observed in NSTI incidence could be attributed to a specific environmental factor.

Methods. Institutional ethics approval was obtained. This retrospective descriptive study included all cases of NSTIs requiring surgical debridement admitted to the Queen Elizabeth II Health Sciences Centre in Halifax, Nova Scotia, Canada, between January 2001 and November 2015. Patients were excluded from the study if they had a necrotizing infection secondary to another pathology (for example, tumor or perforated viscus) or had incomplete data records. Collected data included age, gender, body mass index, comorbidities (smoking, diabetes), anatomic location of infection, surgical management (time to first surgery, number, and nature of procedures), length of stay (in intensive care unit specifically and in hospital), and outcome (mortality, discharge). Ambient air temperature and humidity data were obtained from the Environment Canada agency for the week preceding the day of presentation of each patient. Other weather variables, namely airflow (prevailing winds) or rainfall, were not assessed due to high daily variability and incomplete recording over the study period. The database was accessed online.¹¹ The closest monitoring station to the patient's residence was selected for measurements; most frequently, this was the monitoring station at Halifax Stanfield International Airport (latitude: 44°52'48.060"N; longitude: 63°30'00.050"W) located approximately 32 km north of downtown Halifax. The annual adult Nova Scotia population (>16 years of age) was determined by accessing national census data.¹²

The primary objective of the study was to examine potential associations between ambient air temperature and humidity and the incidence of NSTI, expressed as cases per 100,000 inhabitants per month or year. Secondary objectives included assessing for associations between pathogen species, anatomic site or disease severity, and air temperature or humidity.

Statistical analysis. For the primary outcome of the study, a sample size of 134 patients would represent the minimum number required to identify a correlation with a medium effect size and a power of 0.95. Spearman's rho correlation test was used for continuous and ordinal variables. Categorical variables were analyzed using a Chi-square statistical analysis. Binary logistic regression modelling was performed to assess mortality. A $p < 0.05$ was considered statistically

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significant. Statistical calculations were performed using the Statistical Package for Social Sciences version 23 software program (IBM Corp., Armonk, NY, USA).

Results. Two hundred and nine cases were reviewed, and 170 patients met the inclusion criteria, for an average incidence of 1.4 cases per 100,000 inhabitants per year. The majority of patients were male (119 men, 70%) and the mean patient age was 55 ± 14 years. Ten percent of patients had a documented history of trauma preceding the development of NSTI (Table 1).

The lowest mean monthly temperature occurred in January (-5.5°C), and the highest mean monthly temperature was in July (19.3°C). Mean humidity was lowest in April (72%) and gradually increased, peaking in December (82%) and afterwards decreasing again. The mean temperature of the week preceding the onset of NSTI was $7 \pm 9^{\circ}\text{C}$ and humidity was $80 \pm 7\%$.

The absolute number of cases presented with NSTI was highest when the temperature was $>10^{\circ}\text{C}$. Additionally, admissions of patients with NSTI were higher between March and July in which relative temperature increases were the highest for the year, and less frequent in the fall and winter months (Figure 1). In addition, the incidence rate per 100,000 persons was found to be significantly correlated with higher monthly temperatures ($p<0.01$; Figure 2) but not with humidity ($p=0.67$). A significant inverse correlation between the

monthly incidence of NSTI and mean humidity was identified using Spearman's test ($p=0.005$; Figure 3).

The causative organism of the NSTI was found to be associated with the mean weekly temperature ($p<0.01$) but not with the humidity ($p=0.66$). Clostridium species were associated with the highest mean weekly temperatures (13°C), followed by group *Streptococcus* (9.25°C ; Table 2). The anatomical site involved in a NSTI showed no correlation with air temperature or humidity.

Logistic regression analysis demonstrated that lower body mass index, American Society of Anesthesiologists (ASA) score, length of intensive care unit stay, and overall hospital stay were associated with the outcome of death from NSTI (Table 3). No significant correlations were identified between temperature and humidity with mortality, hospital or intensive care unit length of stay, number of surgeries, or complications.

Discussion. Several reports have previously examined seasonal variation in the incidence of NSTI by bacterial species. Previous studies, for example, have observed a higher incidence of *Vibrio* species necrotizing fasciitis during the summer months of the year.¹³⁻¹⁵ Furthermore, Ullah et al¹⁶ prospectively observed 60 patients with polymicrobial Fournier's gangrene to identify the possible predisposing and etiological factors. The study reported that 65% of patients presented in the hot humid months of the year.¹⁶ On the other hand, overall infections caused by *Streptococcus pyogenes*, including necrotizing fasciitis, showed a higher incidence during the winter or spring season compared to summer and autumn.¹⁷ We observed a similar trend in group A *Streptococcus* related NSTIs. There were no cases related to *Vibrio* species identified in this study.

The current report aimed to examine whether seasonal variations in NSTI could be attributed to specific environmental factors, namely ambient temperature

Table 1 - Characteristics of included patients (N=170).

Variables	n (%)
Male:female	119:51 (70:30)
Age (years)	52.8 ± 11.6
Body mass index	33 ± 11
Diabetes mellitus	85 (50)
Smoking	100 (59)
Recent trauma	17 (10)

Continuous variables represented by mean \pm standard deviation.

Table 2 - Association of causative pathogen and mean weekly temperature preceding presentation.

Pathogen	n (%)	Mean weekly temperature ($^{\circ}\text{C}$)
<i>Clostridium</i> species	4 (2.4)	13
Group B <i>Streptococcus</i>	4 (2.4)	9.3
Polymicrobial	73 (43)	8.1
<i>Staphylococcus aureus</i>	8 (4.7)	4.4
Group A <i>Streptococcus</i>	12 (7.0)	4.3
Methicillin-resistant <i>Staphylococcus aureus</i>	3 (1.8)	1.7
Other	24 (14.0)	2.8
Unknown	42 (24.7)	N/A

Table 3 - Logistic regression analysis for predictors of necrotizing soft tissue infection mortality.

Variable	Odds Ratio	95% CI	P-value
Age	1.05	0.97-1.3	0.208
Body mass index	0.84	0.72-0.97	0.021
ASA score	3.8	1.1-13.2	0.034
Time to first surgery	0.87	0.54-1.4	0.564
Intensive care unit stay	1.09	1.02-1.17	0.011
Length of hospital stay	0.96	0.9-1	0.031
Smoking	4.06	0.7-23.5	0.118
Mean temperature	1.04	0.9-1.2	0.503
Mean humidity	0.87	0.7-1	0.096

ASA - American Society of Anesthesiologist, CI - confidence interval,

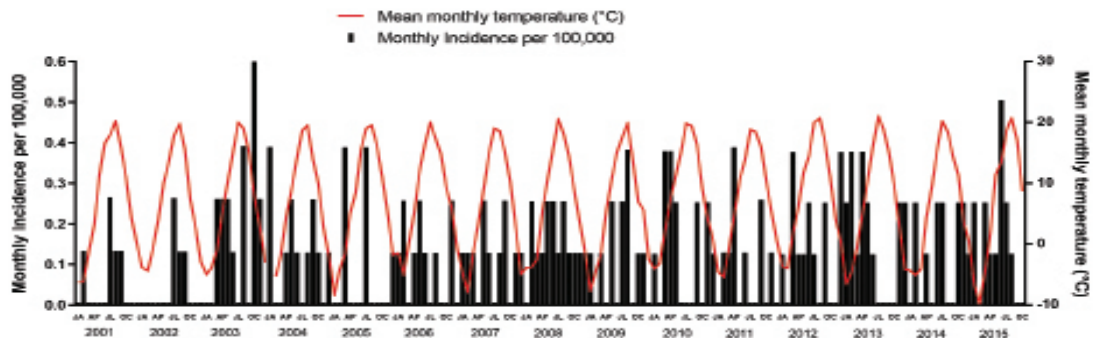


Figure 1 - Relationship between monthly mean temperature (red line) and incidence per 100,000 persons admitted with necrotizing soft tissue infections (black bars) from 2001 to 2015. JA, January; AP, April; JL, July; OC, October. Although no significant association was found year-to-year, fewer cases were noted in the fall and winter months.

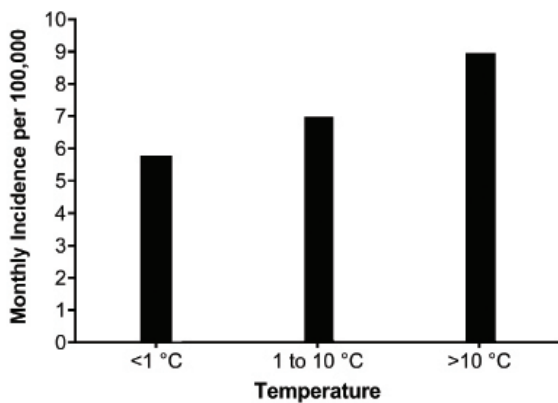


Figure 2 - Relationship between mean monthly temperature and incidence of necrotizing soft tissue infections per 100,000 persons demonstrating a clear trend towards more cases in months with higher temperatures ($p<0.01$).

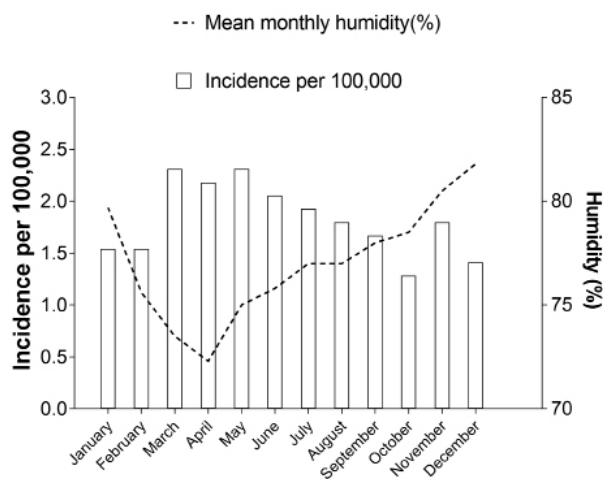


Figure 3 - Relationship between mean monthly humidity and monthly incidence of necrotizing soft tissue infections per 100,000 persons. An inverse relationship was observed ($p=0.005$).

and humidity. We did not identify a significant direct linear correlation between ambient temperature and the incidence of NSTI year-to-year; however, we did observe higher monthly incidence per 100,000 persons with higher temperatures. Our observation that most NSTI infections occurred in the spring and summer months is in keeping with a previous report. Gkrania-Klotsas et al⁹ observed an increased NSTI incidence in the spring and summer months, specifically GAS-related NSTIs. They noted that this was similar to their institution's finding that more non-necrotizing lower-limb cellulitis infections also presented more often in the spring and summer months.¹⁸ Conversely, a study from Denmark showed a higher incidence of cases of GAS invasive infections in colder months, from January to April.¹⁰ Unfortunately, necrotizing infections were not analyzed separately from other invasive GAS infections with respect to seasonal variation, making direct comparison to our results difficult.

The findings of this study revealed differences in causative organisms of the NSTI with different ambient temperatures. Polymicrobial (type I) infections were seen with warmer temperatures. The seasonal variation of some infectious diseases has been variously attributed to changes in atmospheric conditions, the prevalence or virulence of the pathogen, the mode of transmission, or the behavior of the host.^{19,20} Clearly, these factors alone are not able explain all observations of seasonality as these are associated with numerous confounding variables, such as population density, population growth, human movement and environmental changes. Nonetheless, there are established associations reported between some tropical infections and weather variables, such as *Zika*, malaria, leishmaniasis, yellow fever, dengue fever, and West Nile fever.²¹⁻²³ In these cases, the seasonal variations in transmission may be readily attributed to changes in the insect vector population bearing the

viral pathogen. A previous study has examined bacterial infection and specific weather factors. Ehelopola et al²⁴ observed a direct association between rainfall and humidity and leptospirosis infections in Sri Lanka. As the authors point out, this association is likely attributable to improved survival of leptospores in moist soil. In contrast, we observed an inverse association between humidity and NSTI incidence. While the causal pathway for this relationship is less clear than in leptospirosis, we postulate that lower humidity may produce drier skin in patients already predisposed to skin breakdown due to dermatologic conditions such as psoriasis or eczema, making them more susceptible to bacterial infection. Studies have previously suggested a possible link between dermatologic conditions and NSTIs.²⁵

The overall mortality in our study was approximately 22%. Previous series reported slightly higher mortality rates of 25–30%.^{26,27} Logistic regression analysis showed that mortality was associated with lower body mass index (BMI), higher ASA scores, longer ICU stay and shorter overall hospital stay. The inverse relationship between BMI and mortality may represent an unclear phenomenon known as the ‘obesity survival paradox’, which was reported with various chronic conditions.^{28–30} Recently, this phenomenon was studied in patients with NSTI, which revealed that obesity is independently associated with reduced mortality in this acute surgical population.³¹ Our data showed that climate factors were not associated with the severity of NSTI; nor did they predict mortality.

This study was limited by its retrospective nature, including missing data. Additionally, we only had records available for the last 15 years, which decreases the likelihood observing major differences due to climate change which occurs over a minimum of 30 years. The study was limited by the moderate weather conditions of Nova Scotia; areas of the globe with more extreme seasonal variations in temperature and humidity may reveal a more linear or stronger association. Additionally, this study was limited by the lack of climate factors analyzed. Our study focused on temperature and humidity and did not look at the effects of barometric pressure, airflow, or rainfall, owing to incomplete data reporting over the study period. These environmental factors may affect NSTI incidence and should be included in future study.

This study specifically examines the association of ambient humidity and temperature, and not simply season, with NSTI incidence. Based on this study, we would advise physicians in temperate climates like ours to have a higher index of suspicion for NSTIs when

assessing patients with soft tissue infections between March and July or during periods of decreased relative humidity. Additionally, patients with risk factors (diabetes), should be made aware of the increased risk of NSTIs during these periods and advised to practice good skin care during these times.

In conclusion, this study demonstrates a tendency toward more frequent cases of NSTI with warmer but less humid weather, with no effect on severity or mortality. These findings bear repeating in geographic regions with more extreme seasonal environmental variability and may have significant implications for public health policy in the setting of climate change.

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