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Mohamed Yassin

Background: Intensified chemotherapy increases susceptibility to infections. Respiratory viruses, including respiratory syncytial virus (RSV), parainfluenza virus and Influenza virus A and B are widespread in the community and easily transmitted to patients with hematological malignancy.

***Aim* of study**: to assess the prevalence, risk factors and prognosis of community acquired respiratory viruses in severe lower respiratory tract infections in hospitalized pediatric cancer patients.

Patients and Methods: Ninety children with cancer admitted in the Children's Hospital, Ain Shams University during the period from March 31th, 2007 until September 30 th, 2008 suffering from severe lower respiratory tract infections (LRTIs) were included. All were subjected to history and clinical examination; investigations included complete blood picture with differential leucocytic count, erythrocyte sedimentation rate, C - reactive protein and blood culture. Plain chest x-ray and computed chest tomography. A nasopharyngeal swab was examined by multiplex polymerase chain reaction for the following virus genomes: influenza A and B, parainfluenza serotypes 1 and 3 and respiratory syncytial virus. Clinical follow up of patients was done for assessment of clinical outcome.

Results: Hematologic malignancy was the underlying disease in 63.3% (57/90) patients. Forty five % (41/90) were in

remission and 54% (49/90) were in the induction stage. The prevalence of viral infection in the studied patients was 38.5% and 36.3% in patients with hematological and solid tumors respectively (P=0.83). The main presenting symptom of LRTI were fever, cough, expectoration and wheezy chest were prominent in 52.9% of patients with viral infection. Thirty two % (29/90) of patients developed respiratory distress in the form of tachypnea and chest retractions, 27% (8/29) of them were positive for viral infection.

Thirty two % (29/90) have positive blood cultures for bacteria (the main pathogen was Klebsiella) while 67.7% were negative.

Bacteria were identified as a single cause of LRTI in 17.7% (16/90), viruses in 27% (25/90), fungi in 4.4% (4/90) and mixed causes in 14% (13/90) {6.6% (9/13) mixed viral and bacterial, 4.4% (4/13) mixed bacterial and fungal}.

Nasopharyngeal swabs PCR were positive for viral infection in 34/90 (37.7%) patients, most of them were in May. Influenza virus was the commonest virus detected, being of type A in 16/90 (17%) cases, type B in 4/90 (4.4%) cases followed by Parainfluenza 1 in 9/90 cases (10%), and Parainfluenza 3 in 5 cases (5.5%). RSV was not detected in the studied patients.

Eighty seven patients (96%) were neutropenic 31/87 (35%) of them were positive for viral infection. 27/31 (79.4%) had

severe neutropenia, 3/31 (8.8%) had moderate neutropenia and 1/31 (2.9%) had mild neutropenia.

Seventy % of patients with viral infection had abnormal radiological findings in the form of increased bronchovascular marking in (58.8%), while (20.5%) had either patchy infiltrates or lung collapse in CT.

Eight patients (8.8%) were admitted to the pediatric intensive care unit; 6/8 (75%) for septic shock and disseminated intravascular coagulation and 2/8 for respiratory failure 62.5% had mixed viral and bacterial infections and 3/8 37.5% had mixed bacterial and fungal.

Six patients died during the course of the study (6.6%) from infection related sequelae: 2/6(33%) were having mixed viral and bacterial infections (one had parainfluenza 1 and the other had parainfluenza 3), 4/6 (66%) had mixed bacterial and fungal pathogen.

Conclusions: Respiratory viruses are common pathogens in LRTI, either as a single cause or mixed with bacterial pathogens in pediatric cancer patients. Viral etiology should be suspected with incorporation of antiviral therapy in those patients as there are no specific signs or symptoms. Mixed bacterial and viral infections had the worst prognosis. Rapid diagnostic tests for respiratory viruses should be incorporated in the routine workup

of patients with hematological malignancies as most of patients with viral infection had no specific radiological findings.

Abbreviations:

1.	ALL	Acute lymphoblastic leukemia
2.	AML	Acute myeloid leukemia
3.	ANC	Absolute neutrophilic count
4.	BAL	Broncho alveolar lavage
5.	BFM	Berlin-Frankfurt-Munich
6.	BMF	Bonn-Munich-Frankfurt
7.	BMT	Bone marrow transplantation
8.	BVM	Bronchovascular markings
9.	CBC	Complete blood count
10.	CML	Chronic myeloid leukemia
11.	CMV	Cytomegalovirus
12.	CNS	Central nervous system
13.	CRP	C-reactive protein
14.	CSF	Cerebro- spinal fluid
15.	CT	Computed tomography
16.	DIC	Disseminated intravascular coagulopathy
17.	FUO	Fever of unknown origin
18.	G-CSF	Granulocyte colony stimulating factor
19.	GvHD	Graft versus host disease
20.	HIV	Human immunodeficiency virus
21.	HSCT	Hematopoietic stem cell transplantation
22.	HSV	Herpes simplex virus
23.	ICU	Intensive care unit
24.	IDSA	Infectious Diseases Society of America
25.	IFN	Interferon
26.	IL	Interleukin

27.	INF A	Influenza A virus
28.	INF B	Influenza B virus
29.	LRTI	Lower respiratory tract infection
30.	NHL	Non Hodgkin lymphoma
31.	NK	Natural killer cells
32.	PCR	Polymerase chain reaction
33.	PIF	Parainfluenza virus
34.	RD	Respiratory distress
35.	RSV	Respiratory syncytial virus
36.	RT-PCR	Real-time polymerase chain reaction
37.	SARS	Severe acute respiratory syndrome
38.	SD	Standard deviation
39.	TNF	Tumor necrosis factor
40.	VAD	Vascular access device
41.	VZV	Varicella zoster virus
42.	WBC	White blood cell count

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INTRODUCTION

Cancer is a major disease burden worldwide but there are marked geographical variations in incidence overall and at specific organ sites. Reliable estimation of the number of incidence requires population-based cancer registration. Worldwide, approximately 10 million people are diagnosed with cancer annually and more than 6 million die of the disease every year; currently, over 22 million people in the world are cancer patients. In 2005 cancer killed approximately 42,000 people In Egypt 31,000 of those people were under the age of 70. **(W.H.O., 2007)**

The risk of any child developing acute leukemia is about 1 in 2,000. **(Geaves, 2002)**

Leukemia was a fatal illness until the early 1970s when effective chemotherapy and irradiation were introduced. Since then, the outcome of children with leukemia has improved steadily. Overall survival has increased from 25% to 75% with more intensive therapy and treatment adjusted to specific risk groups. **(Ramanujachar et al., 2006)**

Today, an important goal in improving the outcome of children with leukemia is associated with treatment-related factors. Intensified antileukemia treatment increases susceptibility to infections. Despite effective antimicrobial treatment of infections, they still are the leading cause of treatment-related morbidity and mortality. **(Slats et al., 2005)**

The occurrence of febrile episodes during anticancer treatment varies from 2.6 to 4.2 episodes per patient years at risk. The

microbiologic cause of infection or the focus of infection in children with cancer is found in 30% to 40% of the cases. **(Katsimpardi et al., 2006)**

The incidence of bacteremia varies from 8.5% to 28% in febrile episodes, Depending on the intensity of antileukemia therapy. **(Stabell et al., 2007)**

Mortality due to invasive infections is low, usually less than 10% but varying from 3% to 17%, depending on the immunologic status of the leukemic patient and on the microbiologic causal agent. **(Slats et al., 2005)**

Most septicemias occur in association with neutropenia and are caused by gram-positive bacteria. A considerable number of febrile episodes have remained classified as fever of unknown origin (FUO). Respiratory viruses are the most common cause of infections in children, and they are naturally a potential cause of febrile episodes in children with cancer. Respiratory viral infections in children with cancer have not been as common as would have been expected. **(Rahiala et al., 1998)**

Respiratory syncytial virus (RSV) and parainfluenza viruses have been the most common causative viruses. The most common respiratory virus, rhinovirus, has been searched for only in a few studies. **(Christensen et al., 2005)**

The role of these viruses in immunocompromised children is not yet clear. Prompt and reliable etiologic diagnosis of fever is crucial. It determines the patient's treatment and gives information on the clinical course and outcome of the illness. Unnecessary treatments should be avoided. In addition, economic losses, discomfort to the