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ACUTE VIRAL UPPER RESPIRATORY TRACT INFECTIONS IN PEDIATRIC ONCOLOGY PATIENTS UNDERGOING CHEMOTHERAPY

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ABSTRACT

Introduction: The mortality and morbidity in paediatric cancer patients has improved significantly over the last few years. However, viral infections continue to challenge the outcome in these children.

Methodology: A retrospective analysis to determine the etiology of acute upper respiratory tract viral infection in 40 paediatric patients undergoing chemotherapy was conducted. Nasopharyngeal swabs (NPS) were collected in these patients and analysed using Biofire Respiratory kit RP2 plus.

Results: A total of 38 viruses were detected from 40 NPS. In 6 patient samples, more than one virus was detected. Human Rhinovirus/ Enterovirus (n=17) was the most commonly detected isolate in this study. Age group of 1- 6 years (n= 26 viruses) was most commonly affected and prevalence of viral infection was found to be more common among the males (n= 24)

Conclusion: Rapid detection of a viral pathogen may provide the physician with an upper hand in initiating appropriate treatment, thereby reducing the financial burden imposed on the health system, and providing direct improvement in morbidity and mortality of children with cancer.

KEYWORDS : Paediatric cancer, viral infection, NPS

INTRODUCTION:

Viruses commonly affect upper respiratory tract in both adult and pediatric patients. During the last decades, survival rates in pediatric cancer have increased significantly. But despite many improvements in supportive care, infection remains second only to malignancy as a cause of death in pediatric oncology patients. Infections thus lead to mortality, resulting in prolonged hospitalization, delay in chemotherapy and poor quality of life, eventually leading to increased healthcare utilization and costs.[1]

Majority of episodes are due to febrile neutropenia and are accompanied by respiratory tract symptoms, which tends to resolve by next follow up. These results clearly indicate towards a causal relationship between respiratory viral infections and episodes of febrile neutropenia, but the concept is still in theory and further studies need to be conducted postulate an association.[2]

Respiratory syncytial virus (RSV), Rhinovirus, Enterovirus, Adenovirus, Influenza types A and B, Parainfluenza types 1, 2, and 3, Human Metapneumovirus (HMPV), Varicella zoster, Coronaviruses, and Human bocavirus (HBoV) have been recognized as causative agents of acute respiratory tract infection (ARI). Furthermore, paediatric patients on chemotherapy being immunocompromised are vulnerable to such infection with increased severity. [2-5] Incidences of these viruses may show seasonal variation.[6] VZV, HSV, and CMV can remain latent, during the course of chemotherapy or the underlying malignancy, reactivating at a later date.[7]

Several studies have shown that common respiratory viruses such as RSV, Adenovirus and influenza virus A, can cause severe infection in immune compromised patients and readily spread within hospital ward as well.

MATERIALS & METHODS

This study was conducted in the department of Microbiology, at Bai Jerbai Wadia Hospital for Children, Parel. 40 Nasopharyngeal swabs were collected from paediatric patients undergoing chemotherapy and presenting with suspicious acute viral infections, within the study period (September 2018 to February 2019). All samples were analysed using Biofire Respiratory kit RP2 plus. A retrospective analysis of etiology and associated factors in these infections was performed. An attempt was made to find correlation between the etiology, gender and age. Significance of involvement of single pathogen vs. multiple pathogens in the etiology of viral respiratory tract infections was also made. Out of the 40 NPS samples tested, 20 samples showed presence of viral pathogens/ pathogens. In all, 38 vital isolates were detected.

Table 1: Gender Distribution

Gender	No.	%
Males	27	67
Females	13	33
Total	40	

Table 1 show that 67% of NPS were collected from boys, while only 33% were collected from girls.

Table 2: Age vs. Gender Distribution

Age	No. of Patients	Male	Female
< 1	1	0	1
1 – 3	17	12	5
4 – 6	10	8	2
7 – 9	3	1	2
10 – 12	5	3	2
13 – 15	3	3	0
16 -18	1	0	1
Total	40	27	13

It is clearly seen from table 2, that majority of children belonged to age group of 1 to 6 years (n=27).

Table 3: Frequency Distribution of Viruses Detected

Organism	Frequency	Percentage
Coronavirus NL63	4	10.5
Coronavirus OC43	1	2.6
Influenza A H1- 2009	3	7.9
Influenza A H3	1	2.6
Parainfluenza virus 3	5	13.2
Parainfluenza virus 4	1	2.6
Human Rhinovirus / Enterovirus	17	44.7
Respiratory Syncytial Virus (RSV)	6	15.79

It is seen from Table 3 that Human Rhinovirus/ Enterovirus (n=17, 44.7%) is the single most common viral aetiology of acute upper respiratory tract inspection. This was followed by Respiratory Syncytial Virus (n= 6, 15.79%)

Table 4: Aetiology vs. Gender Distribution

Organisms	Detected	Male	Female
Coronavirus NL63	4	4	0
Coronavirus OC43	1	1	0
Influenza A subtype H1-2009	3	0	3
Influenza A H3	1	1	0
Parainfluenza Virus 3	5	2	3
Parainfluenza Virus 4	1	1	0
Human Rhinovirus/Enterovirus	17	12	5
Respiratory Syntial Virus (RSV)	6	3	3
Total	**38**	**24**	**14**

Table 4, depicts that most of the viruses caused infections predominantly in male children (n= 24), except Influenza A subtype H1-2009 which was seen to cause infections exclusively in female

children.

Table 5: Aetiology vs. Age Distribution

Organism Detected	Age in years					
	< 1	1-3	4–6	7-9	10-12	11–15
Coronavirus NL63	0	0	2	0	0	2
Coronavirus OC43	0	0	0	0	0	1
Influenza A subtype H1-2009	0	1	1	1	0	0
Influenza A H3	0	0	0	0	0	1
Parainfluenza Virus 3	0	3	2	0	0	0
Parainfluenza Virus 4	0	1	0	0	0	0
Human Rhinovirus/Enterovirus	0	10	2	1	4	0
Respiratory Syncytial Virus (RSV)	0	3	1	1	1	0
TOTAL	0	18	8	3	5	4

Table 5, shows that most viruses were detected from the NPS in the age group of 1- 3 years (n= 18) followed by 4-6 years (n= 8).

Table 5: Multiple Viruses from single NPS Sample

Age in years	Sex	Result
2	Male	Human Rhinovirus / Enterovirus, Parainfluenza Virus 3
2	Female	Human Rhinovirus / Enterovirus, Influenza A H1- 2009, Parainfluenza Virus 3, Respiratory Syncytial virus (RSV)
6	Female	Influenza A H1- 2009, Parainfluenza virus 3
6	Male	Coronavirus NL63, Human Rhinovirus / Enterovirus
6	Male	Coronavirus NL63, Human Rhinovirus / Enterovirus
15	Male	Coronavirus NL63, Coronavirus OC43

It is seen from Table 6 that, there were 6 patient samples from which more than 1 virus was isolated, the most common being Human Rhinovirus / Enterovirus (n= 5). Of the 6 samples, 4 were from male patients and 2 from female patients.

DISCUSSION:

Upper respiratory infection is the single most common cause why patients visit health care units. The symptoms associated with these infections, often mimic different pathogens. This makes diagnosis and initiation of a specific treatment difficult. As a result, the concept of syndromic testing is been widely accepted and adopted, where multiple agents of respiratory infection can be tested at the same time with a single test.[8,9]

The FilmArray ® 20 Respiratory Panel 2 (RP2) is a novel, multiplex in vitro diagnostic test which works on the principle of syndromic testing. It simultaneously and rapidly (~45 minutes) detects 22 pathogens directly from nasopharyngeal swab (NPS) samples.

This study includes patients with history of ALL, Intraspinal PNET, Primitive Neuroectodermal tumor, BCP – ALL, T-ALL, HLM, AML, B-ALL and T-ALL. Conditions observed in most of the patient are the symptoms of febrile neutropenia, respiratory distress, pneumonia, and cough. The gender ratio study analyses showed that majority of the respiratory infections due to viruses were observed in males than the females (Table.2). It might indicate an association between the hormones and immunity. Further research on this part can also help us to deal and treat hair loss during chemotherapy. Hair loss is associated with depression and is one of socially concern.

This study shows that patients in the age group of 1-3 years are highest affected, followed by 4-6 years age group, and the 10-15 years age group respectively. It indicates that the weaker immune status of the paediatric patients along with neutropenia provides an excellent environment for viruses to proliferate. Another reason is chemotherapy treatment affects the physical conditions, which in turn affects the food intake capacity, thereby altering their immunity. Also with growing age, the intake of nutritious food also increases. Hence age and food intake might be one of the associated factors responsible for increased susceptibility to viral infection. Cases of patient below 1 years of age with upper respiratory infections are comparative less as they are likely to be breast fed, which in turn provides them with passive immunity against such infections.

Aetiological condition shows the highest prevalence of Human Rhinovirus/ Enterovirus, with 45% of the individuals being affected. Rhinoviruses and Enteroviruses are related RNA viruses in the Picornavirus family. Rhinovirus is noted as causing the "common cold", but may also be involved in precipitating asthma attacks and severe complications. Enteroviruses can be associated with different clinical manifestations, including nonspecific respiratory illnesses in infants or adults. Respiratory Syncytial virus and human metapneumovirus are known to cause severe and prolonged lower respiratory disease in infants and children during cancer therapy. They also act as co-pathogens in association with other respiratory infections, in patients undergoing bone marrow transplants.[8] Seasonal Variation, antigenic drift and shift probably explains the lower detection of Influenza A viruses in this study.

86% of the multiple virus detected cases show the occurrence of 2 viruses, whereas a single cases showed the presence of 4 viruses. Detection of multiple viruses represents the immune condition of the patient. Higher the viruses less is the survival rate. Neutropenia condition weakens the immune system which gives rise to the invasion of viral, bacterial and fungal infection.

CONCLUSION:

Extensive study need to be carried out on these viruses, as this viral infection burden up the health condition of the patient. Seasonal variation in occurrence of virus, co- infection, shedding period and replication processes of viruses can help us to plan the treatment procedure efficiently. Instruments like RT-PCR along with the sign and symptoms help to detect virus faster and with accurate serotype. Rapid diagnosis of respiratory infections can lead to decreased length of stay, better antimicrobial stewardship, and better patient cohorting to prevent nosocomial infections.[10-15]

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