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Human Immunodeficiency Virus Infection Associated with Necrotizing Fasciitis: A Cohort Study of Texas Population, 2001-2010

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Abstract

Background: Human immunodeficiency viral (HIV) infection is considered a risk factor for development of necrotizing fasciitis (NF). However, NF in HIV-infected patients has been rarely described, with no population-level data on the epidemiology, clinical features, resource utilization, and outcomes in this group.

Methods: We conducted a retrospective, population-based cohort study, using the Texas Inpatient Public Use Data File to identify hospitalizations with diagnoses of both HIV infection and NF for the years 2001-2010. Denominator data for incidence estimates were derived from the annual reports by the Texas Department of Health on the number of patients living with HIV infection in the state. The incidence of HIV-associated NF, demographic characteristics, clinical features, resource utilization, and outcomes were examined.

Results: There were 27,863,025 hospitalizations during study period, with 74 having reported HIV infection and NF. The annual incidence of NF hospitalizations associated with HIV infection remained unchanged (p=0.3428). The overall incidence of HIV-associated NF was 14 hospitalizations per 100,000 person-years. Among NF hospitalizations 57% required care in an ICU. One or more chronic non-HIV comorbidities were reported in 55% of NF hospitalizations and one or more organ failure in 49%. The mean inflation-adjusted total hospital charges were $106,563 and the mean hospital length of stay was 19 days, with no significant change over study period. Twelve (16.2%) patients died and 47% of survivors had routine home discharge.

Conclusions: The present cohort of HIV-associated NF is the largest reported to date. The incidence of NF was markedly higher than that reported in the general population. Non-HIV chronic illness and organ failure occurred each in about half of NF hospitalizations. Management in an ICU was commonly required and patients had high mortality rate. The sources of the observed findings require further study.

Introduction

Necrotizing fasciitis (NF) is a soft tissue infection manifesting as necrosis of subcutaneous tissues and fascia. Although rare, NF commonly results in severe and often fatal illness with high resource utilization. Case fatality associated with NF has been reported to exceed 40% in single center studies [1] while reports on larger cohorts described case fatality around 5-12% [2,3].

Infection with the human immunodeficiency virus (HIV) is considered a risk factor for NF [4]. However, occurrence of HIV as an underlying illness among NF patients has not been examined at a population level, with only few case reports of HIV-associated NF described to date [5-14]. While the risk of HIV-associated NF may exceed that of the general population, there are sparse data on the epidemiology of NF in these patients.

We therefore sought, in the first population-level study to date, to our knowledge, to examine the epidemiological, demographic, clinical, resource utilization, and outcome characteristics and secular trends of HIV-associated NF.

Material and Methods

Data Sources

We used the Texas Inpatient Public Use Data File (TIPUDF), a longitudinal data set maintained by the Texas Department of State Health Services [15]. The data set includes detailed de-identified inpatient discharge data from all state-licensed hospitals, with the exception of those exempt by state statute from reporting to the Texas Health Care Information Collection. Exempt hospitals include a) those that do not seek insurance payment or government reimbursement and b) Selected rural providers, based on bed number and local county population [15]. The facilities included in the mandated report account for 93% to 97% of all hospital discharges. The TIPUDF data set includes demographic, clinical, resource utilization, and outcome information. The data set includes up to 25 discharge diagnoses, and up to 25 procedures, coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

Data on the annual number of patients living with HIV infection in Texas (based on actual diagnosis, including both HIV and AIDS; see also under sensitivity analysis below) was obtained from the annual reports released by the Texas Department of Health [16]. Because we used a publicly available, de-identified data set, this study was

determined to be exempt from formal review by the Texas Tech Health Sciences Center Institutional Review Board.

Study Population

We used ICD-9-CM codes to identify Texas residents hospitalized with both HIV infection (codes 042.XX) and a primary or secondary diagnosis NF (code 728.86) between 2001 and 2010.

Data Collection

We collected data on patients' age, race (categorized as non-Hispanic black [black], non-Hispanic white [white], Hispanic, and other), health insurance (categorized as private, Medicaid, uninsured, and other), chronic co-morbid conditions (based on the Deyo-Charlson index) [17], obesity, smoking, drug and alcohol abuse, other sites of infection (Supplementary Appendix 1), reported microorganisms (Supplementary Appendix 2), type and number of failing organs (Supplementary Appendix 3), admission to an intensive care unit (ICU), life support interventions [mechanical ventilation, central venous catheterization, hemodialysis, and tracheostomy] (Supplementary Appendix 4), total hospital charges, hospital length of stay, and disposition at the end of hospitalization. Severity of illness was based on the number of failing/dysfunctional organs (OF), as modelled by the coding system reported by Lagu et al. [18]. The gender of hospitalizations with a diagnosis of HIV-associated NF could not be examined due to its masking by the state of Texas among patients with diagnoses of HIV, alcohol, or drug abuse.

Outcomes

The primary outcome was hospital mortality. Secondary outcomes included number and type of OF, resource utilization, and disposition among hospital survivors.

Data Analysis

Because TIPUDF provides discharge-level, rather than patient-level information, we reported HIV-associated NF events as number of hospitalizations. We calculated incidence rates of patients' hospitalizations with a diagnosis of HIV-associated NF per 100,000 populations living with HIV infection.

We performed multiple sensitivity analyses to examine the robustness of our incidence estimates. Although TIPUDF is reported to include 93%-97% of annual hospital discharges, we reanalyzed the annual incidence of HIV-associated NF, assuming the dataset captures only 90% of all hospital discharges. In addition, because the non-reporting hospitals are skewed toward rural facilities, potentially affecting care patterns, we assumed that the incidence of HIV-associated NF in those areas is higher, up to 50% above that for reporting hospitals. In addition, because it is estimated that about 20% of HIV patients in Texas are not aware of their diagnosis [16], we have reanalyzed the annual incidence data, assuming the annual reported number of people living with HIV represents 80% of the actual prevalence.

The mortality among hospitalizations with HIV-associated NF was examined as case fatality (defined as the number of HIV-associated NF hospitalizations who died in the hospital divided by the total number of HIV-associated NF hospitalizations for an examined group).

Group data are reported as numbers (percentages) for categorical variables and mean (standard deviation [SD]) or median (interquartile range [IQR]) for continuous variables, as appropriate. Distribution of normality was examined by Kolmogorov-Smirnov test. Categorical data were compared by 2-sided X^2. Mann-Whitney U test and t-test were used to compare continuous data, as appropriate. Cochran-Armitage test for trend was used to examine trends of categorical data. We used regression analysis to explore the trends of incidence of HIV-associated NF. When examining trends of key characteristics at the start vs. end of past decade we used combined 3-year data to enhance precision of comparisons. Total hospital charges were examined using inflation-adjusted (2010) dollars. All statistical analyses were performed using MedCalc version 12.7.0 (MedCalc Software, Ostend, Belgium) and SAS version 9.3 (SAS Institute, Cary, NC, USA). A 2-sided p value <0.05 was considered statistically significant.

Results

There were 27,863,025 hospitalizations during the 2001-2010 period, of which 74 were with reported diagnoses of both HIV infection and NF. The number of people living with HIV infection in the state rose from 36,266 to 65,077 between 2001 and 2010. The characteristics of HIV-associated NF hospitalizations are detailed in Table 1. Lack of health insurance was reported in 29.7% of HIV-associated NF hospitalizations. When available, Medicaid was the most common (25.7%) health insurance. Chronic comorbid conditions other than HIV infection were reported in 41 (55.4%), with diabetes, chronic pulmonary disease, and congestive heart failure being the most common. Obesity was reported in 2 (2.7%) of HIV-associated NF hospitalizations. One or more organ failures were reported in 36 (48.6%).

Characteristic		n = 74
Age (years, n [%])	18-44	47 (63.5)
	45-64	27 (36.5)
Race, n (%)	Hispanic	18 (24)
	White	33 (45)
	Black	19 (26)
	Other	4 (5)
Health insurance, n (%)	Private	17 (23)
	Medicaid	19 (25)
	Medicare	14 (19)
	Uninsured	22 (30)
	Other	2 (3)
Chronic co-morbidities, n (%)a	Any	41 (55.4)
	Diabetes mellitus	11 (14.9)
	Chronic pulmonary disease	8 (10.8)
	Congestive heart failure	7 (9.5)
	Chronic kidney disease	6 (8.1)
	Deyo-Charlson score (mean [SD])	7.2 (1.4)

Other conditions, n (%)b	Smoking	16 (21.6)
	Drug abuse	10 (13.5)
	Alcohol abuse	6 (8.1)
	Obesity	2 (2.7)

Table 1: Characteristics of hospitalizations with HIV-associated necrotizing fasciitis

The annual incidence of HIV-associated NF ranged from 9 to 23 hospitalizations per 100,000 person-years, with no statistically significant change over study period (p=0.3428). The overall incidence of HIV-associated NF during study period was 14 hospitalizations per 100,000 person-years.

Other sites of infection were reported in 24 (32.4%) hospitalizations. The most common reported sites included intra-abdominal (13.5%), respiratory (8.1%), urinary, and device-related (4.1% each). Microbiology data were reported in 44 (59.5%) hospitalizations. When analysis was restricted to HIV-associated NF hospitalizations with reported microbiology data, who had no other reported site of infection (n=19), polymicrobial isolates were noted in 15.8%. Gram-negative bacterial pathogens were the most commonly reported (41%), followed by Gram-positive isolates (37%) and fungi (22%). Group A streptococci were reported in 1 patient. Among Gram-negative isolates, Pseudomonas species were the most common (33%), while staphylococcal and streptococcal species were evenly represented among Gram-positive isolates.

The key trends of the demographic, clinical, and resource utilization features among HIV-associated NF hospitalizations between 2001-2003 and 2008-2010 are outlined in Table 2. Hospitalizations among the 45-64 years age group, development of ≥3 OF, hospital charges, and case fatality trended upward over the past decade, but did not reach statistical significance. The Deyo-Charlson score rose over study period (p=0.0096). Our estimates of the annual incidence of HIV-associated NF remained unchanged on reanalyzing the data, accounting for those not aware of HIV diagnosis (p values ranging from 0.5839 to 0.7518) or with assumption of lower rate of statewide reported hospitalizations, coupled with higher rates of NF in unreported hospitalizations (p values ranging from 0.6547 to 0.7815).

Variable		2001-2003 (n = 16)	2008-2010 (n = 23)	p
Age ≥ 45 years (%)		31.3	56.5	0.2184
Race (%)	Hispanic	25	21.7	0.7316
	White	37.5	51.2	0.5635
	Black	25	26	0.767
Deyo-Charlson score (mean [SD]a		6.6 (1)	7.6 (1.4)	0.0096
≥ 1 Organ failures (%)		43.8	47.8	0.9399
≥ 3 Organ failures (%)		12.5	26.1	0.7455
Type of organ failure (%)	Respiratory	18.8	26.1	0.8412
	Circulatory	18.8	30.4	0.9314
	Renal	25	37.8	0.9024
Selected life support interventions (%)	Mechanical ventilation	6.3	13	0.9511
	Central venous catheterization	12.5	30.4	0.5478
Hospital length of stay (days)	mean (SD)	17.6 [11.9]	14.9 [13.2]	
	median [IQR]	15.5 [9.5-27.5]	12 [5.5-20.5]	0.3684
Hospital chargesb	(dollars, median [IQR])	72,193[48,877-118,299]	77,761[56,326-115,559]	0.568
Case fatality (%)		18.8	34.8	0.4637
abased on conditions included in the Deyo-Charlson co-morbidity index				
binflation-adjusted (2010 dollars)				

Table 2: Trends of epidemiology, patient characteristics, resource utilization and outcomes of hospitalizations with HIV-associated necrotizing fasciitis

One or more OF was reported in 48.6% of HIV-associated NF, most commonly involving the renal (29.7%), circulatory (25.7%), and respiratory systems (23%). Neurological dysfunction occurred only in 1 patient. Among hospitalizations with OF, 44.4% had 3 or more failing organs. Case fatality rose with development and increase in the number of failing organs. Among HIV-associated NF with 0, 1-2, and ≥3 OF, case fatality was 2.6%, 20%, and 43.8%, respectively (p=0.002). Amputation was required in 6 (8.1%) NF hospitalizations.

Admission to an ICU was required in 56.8% of HIV-associated NF hospitalizations. Use of mechanical ventilation, central venous catheterization, and hemodialysis was reported in 15%, 27%, and 4% of HIV-associated NF hospitalizations, respectively. No patient has required tracheostomy. Though down-trending over the past decade, there was no significant change in hospital length of stay (p=0.3684) among NF hospitalizations. The average inflation-adjusted (2010 dollars) total hospital charges per HIV-associated NF hospitalization were $106,563.

Twelve (16.2%) patients died during hospitalization. Among survivors 29 (47%) had routine home discharge, 16 (26%) required home health care, and 12 (19%) were discharged to another facility. No change was found in transfers to other institutions over the past decade (data not shown).

Discussion

We found that the incidence of HIV-associated NF hospitalizations was markedly higher than that reported in the general population developing NF. Non-HIV chronic comorbidities and OF were each reported in about 1 in 2 NF hospitalizations. Care in an ICU was commonly required in our cohort, with a trend of increasing use of life support interventions. HIV-associated NF required prolonged hospitalization and high hospital charges. Case fatality was high in the present cohort. In addition, hospital survivors sustained persistent morbidity with only about half having a routine home discharge.

The present study is, to our knowledge, the first population-level examination of HIV-associated NF, reflecting the rarity of this complication among HIV-infected patients. Our findings of HIV-associated NF incidence being 14 hospitalizations per 100,000 person-years support the proposed increased risk of NF in HIV-infected patients, markedly above that reported in the general population. A commonly cited multistate incidence estimate of NF in the United States (US) is 4 per 100,000, based on a report by Ellis Simonsen and colleagues [19] using administrative data from 1997-2002. A markedly lower incidence of NF was found by Mulla et al. in another population study, using similar approach, with NF reported in 1.3 per 100,000 hospital discharges in Florida in 2001 [20]. However, the investigators focused only on NF as primary diagnosis. Both studies used a case definition approach for NF similar to our study. In a preliminary report on NF in the general Texas population during the years 2001-2010, we found the incidence of NF ranging between 6 to 8 hospitalizations per 100,000 [21]. Thus, our findings for the present cohort suggest that the incidence of NF among HIV-infected patients is markedly higher than that in the general population, reflecting the impact of the immune dysfunction associated with former. There are no more recent population-level data on the incidence of NF in the US. Further studies are needed to corroborate our findings.

Our findings of the race/ethnicity composition of the patients in the present study differ from recent reports of the population living with HIV in Texas, with whites comprising the major group in our cohort, as compared with blacks among HIV-infected patients Texas [16]. However, the small number of HIV-associated NF hospitalizations in both groups limits the interpretation of these findings, and white race has not been described as a risk factor for NF in the general population. Although the incidence of NF rises with age [22], no NF hospitalizations involved patients older than 64 years, possibly reflecting the overall rarity of NF. The reports produced by the Texas Department of Health do not provide age breakdown above 55 years

among those living with HIV in the state, precluding adequate estimate of the contemporary burden of HIV infection among the elderly in the state. Although not reaching statistical significance, there was an increasing rate of HIV-associated NF hospitalizations in the 45-64 years age group at the end of the last decade. Because the incidence and number of newly diagnosed HIV infection in Texas remained unchanged during study period [16], the rising age trend in our cohort may reflect similar changes observed among the population living with HIV in the state and the associated rising long-term survival among HIV-infected patients. This increased survival may in turn explain the trends of rising rates of non-HIV chronic comorbidities at the end of last decade.

Nearly 1 in 3 HIV-associated NF hospitalizations in our cohort lacked health insurance, a rate nearly twice as high than reported in the general population with NF [2]. No data are available on health insurance coverage among patients living with HIV in Texas and our findings on lack of health insurance are much higher than the 9.3% rate of uninsured hospitalized patients in the state [23]. Further study is needed on the association of health insurance coverage with illness in the HIV-infected population.

Only about half of HIV-associated NF hospitalizations had non-HIV chronic comorbidities. This finding is contrasting reports on NF in the general population, with the majority of patients having one or more (non-HIV) chronic comorbid conditions [2]. The differing pattern likely reflects the major role played by HIV in development of NF. When chronic comorbidities were present in our patients, diabetes was the predominant one, similar to reports in the general population with NF [2,3]. However, diabetes was reported only in about 1 in 7 HIV-associated NF hospitalizations, as compared to about 1 in 2 in the general population with NF [2]. Chronic comorbidities were inconsistently described in reported cases HIV-associated NF though, when described, most affected patients had no non-HIV chronic illness [10,12-14] or only a single one [7,11]. The reported chronic comorbidities included hypertension [7] and non-Hodgkin's lymphoma [11], with the later possibly a sequela of AIDS in the affected patient. Obesity was reported in 2.7% of our patients, markedly lower than in population studies of NF in the general population [2,24], possibly reflecting direct impact of HIV infection and its sequelae. Previous case reports on HIV-associated NF provided limited data on general physical exam, with only one describing an obese patient [7].

The site of infection in our patients could not be described due to use of administrative data. The site of infection was described inconsistently in case reports of NF in HIV-infected patients. Two case reports indicated NF involving limbs [5,13], while cervical infection was described in 3 patients [7,10,11], and breast involvement in one [14]. While the small number of patients precludes meaningful analysis, the available data from these cases suggest involvement of uncommon body sites in patients with HIV-associated NF. These anecdotal reports contrast the prevalent involvement of limbs in 60%-100% of patients in the general population with NF [25], with head and neck involvement between none to 7.7% [25].

An additional site of infection was reported in about 1 in 3 HIV-associated NF hospitalizations, mostly involving the intra-abdominal and respiratory tracts. It is unclear whether reported infections preceded, followed, or occurred synchronously with NF. An infection other than NF was described only in one case report of HIV-associated NF (oral candidiasis) [10]. As noted earlier, clinical details other than those pertaining to NF were commonly limited in prior descriptions of

patients with HIV-associated NF. Other sites of infection were reported in the general population with NF in 30% [26] to 76% [27] of patients.

Microbiology data were not reported in 40.5% of HIV-associated NF hospitalizations. Underreporting was also noted by others in national data sets, with microbiology information absent in up to 65% [28]. We found predominance of monomicrobial pathogens in our cohort, mostly Gram-negative bacteria, with rare reporting of Group A streptococci. However, HIV infection (as well as other immunosuppressive states) has been considered among the risk factors for a polymicrobial type of NF [4], and our findings are in contrast with the polymicrobial etiology of most events of NF in the general population [4]. Our findings may have been affected by underreporting of microbiology, analysis restricted to HIV-associated NF hospitalizations without other reported sites of infection, and administrative data precluding information on specimen sources. Microbiology findings were often not described in case reports [1,5,8,9,12], though tended to be monobacterial isolates when reported [6,10,13].

Necrotizing fasciitis is commonly considered to be a critical illness, with reports in the general population often focused on patients managed in the ICU [26]. There are no reports from the US describing ICU utilization in NF in the general population. We found that 57% of HIV-associated NF hospitalizations required ICU care. Use of ICU was mentioned in 4 patients described in prior case reports of HIV-associated NF [7,8,11,13]. Our findings are similar to those reported by Widjaja et al. [27] and Das et al. [24], showing need for ICU care in 63% and 56% of their patients, respectively. Nevertheless, critical care utilization patterns vary across countries [29] and regionally [30], limiting a direct comparison. Indeed, focus only on ICU-managed NF can underestimate the burden of NF in the population.

The renal, circulatory, and respiratory systems were the most commonly involved with OF in the present study. Three case reports of HIV-associated NF described OF, including shock [13,14], renal failure [14] and disseminated intravascular coagulation [8]. Studies in the general population with NF by other investigators did not systematically describe patterns of OF. When selected organ failures were systematically examined, Endorf and colleagues reported findings similar to our study, with renal, circulatory, and respiratory systems as the most commonly affected in the national population [30]. However, the investigators restricted their definition of respiratory failure to patients requiring invasive mechanical ventilation, thus likely underestimating the frequency of this complication and overall OF. In a recent report of New Zealand population by Das et al., focusing on selected OF, shock and renal failure were each present in 42-43% of their NF cohort [24]. In the preliminary report cited earlier, the respiratory, renal, and circulatory systems were the most common failing organs in the general population in Texas with NF, ranging between 16% to 21% [21]. OF was present in nearly 1 in 2 HIV-associated NF hospitalizations in our cohort. When clinical details were provided in prior case reports 3 of 7 patients with HIV-associated NF had OF [7,8,10-14]. The rate of OF in the present study is markedly higher than those reported by Endorf and colleagues [31] in the general population, finding any OF in 30.7% of hospitalizations with necrotizing soft tissue infections. However, as noted earlier, the latter study likely underestimated the rate of OF in their population. Indeed, in a preliminary report on NF in the general population in Texas, we found a development of OF in 40% [21]. When OF was present in the present cohort, nearly half had 3 or more failing organs,

reflecting marked severity of their illness. Prior reports on NF in the general population by other investigators did not describe the distribution of the number of OF. However, the steep rise of case fatality with development and increase in number of OF noted in the present study is similar to that described by others [31]. In our preliminary report on NF in the general population in Texas, 3 or more OF were reported in 29% of those with any OF [21]. The latter finding underscores the markedly higher severity of illness among patients with HIV-associated NF, as compared to the general population with NF. The substantial morbidity of HIV-associated NF in our cohort is also reflected in an amputation rate of 8.1% in our cohort, which is markedly higher than the amputation rates found in the general population with NF, recently reported between 1.2% and 2% in a national population study [2]). The sources of the difference are unclear. However, the small number of events in our cohort limits adequate comparison.

We found prolonged hospital length of stay among HIV-associated NF hospitalizations. Only few case reports to date described resource utilization, with hospital length of stay from 10 days [11] to 4.5 months [10]. Our findings are comparable to prior reports on NF in the general population in the US [2,20]. The fiscal burden of HIV-associated NF has not been previously reported. The average, inflation-adjusted, total hospital charges per hospitalization in our cohort make HIV-associated NF, though rare, the most expensive condition in the state, with the second being respiratory failure ($103,112) [23]. The average hospital charges in our population were also markedly higher than those reported in the general population with necrotizing soft tissue infections, even when adjusted for inflation ($89,529) [31], though the sources of higher charges among HIV-associated NF hospitalizations are unclear. The latter findings further underscore the high morbidity of HIV-associated NF. Although we found no statistically significant change in hospital charges over the past decade, the downward trend of hospital length of stay may have resulted from increasing care efficiencies, with no rise in discharges to other facilities.

Our finding of case fatality of 16.2% is markedly higher than contemporary population-based studies of NF in the general population [2,31]. We found a trend of rising case fatality over the past decade among HIV-associated NF, possibly reflecting similar trends in development of multiple organ failure and rising non-HIV chronic comorbidity. A recent national study of necrotizing soft tissue infections by Psoinos et al. demonstrated that hospital mortality decreased from 9% to 4.9% between 1998 and 2010 [2], though the described population was older with prevalent chronic illness. In our preliminary report on NF in the general population in Texas, case fatality was 9.2% [21], supporting the likely markedly higher case fatality among patients with HIV-associated NF. However, the very small number of events in our cohort limits interpretation of these findings and further comparison with the aforementioned trends in the general population.

Our findings should be considered in the context of several limitations. A retrospective design and use of an administrative data set with their attendant limitations affects the interpretation of our results. However, the rarity of HIV-associated NF precludes practical approach to capture prospectively patient-level data, and similar approach was used by other investigators of NF in the general population [2,31].

The accuracy of case definition of NF in the present study has been based on ICD-9-CM coding at reporting hospitals. Administrative

data sets do not provide information on pathological confirmation of NF diagnosis, raising a potential of misclassification. Nevertheless, NF diagnoses were reported very sparingly in our population. Indeed the small number of HIV-associated NF hospitalizations, even at a population-level examination over a 10-year period, has limited our trend analyses and overall estimates of patient, resource, and outcome attributes. In addition, the morbidity burden of HIV-associated NF in the present study, as judged by rate of ICU admission and hospital length of stay, is comparable to reports on NF in the general population [2,24,27,31]. On the other hand, we cannot exclude underestimation of HIV-associated NF in our cohort. Finally, our case identification approach is similar to prior investigations of NF in the general population [20,31].

Microbiology data were not reported in the many of HIV-associated NF hospitalizations in our cohort, with similar limitation noted by others [28]. In addition, we restricted our analysis to HIV-associated NF hospitalizations without additional reported sites of infection. Both factors affect the interpretation of our findings. However, alternative approaches at a population level can be impractical.

The use of administrative data in our study precluded access to information on the timeliness of diagnosis of HIV-associated NF and to details, time course, and appropriateness of antimicrobial therapy and resuscitative interventions, all of which may vary across institutions and individual clinicians and likely have affected the observed resource utilization and outcomes. However, as noted earlier, similar constraints affect interpretation of prior studies in the general population with NF [20,31]. The masking of patients' gender by the state precluded examination of its patterns and associations in this study. Finally, because the state of Texas does not provide tools to convert hospital charges to costs, we reported hospital charges rather than costs of care, limiting comparisons with other cost data. However, the available charge data allowed comparisons within state population and with selected studies of NF in the general population.

Conclusion

We report the first population-level study to date of HIV-associated NF, describing markedly higher incidence than in the general population. Nearly 1 in 3 NF hospitalizations were associated with an additional site of infection. The majority of HIV-associated NF hospitalizations required care in an ICU, often requiring use of life support interventions. The patients required prolonged hospitalization with hospital charges higher than those reported for NF in the general population, making HIV-associated NF the costliest (per hospitalization) hospital diagnosis in the state. Case fatality was higher than described in recent population-level reports of NF in the general population and HIV-associated NF was associated with substantial residual morbidity among hospital survivors. Further studies of HIV-associated NF are needed in other populations to provide further insight into this rare complication.

Acknowledgement

Conflicts of Interest

The author declares no conflict of interest.

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