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Under Recognized Respiratory Tract Infections in Non-Neutropenic Fever Children with Cancer: Real-World Insights from Mass Religious Gatherings and Influenza Seasons

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: No existing research has addressed respiratory tract infections (RTIs) in children with non-neutropenic fever (NNF) who are present during seasons of religious mass gatherings (Hajj, Ramadan), especially if this coincides with the influenza season. The treatment approach for RTI cases in NNF children during mass religious gatherings may not be applicable in the normal season.

Methods: This study includes a retrospective analysis of RTI in NNF children who were present during mass religious gathering seasons and/or flu season, and who were being treated for malignancy at Princess Noorah Oncology Center from May 1, 2016 through December 2017.

Results: A total of 4599 spikes in fever were identified in 124 non-neutropenic children in whom 455 spikes (9.9%, 455 out of 4599) were documented during mass religious gatherings and/or the flu season. NNF secondary to RTIs was documented in 59.7% of patients during the study seasons with a total of 245 fever spikes recorded. Ceftriaxone-based therapy was the main treatment approach for NNF including the RTI cases that were associated with 50% of subsequent hospitalization for further management. Among all the examined risk factors, a prolonged fever of more than three days was significantly associated with NNF secondary to RTI during mass religious gatherings if coincident with the flu season, OR=0.034 [95% CI, 0.013 - 0.09] P-value <0.001.

Conclusions: The present study showed that the prevalence rate of NNF of RTI in NNF children increased during periods of mass gathering. There is need therefore for a national consensus to address NNF management during mass religious gatherings, particularly if coincident with the flu season.

Keywords: Respiratory tract infections RTI; cancer; non-neutropenic fever (NNF) religious mass gatherings; influenza season.

1. INTRODUCTION

Infection is the most common cause of treatment-related morbidity and mortality in children with cancer, where for the most part fever is the only symptom of infection [1,2]. In the last 20 years, a couple of published studies have found that almost half of the children with cancer develop at least one fever episode during the neutropenia phase (fever neutropenia) which is a common complication in chemotherapy treatment and respiratory tract infection among neutropenic patients. However, the frequency of non-neutropenic fever (NNF) episodes is scarce [3-5].

Respiratory tract infection (RTI) is well documented as one of the common causes of fever around the globe, especially during the influenza season, subsequently causing significant delays in delivering cancer-specific therapy in up to 80% of children with cancer in the Middle East, Europe, and Canada. However, the clinical presentation of respiratory infection in children with cancer compared to the general population is not specific [6-8]. During the 2009 influenza pandemic, more than 60% of children with cancer were diagnosed with influenza or influenza-like illnesses, of which 20% experienced severe symptoms that required hospitalization and further modification of their initial infection treatment course [9-12]. In September 2012, the Middle East respiratory syndrome coronavirus MERS-CoV was isolated in Saudi Arabia with few fatality cases reported in patients with cancer. The association of cancer with MERS-CoV-related fatality is yet to be confirmed [13-22].

The comprehensive care management for influenza infection includes the use of influenza vaccines and antiviral drugs, which subsequently aid in planning the use of antibiotics and other treatment modalities. However, every flu season is different. The Saudi Arabia Ministry of Health (MOH) published its data in 2015 and stated that the influenza season in Saudi Arabia starts in September and ends in March of each year, during which the flu vaccine is annually offered in October [23].

The Hijri calendar, also known in English as the Islamic calendar, consists of 12 months similar to the Gregorian calendar. Mass religious gatherings follow the Arabic Hijri Calendar in which Ramadan is in month 9 and Dhul Hijja is in month 12. According to data from the Ministry of Haj and Umrah, the umrah season opens for nine months according to the Hijri calendar (Safar, Rabi'- Al-Awal, Rabi' Al-Thani, Jumada Al-Aula, Jumada Al-Thani, Rajab, Sha'ban,

Ramadan, Shawal), while Hajj begins on the eighth day of Dhul Hijja and ends on the thirteenth day of the same Islamic month. Noteworthy is that the Kingdom of Saudi Arabia is the Custodian of the Two Holy Mosques (Al-Masjid al-Haram in Mecca city and Al-Masjid al-Nabawi in Medina city), considered the holiest in Islam. This attracts millions of Muslims from diverse geographical countries across the Muslim world to Jeddah, as it is the main gateway to the two holy cities especially during the months of Ramadan, or Hajj season annually, and/or to perform Umrah, which is allowed at any time of the year [24]. During these occasions of religious mass gatherings, the risk of transmitting respiratory illnesses, and introducing new pathogenic strains, or resistant organisms increases, especially if this coincides with the influenza (flu) seasons [25].

There are no existing reports addressing patients who present themselves to hospital care with fever during seasons of religious mass gathering, especially if this coincides with the flu seasons, hence the treatment approach of such cases may not be applicable to patients with NNF in a normal season. With this background, we conducted this study to determine the prevalence and clinical outcome of RTI in NNF children with cancer during major seasonal changes (mass gathering and flu season).

2. MATERIALS AND METHODS

This is a retrospective secondary analysis of our previous study aimed at evaluating the prevalence of RTIs in NNF children with cancer.

All children aged less than 15 years who were treated for malignancy at Princess Noorah Oncology Center (PNOC)-King Abdulaziz Medical City (KAMC)-Jeddah, Saudi Arabia from May 1, 2016 through December 2017 were eligible.

We followed the same analysis and methodology for collecting the missing data as in our previously published paper [3]. We also used the same chart review method for data collection, definition, classification, and data analysis as per our previously published study.

2.1 Definition

- Fever is defined as two spikes in temperature of more than 38° Celsius orally for over 30 minutes or at least 38.3° Celsius orally for over one hour.
- Non-Neutropenia episode is defined as a hospital visit with an absolute neutrophil count (ANC) ≥500 /µl.
- Respiratory tract infection (RTI) is an infectious process of the respiratory tract and can include both upper respiratory tract infection (URTI) or/and lower respiratory tract infection (LRTI) [26].
    - URTI includes common cold, laryngitis, pharyngitis/tonsillitis, acute rhinitis, acute rhinosinusitis, and acute otitis media.
    - LRTI includes acute bronchitis, bronchiolitis, pneumonia, and tracheitis.
    - If the patient had both symptoms of URTI and LRTI, they were classified as LRTI.
- Children were classified as ‘appearing well’ if the child was active, tolerating good oral intake, with no obvious focus of infection, abnormal exam, or hemodynamic instability such as unexplained tachycardia, tachypnea, desaturation, and hypotension. These patients were treated empirically with antibiotics in the outpatient setting along with a daily clinic follow-up until they were febrile for two consecutive days.
- Patients were admitted to hospital care if they did not meet the well-appearing criteria (i.e. lethargic, hypoactive, hypotensive, irritable, dehydrated, has decreased oral intake, or has prolonged duration of fever beyond 72 hours despite outpatient management).
- Diagnoses were classified using the International Classification of Childhood Cancer (ICCC) -O-3/WHO 2010 and grouped as lymphoma/ leukemia, neuroblastoma (NBL), brain tumor, and other tumor diagnoses [27].

2.2 Inclusion and Exclusion Criteria

Subjects were eligible for inclusion if they had at least one documented spike of fever at presentation during mass religious gathering seasons (Hajj, Ramadan) and/or the flu season.

Exclusion criteria:

- No respiratory symptoms indicating RTI
- Presented with a clear clinical focus of infection other than RTI during physical examination

- Cancer patients with underlying primary immunodeficiency
- Hematopoietic stem cell transplant recipients on active immunosuppression therapy
- Patients with Down's syndrome
- Patients on active chemotherapy with their neutrophil count expected to decline to less than 500 /µl in the next 48 hours

Outcome measures:

- Failure of primary treatment option determined by:
- Number of fever spikes
- Number of patients needing subsequent therapy (antibiotic modification and/or hospitalization)
- Prevalence rate of RTI in patients with NNF

Comparing the RTI rate during major seasons (mass religious gatherings and influenza seasons vs normal seasons).

In order to avoid biases in misclassification and to overcome missing data, we applied the same methodology for measuring or evaluating the treatment outcomes during the study period of mass religious gatherings and flu season versus the normal season.

2.3 Data Analysis

Descriptive statistics was done to summarize the demographic and baseline clinical characteristics using numbers and percentages in categorical data and means and standard deviations for continuous data if the data were normally distributed, while medians and quartiles were used if the data were not normally distributed. Comparison between categorical data was done using chi-square statistics, while a t-test was used to compare continuous with categorical data. A logistic regression analysis was conducted to examine the association of RTI with mass gathering in subjects with FNN after controlling for potential confounders. The odds ratio (OR) was used as a measure of this association with its 95% confidence interval (CI). All data were entered and analyzed through the statistical package SPSS 25 software (SPSS Inc., Chicago, IL, USA).

3. RESULTS

During the 20-month study period, a total of 480 non-neutropenic fever (NNF) episodes were identified in 131 children. Among these 131 children, 42 NNF children with a total of 136 NNF episodes were presented during religious mass gatherings (28 during Ramadan, 10 during Hajj, and 4 during Hajj concurrent with the flu season), and 89 NNF children with a total of 344 NNF episodes were presented during the Umrah season (35 during normal Umrah season and 54 during Umrah coincident with the flu season).

Among the 131 NNF children, 76 patients had respiratory tract infection symptoms (43 were RTI and had 4599 spikes of fever (92.4%). Of those 4599 spikes of fever, 455 spikes (9.9%) were documented during mass religious gatherings and the flu season. The overall rate of NNF spikes during mass religious gatherings was 5% (233 out of 4599), during the flu season it was 3.4% (156 out of 4599), and during mass gathering coincident with the flu season it was 1.4% (66 out of 4599) (Fig. 1).

The mean age of the patients was 6.4 ± 3.4 years, and 60.5% of the patients were male. A majority (71.8%) of the patients had a central venous catheter (CVC) implanted. Using the International Classification of Childhood Cancer (ICCC) -O-3/WHO 2010, the majority of the patients had leukemia, myeloproliferative diseases, and myelodysplastic diseases (66.9%). Table 1 summarizes the patients' basic demographic data.

3.1 The Prevalence of RTIs and Patient Characteristics

The prevalence of RTIs was 59.7% (74 out of 124) with a total of 245 fever spikes (245 out of 455, 53.8%). The mean temperature was 38.52°C with SD ± 0.56 and a mean CRP level (± SD) of 32.9 (± 47.9) mmol/L. Using the ICCC for diagnosis, a majority of the patients had leukemia (67.9%).

URTI was the most documented symptom in 87.8% (34 out of 74, 45.9% presented during mass religious gatherings (20 patients during Ramadan and 14 patients during Hajj), and 30 out of 74 (88.2%) were presented during the flu season. Cough, sore throat, and runny nose were the most common presented symptoms of URTI (29 out of 74, 39.2 %). Table 2 summarizes the demographic data of patients with fever presented with RTI during the study period.

3.2 Patient Characteristics and Outcomes during Mass Religious Gatherings

The RTIs rates: a total of 34 NNF patients were present during mass religious gatherings (20

patients during Ramadan and 14 patients during Hajj). The vast majority of these patients (26 out of 34, 76.5%) had an implanted central venous catheter (CVC). More than 80% (29 out of 34, 85.3%) of patients were presented with URTI, followed by 8.8% (3 out of 34) who had mixed symptoms of URTI and LRTI, and only 5.9% (2 out of 34) of patients had LRTI (one patient during Ramadan and one patient during Hajj). Table 3 summarizes the patients' characteristics presented with respiratory tract infection (RTI) during religious mass gatherings.

3.3 Failure of Primary Treatment Option

The total number of fever spikes recorded was 114 (64 spikes during Ramadan and 50 spikes during Hajj). None of the cases developed any microbiological positive culture.

Ceftriaxone-based therapy plus or minus oral macrolide (azithromycin or clarithromycin) was the main treatment approach for the majority of cases (76.5%, 26 out 34), followed by oral macrolide in addition to one of the beta-lactam antibiotics (14.7%, 5 out of 34), two patients (5.9 %, 2 out of 34) were treated with piperacillin-tazobactam plus gentamicin, and one patient (2.9 %, 1 out of 34) was treated with second-line antibiotics (meropenem in addition to vancomycin). Median days to fever resolution after starting antibiotics were 1 day (IQR 1-4), while the median duration of antibiotics use was 5 days (IQR 5-7). Out of 34 patients, 22 patients (64.7%) needed hospitalization. All of them (100%) had implanted CVC. The total documented spikes in fever were 68 with a maximum of 40-Celsius ± 0.66. Causes of hospital admission were decreased oral intake (1), lethargy (1), query relapse (1), prolonged fever (12), and persistent RTI symptoms despite fever resolution (7). None of the included cases needed intensive care (ICU) admission, and there was no case fatality associated with RTI.

3.4 Patient's Characteristics and Outcomes during the Flu Season

The RTIs rates: a total of 30 NNF patients were present during the flu season. A majority of patients were presented with URTI (26 out of 30, 86.7%). More than 60% of the patients had implanted CVC (19 out of 30). The total recorded number of fever spikes was 91 (maximum fever was 41-Celcius with ±0.66). None of the cases developed any microbiological positive culture. Table 4 summarizes the patients' characteristics presented with respiratory tract infection (RTI) during the flu season.

3.5 Failure of Primary Treatment Option

Ceftriaxone monotherapy was the main treatment approach for the majority of cases (60%, 18 out of 30). Modification of initial treatment was noted in 40% of patients (12 out of 30) as follows: oral clarithromycin or augmentin or IV vancomycin was added to ceftriaxone in 16.7% of patients (5 out of 30), five patients (16.7%, 5 out of 30) received oral antibiotic only with augmentin (2), penicillin (1), ciprofloxacin (1), and azithromycin (1). Two patients were treated with piperacillin-tazobactam plus gentamicin (6.6%, 2 out of 30). Median days to fever resolution after starting antibiotics were 1.5 days (IQR 1-4), and the median duration of antibiotics used was similar to the median duration of antibiotics used during mass gatherings which was 5 days (IQR 5-7). Out of 30 patients, 11 patients (36.7%) needed hospitalization. Only one of them had no CVC.

The total documented spikes in fever was 32 with a maximum of 39.1-Celsius ± 0.69. Causes of hospital admission were decreasing oral intake (1), prolonged fever (3), and fever resolved but symptoms persist (7).

3.6 NNF Cases during Mass Religious Gatherings Coinciding with the Flu Season

Of note, 10 out of 74 patients (13.5%) were presented with fever secondary to RTIs during mass religious gatherings (mainly Hajj) that coincided with the flu season. The vast majority of patients had CVC implanted (60%, 6 out of 10). The total documented spikes in fever was 40 with a maximum of 39.5-Celsius ± 0.53.

Table 5 summarizes the patients' characteristics presented with respiratory tract infection (RTI) during religious mass gatherings coincident with the flu season.

Ceftriaxone was the main treatment approach used in 90% (9 out of 10 patients). Of those, two patients received oral azithromycin in addition to ceftriaxone. Only one (10%) dehydrated unwell-looking child patient received piperacillin-tazobactam in addition to vancomycin. Four patients needed subsequent hospitalization with a mean CRP level of 52.6 ± 58.2. The main reasons for hospitalization were dehydration (1),

prolonged fever (1), and no fever but with RTI symptoms that persisted (2).

3.7 Anti-viral or Flu Vaccine

None of the included patients received the prophylactic flu vaccine for the flu season and none of the patients who were presented with RTI received the oral antiviral (oseltamivir).

3.8 Cases with Documented Respiratory Viral or Bacterial Infections

None of the clinically documented cases had microbiologically confirmed viral or bacterial infections.

4. DISCUSSION

In this study, RTI is found to be quite prevalent in NNF children with cancer. RTI was recognized in nearly 60% of NNF episodes. To our knowledge, no previous study has addressed RTI in children with cancer who were presented with fever and non-neutropenia during religious mass gatherings or the flu season. The majority of published studies have focused on respiratory viral infection in children with fever neutropenia (FN) [28-30]. Although in the current study we did not identify any respiratory pathogen in all included cases, which does not rule out respiratory viral infections, it may however co-exist with other pathogens [31].

The influenza pandemic is an unpredictable viral disease that can cause severe complications and result in hospitalization and death [32]. Children with cancer are special cases that are highly susceptible to developing severe infections by different respiratory viral pathogens including influenza (flu) [1,6,31,32]. We have reported a previously high failure rate of using ceftriaxone mono-therapy in children with NNF, and almost 43% of them were presented with respiratory symptoms [3]. Of note, in the current study, none of our included cases received a prophylactic flu vaccine and none of them received antiviral therapy during their treatment course. Additionally, mass gatherings, especially if coincident with the flu season, might be responsible for the RTI prevalence rates. Different approaches in managing such cases during important and special occasions or seasons may result in a delay in delivering appropriate therapy, inappropriate use of broad antimicrobials, treatment failure, overlooked important clinical findings, thereby resulting in re-admission or prolonged hospitalization.

The United States Advisory Committee on Immunization Practices (ACIP) has published updated guidelines in 2020 and they recommend using inactivated influenza vaccine for a variety of patient populations who are at an increased risk of complications from influenza including immunosuppressed patients (including immunosuppression caused by medications) [32]. It is the reality that there is neither any clear national data about the seasonality of different influenza strains nor is there data on the burden and impact of influenza infection or respiratory viral illness in children with cancer diseases.

Nowadays, people around the globe are facing a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the International Committee on Taxonomy of Viruses (ICTV) causing coronavirus disease 2019 (COVID-19). The novelty of the SARS-CoV-2 is that it quickly spread from Wuhan, China to other countries around the globe. The typical signs and symptoms range from mild to moderate such as fever, dry cough, dyspnea, fatigue, severe pneumonia, or even death [33-36]. At the time of writing this paper, no identified evidence-based treatment is readily available for use in pediatrics with cancer [37,38]. Of note, the first COVID-19 disease case caused by SARS-CoV-2 in Saudi Arabia was identified on March 2, 2020 [39].

Future studies looking at withholding unnecessary antibiotics use in children NNF with respiratory viral infections based on diagnostic microbiological and/or molecular results are highly recommended. This approach is particularly important since Jeddah city is year-round the main gateway to the two holy cities (Makkah and Madinah) during religious mass gathering seasons (Ramadan, and Hajj), and if coincident with the flu season the risk of viral infection may be higher.

The results of our study are important in the context of the current COVID-19 pandemic. During this time, the Saudi government took certain initiatives to reduce mass gatherings including halting all visits to Makah and Medina in addition to different measures of social distancing. These measures are important particularly in our region, as the present study showed that the rate/prevalence of NNF

secondary to RTI in children with cancer is increased during periods of mass gathering.

Major study limitations include the lack of national data on FNN during the flu season and religious mass gathering incidence and approach. The retrospective nature of the study has limited access to certain important information such as testing of respiratory pathogens. In addition, this is a single institution study that represents but a small number of patients.

Larger, multi-organization, nationwide studies should be conducted in the foreseeable future to corroborate our findings. Ultimately, we recommend setting up a national consensus guideline aimed at standardizing the clinical approach to NNF children with a suspected respiratory viral infection, providing evidence, sound effective antiviral therapy guide, and limiting unnecessary broad-spectrum antibiotics in this vulnerable patient population.

Table 1. Basic demographic and clinical characteristics of included NNF cases

Variables	**N=124**
Gender (%)	
Male	75 (60.5)
Female	49 (39.5)
Median Age in year ± SD	6.4 ±3.4
Location of preliminary treatment (%)	
Outpatient with follow up	116 (93.5)
Inpatient	8 (6.5)
Diagnosis (%)	
Leukemias, Myeloproliferative Diseases, & Myelodysplastic Diseases	83 (66.9)
Renal Tumors	8 (6.5)
Neuroblastoma & Other Peripheral Nervous Cell Tumors	7 (5.6)
CNS & Miscellaneous Intracranial & Intraspinal Neoplasms	5 (4)
Soft tissue and other extraosseous sarcomas	4 (3.2)
Malignant Bone Tumors	4 (3.2)
Other & Unspecified Malignant Neoplasms	3 (2.4)
Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	3 (2.4)
Lymphomas & Reticuloendothelial Neoplasms	2 (1.6)
Hepatic Tumors	2 (1.6)
Intracranial & Intraspinal Embryonal Tumors	2 (1.6)
Soft Tissue & Other Extraosseous Sarcomas	1 (0.8)
CVC (%)	
Central Line	89 (71.8)
Peripheral Line	35(28.2)
Mean Temperature °C ±SD	38.5 (0.57)
Median Absolute Neutrophil Count (IQR)	3.4 (1.9 – 5.7)
Religious Mass Gathering Seasons (%)	
Ramadan	40 (32.3)
Hajj	26 (20.9)
Coincidence flu season with Hajj (%)	14 (11.3)
Flu Season (%)	44 (35.5)
NNF cases presented with RTI (%)	
Yes	74 (59.7)
Need Subsequent Hospitalization	37 (50%)
No	50 (40.3)
Total Number of Fever episodes N, (%)	455
Mass gathering and flu season	154 (33.8)
No season	301 (66.2)

N: Number; SD, Standard Deviation; RTI, Respiratory Tract Infection; CVC, Central Venues Catheter; IQR, Interquartile Range; NNF, Non-Neutropenic Fever

Table 2. Characteristics of RTI cases presented with fever during major seasonal occasions (N= 245 Fever)

Number of fever episodes N=245, (%)		Mass gathering, No Flu	Flu season No mass gathering	Flu season coincident with mass gathering
		114 (46.5)	**91 (37.2)**	**40 (16.3)**
Gender	Male	74	48	22
	Female	40	43	18
Age	≤ 6 year	76	49	7
	6.1 – 12 year	37	39	31
	> 12	1	3	2
Fever days	<3 days	67	60	28
	3-7 days	47	29	12
	> 7 days	0	0	2
Chemo phase	Consolidation	35	5	3
	Maintenance	45	49	34
	Off chemotherapy	34	37	3

Table 3. Characteristics of NNF cases presented with respiratory tract infection (RTI) during religious mass gatherings

Variables	N=34
Gender (%)	
Male	20 (58.8)
Female	14 (41.2)
Median Age in year (IQR)	6 (3-8.85)
Phase of chemotherapy treatment (N)	
Induction	0
Consolidation	11
Maintenance	13
Off-treatment	12
RTI types (%)	
URTI	29 (85.3)
LRTI	2 (5.9)
Mixed	3 (8.8)
CVC (%)	
Central	26 (76.5)
Peripheral	8 (23.5)
Religious mass gathering season (%)	
Ramadan	20 (58.8)
Hajj	14 (41.2)
Location of preliminary treatment (%)	
Outpatient with follow up	31 (91.1)
Need Subsequent Hospitalization	22 (64.7%, 22 out of 31)
Inpatient	3 (8.8)
Total number of Fever episodes N, (%)	N=114
Ramadan	64 (56.1)
Hajj	50 (43.9)

N: Number; SD, Standard Deviation; RTI, Respiratory Tract Infection; CVC, Central Venues Catheter; IQR, Interquartile Range; NNF, Non-Neuropenic Fever

Table 4. Characteristics of NNF cases presented with respiratory tract infection (RTI) during flu season

Variables	N=30
Gender (%)	
Male	14 (46.7)
Female	16 (53.3)
Median Age in year (IQR)	7 (4.25-8)
Phase of chemotherapy treatment (N)	
Induction	0
Consolidation	3
Maintenance	14
Off-treatment	13
RTI types (%)	
URTI	26 (86.7)
LRTI	4 (13.3)
Mixed	0
CVC, (%)	
Central	19 (63.3)
Peripheral	11 (36.7)
Location of preliminary treatment (%)	
Outpatient with follow up	26 (86.7)
Need Subsequent Hospitalization	11
Inpatient	4 (13.3)
Total number of fever episodes (N)	**N=91**

N: Number; SD, Standard Deviation; RTI, Respiratory Tract Infection; CVC, Central Venues Catheter; IQR, Interquartile Range; NNF, Non-Neuropenic Fever

Table 5. Characteristics of NNF cases presented with respiratory tract infection (RTI) during mass religious gathering co-incidence with flu season

Variable	N=10 (%)
Gender (%)	
Male	6 (60%)
Female	4 (40%)
Median Age in year (IQR)	8 (7.25-9.75)
Phase of chemotherapy treatment (%)	
Induction	0
Consolidation	2 (20%)
Maintenance	7 (70%)
Off-treatment	1 (10%)
RTI types (%)	
URTI	8 (80%)
LRTI	2 (20%)
Mixed	0
CVC, (%)	
Central	6 (60%)
Peripheral	4 (40%)
Location of preliminary treatment (%)	
Outpatient with follow up	9 (90%)
Need Subsequent Hospitalization	4
Inpatient	1 (10%)
Total Number of fever episodes (N)	**N=40**

N: Number; SD, Standard Deviation; RTI, Respiratory Tract Infection; CVC, Central Venues Catheter; IQR, Interquartile Range; NNF, Non-Neuropenic Fever

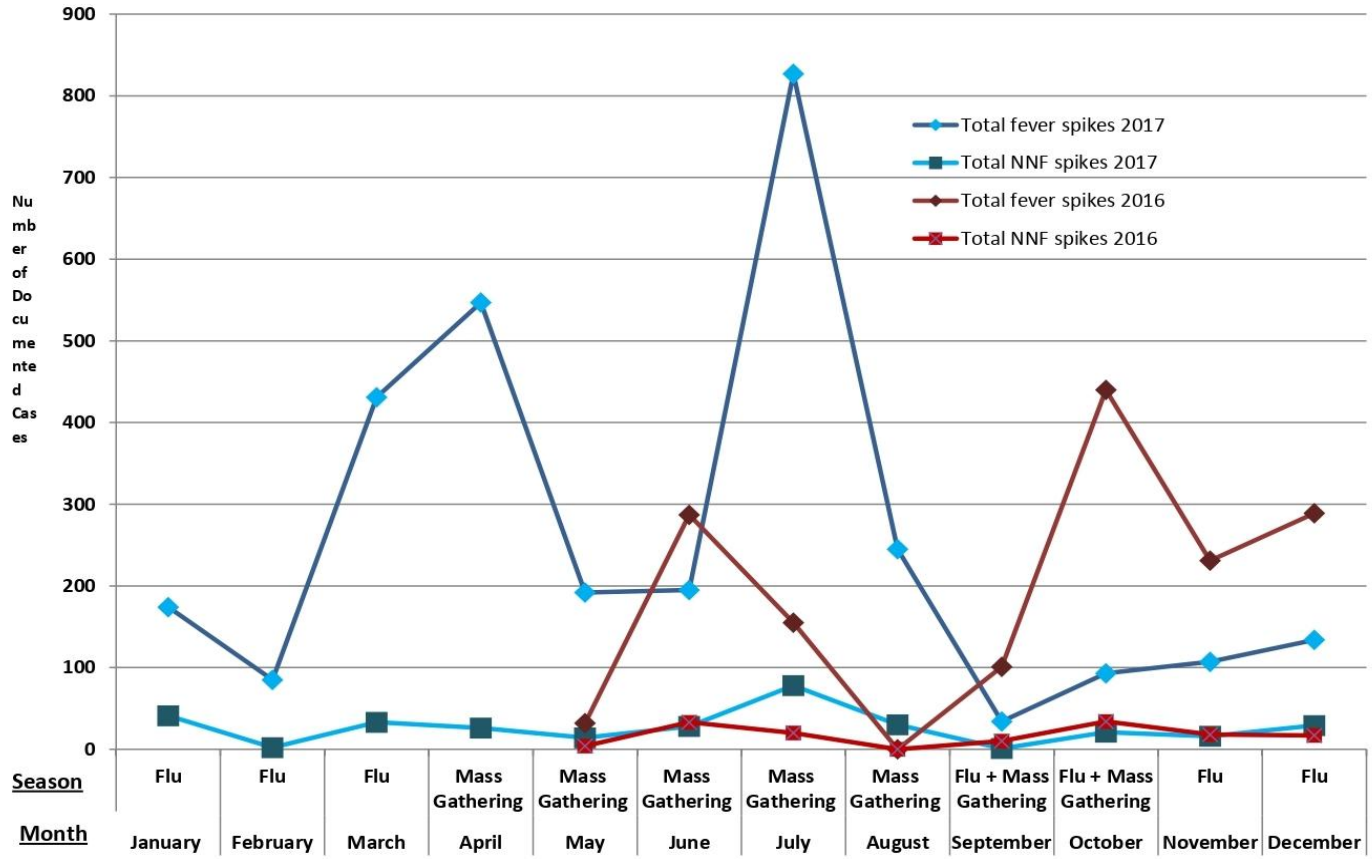

Fig. 1. Overall rate of fever spikes in NNF children with cancer in relation to total documented fever spikes over study period (May 2016 to December 2017)

5. CONCLUSION

Children with cancer are vulnerable to respiratory infections due to their chronic illness even if they are non-neutropenic, especially during major seasonal occasions (religious mass gatherings and flu season). RTI symptoms are associated with a prolonged period of fever, days of antibiotic use, and may result in subsequent hospitalization. Proactively implementing a surveillance program to ensure proper vaccination, early screening of virus during the season, proper education of patients and their families regarding appropriate infection control measures, and proper personal protection during major seasonal changes will help optimize their management.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

CONSENT

As per international standard or university standard, parental written consent has been collected and preserved by the author(s).

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https://www.eventscribe.com/2020/midyear/fsPopup.asp?efp=V1hQQ1pSWlc5NTcx&PosterID=325977&rnd=0.6944853&mode=posterinfo
https://midyear.ashp.org/-/media/midyear-conference/docs/2020/VMCM20-Professional-Poster-Listing-by-PA-Last-Name.ashx?la=en&hash=9D485E020DC2E54DDEA7402656409E48EAF35435
https://saudijclinpharm.com/article.asp?issn=WKMP0249;year=2022;volume=1;issue=1;spage=22;epage=43;aulast=.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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