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Nosocomial influenza in patients with cancer before the coronavirus disease 2019 (COVID-19) era and one year after the pandemic: Can we do any better in hospitals?

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To the Editor—The nosocomial influenza rate among cancer and severely immunosuppressed patients (ie, transplant recipients) has been reported to be between 9% and 28%.[1,2] Healthcare workers (HCWs) with influenza can transmit the virus to patients, and this transmission can be particularly problematic when HCW vaccination rates are low.[3] High rates of influenza vaccination in HCWs have been associated with lower morbidity and mortality among patients in long-term care facilities.[4]

During the coronavirus disease 2019 (COVID-19) pandemic, most hospitals established measures to limit the spread of severe acute respiratory coronavirus virus 2 (SARS-CoV-2); therefore, the transmission of other respiratory viruses was also limited. In this study, we examined the demographics, clinical presentation, and outcomes of patients with nosocomial influenza in a Mexican cancer-referral center over 13 years, including the first year of the COVID-19 pandemic.

Methods

This cross-sectional study was conducted from 2008 to 2021 at the Instituto Nacional de Cancerologia, an oncological referral center in Mexico City. We included adult patients with solid and hematological malignancies and confirmed nosocomial influenza. Informed consent was waived, and patient confidentiality was protected. Nosocomial influenza was suspected in patients who developed influenza-like symptoms >48 hours after admission. Influenza was confirmed by polymerase chain reaction from nasal swabs, endotracheal tube aspirates, or bronchoalveolar lavage samples.

Demographic and clinical data were obtained from influenza surveillance databases and electronic medical records. Categorical variables are described using proportions, and continuous variables are described using mean and standard deviation (SD) or median and interquartile range (IQR). The Pearson χ^2 test was used to compare categorical variables, the Student *t* test was used for means, and the Mann-Whitney *U* test was used for medians. In addition, we compared HCW influenza vaccination rates from 2015 to 2021.

Before COVID-19, any patient with an influenza-like illness was isolated in an individual room, with droplet and contact precautions. Relatives of patients with influenza-like illnesses had to wear surgical masks, and hand hygiene was also reinforced. In March 2020, tighter infection control practices were introduced, with mandatory face mask use, increased hand hygiene, restrictions for accompanying persons, and cohort isolation in a specific in-hospital ward for patients under evaluation for respiratory symptoms.

Results

In total, 1,808 influenza-like illness cases were evaluated between 2008 and March 2021. Among them, 289 (15.3%) had confirmed influenza. Of these, 30 (10.38%) were diagnosed with nosocomial influenza. The median number of nosocomial influenza cases per year was 2 (IQR, 0–3).

Overall, the median age of these patients was 43 years (IQR, 22–55), and most (70%) had hematologic malignancies. Oseltamivir was prescribed for 29 patients (96.6%). In addition, 10 patients (33.3%) with nosocomial influenza died. Clinical and sociodemographic characteristics are summarized in Table 1.

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Table 1. Clinical and Sociodemographic Characteristics, and Comparison Between Alive and Dead Cases

Variable	N (%) (n=30)	Alive (n=20)	Dead (n=10)	Crude OR (95% CI)	*P* Value
Age, median y (range)	43 (22–55)	34.5 (22–48.5)	53.5 (43–62)	1.058 (1.002–1.117)	**.043**
Sex, male	19 (63.3)	14 (70)	5 (50)	2.167 (0.45–10.439)	.432
Comorbidities (Y/N)	18 (60)	12 (60)	6 (60)	1 (0.212–4.709)	1
Diabetes mellitus	5 (16.6)	3 (15)	2 (20)		
Systemic hypertension	3 (10)	2 (10)	1 (10)		
HIV	3 (10)	2 (10)	1 (10)		
Obesity (BMI $\geq$ 30 kg/m^2)	3 (10)	2 (10)	1 (10)		
Smoking	4 (13.3)	3 (15)	1 (10)		
Cancer type					
Solid organ	9 (30)	7 (35)	2 (20)	2.333 (0.383–14.233)	.431
Hematological malignancy	21 (70)	13	8	2.15 (0.350–13.04)	.674
Steroid use	15 (50)	9 (45)	6 (60)	1.833 (0.392–8.566)	.700
Influenza vaccination	2 (6.7)	1 (5.3)	1 (10)		
Symptoms					
Fever	23 (76.7)	14 (73.7)	9 (90)	3.214 (0.312–32.206)	.633
Cough	24 (80)	14 (73.7)	10 (100)	1.714 (1.222–2.404)	.134
Dyspnea	17 (56.7)	8 (40)	9 (90)	13.5 (1.421–128.25)	**.017**
Laboratory markers					
Lymphopenia (<200 cells/mL)	15 (50)	9 (45)	6 (60)	1.833 (0.392–8.566)	.700
Neutropenia (<500 cells/mL)	6 (20)	17 (85)	7 (70)	2.429 (0.391–15.08)	.372
Albumin (mg/dL)[a]	2.85 (2–3.2)	3.1 (2.3–3.3)	2.1 (1.9–2.8)	0.134 (0.023–0.777)	**0.035**
Creatinine (mg/dL)[a]	0.62 (0.51–0.80)	0.60 (0.52–0.769	0.71 (0.47–0.87)	2.35 (0.12–45.81)	.559
LDH[a]	260.5 (173–352)	260.5 (173–356)	263 (173–335)	1.0 (0.996–1.006)	.880
Influenza virus type					
A (H1N1)pdm 09	19 (63.3)	10 (50)	9 (90)	8.1 (0.851–77.137)	.098
A (H3N2)	7 (23.3)	6 (30)	1 (10)	0.241 (0.025–2.357)	.367
B	3 (10)	3 (15)	0		
No classified	1 (3.3)	1 (5)			
Concomitant infection	13 (43.3)	8 (40)	5 (50)	0.815 (0.174–3.087)	1.000
Days of hospital stay before NI	13.5 (7–20)	13 (6.5–20.5)	15 (8–22)	0.879 (0.742–1.041)	.681
Days of hospital stay after NI	3.5 (0–10)	5 (0.5–12)	2.5 (0–9)	0.843 (0.610–1.165)	.588
Mechanical ventilation days [a]	0 (0–6)	0	5.5 (2–12)	1.349 (1.01–1.80)	**.006**

(*Continued*)

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Table 1. (*Continued*)

Variable	N (%) (n=30)	Alive (n=20)	Dead (n=10)	Crude OR (95% CI)	*P* Value
Days of oseltamivir[a]	5 (5–10)	7.5 (5–10)	4.5 (2–12)	0.848 (0.629–1.145)	0.198
Oseltamivir administration within 72 h after onset of symptoms	20 (66.6)	16	4	0.167 (0.031–0.889)	**.045**
Length of stay, d (range)	21 (13–32)	19.5 (13–32)	23 (10–28)	0.982 (0.934–1.032)	.470

Note. IQR, interquartile range; OR, odds ratio; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase; NI, nosocomial influenza.
[a]We used median and IQR for continuous variables.

Influenza vaccination among HCWs increased from 2015 to 2019, with a sharp increase in 2020. From 2015 to 2019, the mean rate of influenza vaccination among HCWs was 54.64%. In 2020, this rate increased to 95.3%, and there were no cases of community-acquired influenza nor nosocomial influenza. The difference between 2015 to 2019 versus 2020 was statistically significant ($P < .001$).

Discussion

In this observational study, we reviewed 30 cases of nosocomial influenza in 13 years. Notably, one-third of the patients died, and we observed that early administration of oseltamivir (within 72 hours after onset of symptoms) was related to survival. In February 2014, during the 2013–2014 season, we had an influenza outbreak among unvaccinated HCWs that correlated with a remarkable increment of nosocomial influenza cases in patients (Supplementary Fig. 1 online).

A few studies have described nosocomial influenza among cancer patients. A study from MD Anderson Cancer Center in Texas reported a nosocomial influenza rate between 0% and 6.6% in a 7-year period,[5] which is lower than ours. In contrast, a German study reported a nosocomial influenza rate of 20%.[6] Regarding mortality, Chemaly et al[1] in 2006 reported a rate of 15%, which is lower than ours. This difference may be related to more advanced underlying malignancies in and poorer functional status of our patients. Also, 50% of our patients had lymphopenia (<200 cells/mm^3), which has been reported as an independent factor for a poor prognosis and death.[1] Similar to our report, early initiation of oseltamivir was associated with better outcomes.[7] In our study, coinfections were not associated with increased mortality.

At the beginning of 2020, the COVID-19 pandemic caused the reformulation of infection control practices worldwide. Mandatory face mask use and social distancing have probably contributed to lower transmission of respiratory infections.[8] These measures have positively affected the dynamics of respiratory virus transmission, and we need to consider those for regular medical care, even when the pandemic comes to an end. It is also remarkable that vaccination against influenza in HCWs in our hospital almost doubled last year, demonstrating that wide vaccine availability, political will, and most importantly, HCW responses are critical factors in prevention.

This study has several limitations. It included a small number of cases over an extended study period. In addition, this is a single-center report, so the results may not be generalizable. During the first years after the 2009 pandemic influenza, testing was limited. Finally, influenza vaccination rates among HCWs were available from 2015 onward.

The rate of nosocomial influenza in cancer patients at our institution is similar to that of other reports. The high mortality rate highlights the relevance of strict infection control and prevention practices in cancer patients and the importance of HCW vaccination as a preventive measure to reduce influenza in hospitals. The increased uptake of the influenza vaccine in 2020, universal face mask use, social distancing, and more strict visitor policies correlated to the absence of cases of influenza in 2020, and should make us reconsider infection prevention policies overall.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2021.337

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