

## Review Article

## Viral Infections in Intensive Care Unit Patients

Donya Taghizadeh Maleki<sup>1</sup>, Amir Mohammad Goudarzi<sup>2</sup>, Morvarid Golrokh Mofrad<sup>3</sup>, Ebrahim Faghihloo<sup>1\*</sup>

<sup>1</sup> Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup> Asphalt and Bitumen Research Center (ABRC), School of Civil Engineering, Iran University of Science and Technology (IUST), Tehran, Iran

<sup>3</sup> Department of virology, Razi Vaccine and Serum Research Institute, Karaj, Iran

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### Abstract

**Background and Aim:** Viral infections in the intensive care units (ICUs) often involve the central nervous system or respiratory tract. These infections can cause significant morbidity and mortality. Science the fact that there is effective treatment against some viruses, knowing the viruses that cause infections in ICU can be a great help in managing these patients. Hence, the study reviewed the major viruses in the ICU.

**Materials and Methods:** We searched published articles on trends of viral infections in the intensive care units (ICUs). The articles were retrieved from databases of PubMed, Scopus, Google Scholar, and MEDLINE.

**Conclusion:** Due to the significant outbreak of viruses in the ICU and the presence of effective treatments against some viruses, knowing the important viruses in this area and rapid diagnosing and treatment can be important.

**Keywords:** Virus, Infection, ICU

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\*Corresponding Author: Ebrahim Faghihloo, PhD, Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: faghihloo@gmail.com

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### Introduction

Viruses are small structures which known as obligatory intracellular parasites, therefore they need host-cell machinery to replicate their DNA or RNA genome<sup>1</sup>. Viral diseases may be cause of significant morbidity and mortality. Patients with severe viral infections are often hospitalized in intensive care units (ICUs); on the other hand recent studies have shown the frequency of virus detection in ICU patients<sup>2</sup>.

ICU-acquired infections were defined as those acquired no less than 48 h after ICU admission. Patients hospitalized in ICUs are 5 to 10 times more

likely to acquire nosocomial infections than other hospital patients<sup>3</sup>. Viral infections in the ICU often involve the respiratory or the central nervous system and can cause significant morbidity and mortality especially in immunocompromised patients. Different types of viruses in ICU include *Orthomyxoviridae*, *Paramyxoviridae* (RNA viruses). *Adenoviridae*, *Herpesviridae* (DNA viruses)<sup>2</sup>. In addition, bacterial and viral co-infections may be a risk factor for ICU admission, severity of disease, and mortality. Like pneumonia that derived from both viral and bacterial agents<sup>4</sup>. Therefore in this study we survey the importance of viruses in ICU infections.

## Materials and Methods

The databases of PubMed, Scopus, Google Scholar, and MEDLINE were searched for published articles on trends of viral infections in the intensive care units (ICUs).

### Human rhinoviruses (HRV)

*Human rhinoviruses (HRV)* belongs to the *Picornaviridae* that is a family of small, icosahedral viruses with single-stranded, highly diverse positive strand RNA genomes. These viruses are responsible for more than one-half of cold-like illnesses<sup>5</sup>. HRV is divided into 3 distinct species: HRV species A, B, and C<sup>6</sup>. HRV is one of the most important viral agents that cause acute respiratory tract infections and has been detected in upper and lower respiratory tract<sup>7</sup>. HRV infections occur during all four seasons and were more common in spring and autumn. Respiratory syncytial virus predominated from November to February<sup>8</sup>. RSV and HRV were the viruses identified most frequently in mixed infections in infants hospitalized with bronchiolitis<sup>9</sup>. HRV species C is associated with respiratory tract infections, severe asthma exacerbations in children, apnea in infants and neonatal intensive care unit (NICU) infections<sup>10,11</sup>.

In 2011, Reid et al studied the prevalence of human rhinovirus species C infection in a neonatal intensive care unit in the state of Tasmania, Australia. During this study, all infants in NPICU and SCN underwent screening for HRV using nasopharyngeal swabs. From 21 infants in the collocated NPICU/SCN, 15 infants underwent screening for HRV, Eight infants were tested for HRV in the NPICU; 3 were positive (37.5%). Two infants had respiratory tract signs at the time of screening and one of them had a positive PCR for HRV. Of the 6 infants who had no signs of respiratory disease at the time of screening, 2 had positive PCR for HRV. Seven infants were tested in SCN and 1 was positive (14.3%). Three of these infants had signs of respiratory disease with 1 having a positive PCR for HRV. No children without signs of respiratory disease tested positive in the SCN. All infants with positive HRV PCR were managed with droplet and contact precautions and cohorted in their

respective units<sup>6</sup>.

In another study, viral infections in patients with severe pneumonia requiring intensive care unit admission were performed in Seoul, Republic of Korea. From a total of 198 patients, 104 patients were tested for respiratory viruses by BAL fluid RT-PCR. The results shown that 72 patients (36.4%) had a viral infection. Rhinovirus was the most common identified virus (23.6%)<sup>8</sup>.

In 2016, Reese et al. studied Evidence of nosocomial transmission of human rhinovirus in a neonatal intensive care unit. All visitors are screened by the patient's nurse for signs of illness and asked to leave if they are ill. Respiratory symptoms were seen in 2 infants. Respiratory viral testing and routine bacterial cultures were undertaken. The results show that 2 nosocomial cases of HRV species C<sup>12</sup>.

### Influenza virus

The *influenza* virus is an epidemic infectious agent that belongs to the Orthomyxoviridae<sup>13</sup>. This family includes the influenza viruses A, B, C and D. They are pleomorphic viruses, with 7–8 single strand RNA, segments assembled with proteins to form a helical nucleocapsid. It has an envelope with two types of long glycoprotein spikes: one type with haemagglutinin activity (HA) and one type with neuraminidase activity (NA). Type A viruses can infect and transmit across a broad host range (humans, mammals and birds), whereas types B and C do not appear to be capable of animal-to-animal or animal-to-human transmission. Type A is the cause of global pandemics, whereas types B and C tend to produce more localized outbreaks and milder forms<sup>14</sup>. Severe acute respiratory viral infections, including *influenza*, are the principle causes of global morbidity and mortality. *influenza* infects approximately 10%-20% of the world's population, annually<sup>15</sup>. Therefore, H1N1 and H3N2 are known as the seasonal *influenza* A virus subtypes<sup>16</sup>. Influenza remains an important epidemic viral infection. Influenza virus is the most common causative agent for severe respiratory viral infections in the intensive care unit (ICU), and frequently encountered viruses that usually cause mild disease<sup>17</sup>. Medical and neonatal ICUs, transplant units, chronic care wards, and nursing homes are at increased risk for nosocomial outbreaks of influenza,

which are characterized by abrupt onset and rapid spread. In April 2009, a new swine-origin H1N1 influenza A virus was detected in Mexico, which was called pandemic H1N1 (pH1N1). In the intensive care units (ICUs), patients with influenza A (H1N1) pdm09 virus infection continue to be a seasonal problem, and experience a high mortality rate<sup>18</sup>.

In 2009, Tabarsi et al. assayed death factors associated in intensive care unit admission due to pandemic 2009 influenza A (H1N1) infection. Samples including nasopharyngeal aspirates/swabs and endotracheal/bronchoscopic aspirates from 46 hospitalized patients were admitted to the ICU, 20 (43%) were admitted to the ICU and 7 (15%) died. The mean age of patients was  $36.9 \pm 12.92$  years (range: 15–66, median: 32) and only one patient was over 65 years old. The male-to-female ratio was 1.3:1 (26:20). Out the seven patients (15.2%) were cigarette smokers and 10 (21.7%) were drug abusers. H1N1 infection was confirmed by real-time reverse transcriptase polymerase chain reaction (rRT-PCR)<sup>19</sup>. In 2012, Choi et al. studied the prevalence of viral infections in patients with severe pneumonia requiring intensive care unit admission using bronchoalveolar lavage (BAL) samples from 198 patients (64 with community acquired pneumonia (CAP) and 134 with healthcare-associated pneumonia (HCAP)). The RT-PCR results showed that influenza virus detected in 16.7% of samples (9.4% CAP, 4.5%HCAP)<sup>8</sup>.

In 2010, Hashemian et al. performed secondary infection and clinical aspects after pandemic swine-origin influenza a (H1N1) admission in an Iranian critical care unite. The patient's throat discharge swab was cultured and evaluated with RT-PCR. Of 46 patients hospitalized with confirmed diagnosis of swine flu pneumonia (H1N1), 20 cases (43.7%) admitted in ICU<sup>20</sup>.

Pérez-Carrasco et al. studied influenza infection in the intensive care unit. From 163 patients, influenza infection was detected in 41 patients, and influenza A viruses were mainly responsible. Only five patients had influenza B virus infection<sup>18</sup>.

## Human parainfluenza virus (HPIV)

Acute respiratory tract infections (ARTIs) in childhood major cause of morbidity and mortality, with pneumonia being the leading cause of death among children between one and five years old<sup>21, 22</sup>. The human *parainfluenza* viruses are single-stranded and first discovered in 1950<sup>23-25</sup>. HPIVs account for a wide range of clinical reflections including colds, croup, bronchiolitis, and pneumonia<sup>5</sup>. Seasonal HPIV virus epidemics result in a significant burden of disease in children and account for 40% of pediatric hospitalizations for lower respiratory tract illnesses (LRTIs) and 75% of croup cases<sup>26, 27</sup>.

In 2013, Sahar Essa et al. performed the potential influence of human parainfluenza viruses detected during hospitalization among critically ill patients in Kuwait, 2013-15. Of 1510 patients admitted to ICU (37.5%) and PICU (62.5%) with viral infections. A total of 39 (2.6%) patients were found to have confirmed PIV infections, with 21 (1.4%) in ICU and 18 (1.2%) in PICU. The most frequently isolated PIV type was type 3 (28, 71.8%) followed by type 1 (9, 23.1%). The least frequently isolated PIV type was type 4 (2, 5.1%), and type 2 was not detected. Samples were detected by reverse transcriptase-polymerase chain reaction (RT-PCR)<sup>25</sup>.

In 2012, Choi et al. studied the viral infections in intensive care unit hospital in Seoul, Republic of Korea. From 198 patients, 72 patients (36.4%) had a viral infection and after detection by reverse-transcription polymerase chain reaction (RT-PCR), the rate of parainfluenza virus was (20.8%)<sup>8</sup>.

Retrospective study from January 2003 through December 2009 was carried out on influenza and parainfluenza associated pediatric ICU Morbidity. Every child in the PICU with a laboratory-confirmed influenza or parainfluenza infection was included. A total of 17 parainfluenza admissions were identified over the 7-year period. Parainfluenza type 3 (n=9) was the commonest subtype of parainfluenza infection. The results illustrates the important of parainfluenza viruses in PICU morbidity<sup>28</sup>.

## Human Respiratory Syncytial Virus (HRSV)

Human Respiratory Syncytial Virus (HRSV) belongs to the family *paramyxoviridae* of RNA viruses and has ssRNA genome<sup>14</sup>. This virus is divided into two major antigenic groups A and B on the basis of the G protein variability<sup>29</sup>. It has envelope that contains a fusion protein that causes host cells to form multinucleated giant cells (syncytia)<sup>14</sup>.

Human respiratory syncytial virus is a major cause of acute lower respiratory infection (ALRI) in young children; it also affects adults and the elderly people and immunocompromised patients. RSV infection manifests symptoms ranging from sinusitis and otitis media to bronchiolitis and pneumonia<sup>30</sup>. But general symptoms include fever, headache, myalgia, sneezing, sore throat, dry cough, rhinorrhea, bronchitis and otalgia, but the infection can spread to the lower respiratory tract of the risk groups mentioned above, which subsequently leads to severe bronchiolitis and pneumonia<sup>29</sup>. HRSV can cause considerable morbidity and mortality in leukemia patients<sup>31</sup>.

Approximately 0.5% to 2.0% of all children are hospitalized with lower respiratory tract disease, of which 50% to 90% have bronchiolitis and 5% to 40% have pneumonia<sup>32</sup>. 90% of children are infected with RSV during the first 2 years of life and up to 40% of them will develop acute lower respiratory tract infection (LRTI)<sup>33,34</sup>.

Antonio Piralla et al worked on respiratory patients admitted to 26 intensive care units in seven consecutive winter-spring seasons from 2009 to 2016 in Northern Italy. During the study period, 414 (266 males and 148 females) patients were hospitalized in 26 ICUs with severe respiratory distress. Respiratory samples were tested with a panel of laboratory-developed real-time RT-PCR or real-time PCR able to detect the viruses: hRSV types A and B. Overall, results for hRSV showed 13/226 or 5.8%<sup>35</sup>.

Caroline Breese Hall et al. performed a study about RSV-associated hospitalizations among children less than 24 months of age. from 2000 to 2005 they studied on 2149 patients and they found 559 positive RSV cases by RT-PCR<sup>36</sup>.

Leung et al. worked on epidemiology and risk factors

for RSV infections requiring pediatric intensive care admission in Hong Kong children from 2009 to 2011. Respiratory samples were detected by direct immunofluorescence and/or viral culture. A total of 118 (2.4%) PICU admissions were identified among 4,912 RSV-positive pediatric cases in eight hospitals<sup>37</sup>. In 2014, Faghiloo et al. performed a study to determine genotype circulation pattern of both group of A and B of HRSV strains in Iran. From 485 children <2years of age who were negative for influenza viruses, showed for the presence of HRSV in this research. HRSV was detected in 94 (19.38%) of the samples using nested RT-PCR. Group A viruses were isolated during each year, while group B viruses were isolated during 2009 and 2013<sup>38</sup>. And in the same study revealed that multiple genotypes of subgroup A co-circulated during the season 2007–2008 in Iran<sup>39</sup>. In another investigation, Faghiloo et al studied on genetic diversity in the G protein gene of HRSV among Iranian children less than 5 years with acute respiratory symptoms in 2011. A total of 107 throat swabs were tested by RT-PCR. Of the 107 samples, 24 (22.42%) were positive for HRSV, of which 16 (66.6%) belonged to subgroup A and 8 (33.4%) to subgroup B. Phylogenetic analysis showed that subgroup A strains fell in two genotypes GA1 and GA2, whereas subgroup B strains clustered in genotype BA<sup>40</sup>.

## Herpes simplex viruses (HSV)

*Herpesviridae* includes a large family of double-stranded DNA viruses that infect both animals and humans. Eight herpesviruses are known to infect humans: herpes simplex virus type-1 and 2 (HSV1, HSV2), varicella zoster virus (VZV), human cytomegalovirus (HCMV), Epstein-Barr virus (EBV), human herpesvirus 6 type-A and B (HHV6), human herpesvirus type-7 and 8 or Kaposi's sarcoma virus (HHV7, HHV8)<sup>41,42</sup>.

Humans are the only species known to be infected with two distinct herpes simplex viruses: HSV-1 and HSV-2. Human herpes simplex viruses are ubiquitous, with over two-thirds of the human population infected by at least one virus<sup>43</sup>. HSV-1 and HSV-2 establish latency in different neuronal subtypes (A5+ and KH10+) in murine trigeminal ganglia, results which

**Table 1:** Virus detection in ICU.

Authors	Date	Patients	Diagnostic Method(s)	Detected Viruses in ICU								
				Adenovirus	RSV	HSV1,2	CMV	EBV	Influenza	Parainfluenza	Rhinovirus	
Cassir N et al.	2012	30	Real-Time PCR	7 (23.3%)	-	-	-	-	-	-	-	-
Ganime AC et al.	2014	141	qPCR (Taq man)	63 (44.7%)	-	-	-	-	-	-	-	-
Dingyu Tan et al.	2012_2014	15	Real-Time	15 (100%)	-	-	-	-	-	-	-	-
Ersoy et al.	2102	24	PCR	14 (58.3%)	-	-	-	-	-	-	-	-
Antonio Piralla et al.	2009 - 2016	226	RT-PCR, Real-Time	-	13 (5.8%)	-	-	-	-	-	-	-
Caroline B.H et al.	2000 - 2005	2149	RT-PCR	-	559 (26%)	-	-	-	-	-	-	-
Leung T.F et al.	2009 - 2011	4912	Direct Immunofluorescence	-	118 (2.4%)	-	-	-	-	-	-	-
Andrew H.walton et al.	2014	560	qPCR	-	-	76 (14.1%)	-	-	-	-	-	-
Lepiller Q et al.	2015	1556	PCR	-	-	185 (11.8%)	-	-	-	-	-	-
Andrew H.walton et al.		560		-	-							
Lepiller Q et al.		1556	PCR	-	-							
Pica F et al.	2013 - 2014	49	Real-Time PCR	-	-	19 (38%)	-	-	-	-	-	-

Ali A et al.	2018	83	qPCR	-	-	2 (2.4%)	-	-	-	-
Coisel et al.	2012	93	PCR	-	-	-	22 (23.6%)	-	-	-
Heininger et al.	2011	86	PCR	-	-	-	35 (40%)	-	-	-
Narvaez-Arzate RV et al.	2013	135	Nested PCR	-	-	-	2 (1.48%)	-	-	-
Osawa R et al.	2016	100	PCR	-	-	-	20 (20%)	-	-	-
David S.Yong et al.	2011	544	q-PCR	-	-	-	271 (68%)	-	-	-
Amanati A et al.	2017	44	PCR	-	-	-	6 (13.6%)	-	-	-
Tabarsi et al.	2009	46	RT-PCR	-	-	-	-	20 (43.4%)	-	-
choi et al.	2012	72	RT-PCR	-	-	-	-	12 (16.7%)	15 (20.8%)	17 (23.6%)
Hashemian et al.	2010	46	RT-PCR	-	-	-	-	20 (43.7%)	-	-
Sahar Essa et al.	2013	1510	RT-PCR	-	-	-	-	-	39 (2.6%)	-
AB Reid et al.	2010	21	PCR	-	-	-	-	-	-	6 (28.5%)
Reese S et al.	2016	32	PCR	-	-	-	-	-	-	2 (6.25%)

connect with restricted productive infection in these neurons *in vitro*<sup>44</sup>. HSV-1 is associated mainly with infectious of the mouth, pharynx, face, eye, CNS and HSV2 is associated principally with infectious of the anogenital region, although both serotypes may infect any area<sup>45</sup>. HSV infections in the ICU often involve the respiratory (pneumonia) or the central nervous system (encephalitis, meningitis, myelitis) and can cause significant morbidity and mortality especially in immunocompromised patients<sup>2</sup>. Walton et al. studied on reactivation of multiple

viruses in patients with sepsis. A total of 560 septic patients were analyzed by quantitative PCR. Cumulative HSV DNA detection rates in blood were 14.1% among other viruses. Patients who had HSV in blood had increased risk of developing opportunistic bacterial infections which was independent of length-of-stay. For CMV and HSV, the number of ICU days was roughly doubled in patients who were viral positive versus viral negative<sup>46</sup>. Lepiller et al. performed a study to determine the clinical relevance of herpes simplex

virus viremia in ICU patients. 1556 blood samples obtained for HSV PCR analysis in ICU patients over 4 years. HSV DNA was detected in 11.8% of samples. The mortality rate in HSV-viremic patients was not significantly increased compared to the overall mortality rate in the ICU. Only patients with high HSV viral loads tended to have a higher, though non-significant, death rate. Our results suggest HSV viremia is common in ICU patients, potentially preferred by immunocompromised condition and mechanical ventilation<sup>47</sup>.

In another investigation by Pica et al. studied on clinical features and outcome of hospitalized patients with HSV-1 DNA in the lower respiratory tract 49 patients of University Hospital Tor Vergata, Rome, Italy, from May 2013 to June 2014, were analysed for presence or absence of HSV-1 DNA. 19 individuals were positive. These results recommend that detection of HSV-1 DNA in BAL fluid specimens is a marker of disease severity and poor outcome. More prospective studies are necessary to deepen the HSV-1 DNA detection in the lower respiratory tract of hospitalized patients<sup>48</sup>.

Ali A et al. performed a study in 2018 in IRAN to determine Prevalence of HSV in 140 Bronchoalveolar Lavage samples (BAL) of 83 critically ill children undergoing mechanical ventilation at a PICU. Samples were analyzed by qualitative PCR. The estimated prevalence of HSV1 was 2.4%<sup>49</sup>.

## Epstein-Barr virus (EBV)

The *Epstein-Barr virus (EBV)*, also called human herpes virus 4 (HHV-4), is one of eight known human herpes virus types in the herpes family. And it is latent in at least 90%–95% of people, which is the highest rate for herpes virus<sup>50</sup>. EBV infection may suppression of patient immune system in several ways, like influence the proper host response to other pathogens and may lead to a bad outcome for critically ill patients. Detection of EBV in lower respiratory tract (LRT) and serum samples have been reported in the ICU population<sup>51,52</sup>.

In 2017, Amanati et al. performed prevalence of human herpes viruses in bronchoalveolar lavage of critically ill children undergoing mechanical

ventilation a pediatric Intensive Care Unit. Out of 83 patients, 44 cases were male (53%) and (47%) were female. The average age of patient was 29 months. Overall, 19 patients were positive for HHVs. Among them the rate of EBV-PCR in 6 patients were (7.2%), and CMV-PCR in 2 patients were (2.4%)<sup>48</sup>.

## Cytomegalovirus (CMV)

Cytomegalovirus is known as an important cause of viral intrauterine infection and disease in immunocompromised patients<sup>53</sup>. Although nearly all CMV infections remain latent and asymptomatic, numerous studies have found that systemic viral reactivation is common in immunocompetent critically ill adults. Some studies have demonstrated an association between CMV infection and increased mortality rates and prolonged intensive care unit and hospital length of stay<sup>54</sup>.

Cytomegalovirus (CMV) is a member of the *herpesviridae* family. It has an envelope with icosahedral symmetry containing a large genome of double stranded DNA<sup>55</sup>.

More than two decades ago, Domart and colleagues were the first to indicate a pathogenetic role for Cytomegalovirus in non-canonically immunosuppressed patients. In a cohort of 115 consecutive adult patients with mediastinitis after cardiac surgery, CMV shedding in urine, as determined by viral culture, was documented in 25% of patients of whom 79% had viremia<sup>56</sup>. study performed by Kalil and Florescu showed that the diagnosis rate of CMV infection increased significantly (from 1 to 21%) when patients who spent five or more days in the ICU<sup>57</sup>.

with review of studies indicating the clinical manifestations of severe CMV disease in immunocompromised ICU patients found that the gastrointestinal tract (hepatitis, gastroenteritis, duodenitis, enteritis, colitis, proctitis) is to be the most common, followed by central nervous system (encephalitis, myelitis, encephalomyelitis, meningitis, and meningoradiculopathy), and hematological system (hemolytic anemia, thrombocytopenia, disseminated intravascular coagulation, and pancytopenia)<sup>58-61</sup>. Papazian et al. studied patients presenting ARDS and their open-lung biopsies to report that pneumonia is a well-known clinical

manifestation of CMV disease in immunocompromised patients<sup>62</sup>. A study performed by Ong et al. showed that immunocompetent patients with ARDS and found a CMV reactivation incidence of 27%, which was associated with significant increase in ICU mortality<sup>63</sup>.

Osawa et al. showed that CMV reactivation was associated with fewer ICU- and ventilator-free days, however overall mortality was not affected. Patients already in the ICU at the onset of sepsis had higher risk of CMV reactivation<sup>64</sup>.

Coisel et al. studied patients mechanically ventilated who are seropositive for CMV and found serious increased mortality in CMV-positive group; in addition, the diagnostic yield of BAL CMV PCR was 73% in comparison with the detection of CMV antigenemia which was 46%<sup>65</sup>.

Heininger et al. studied patients admitted with severe sepsis of whom 31% developed ICU acquired pneumonia and have shown slightly different diagnostic yield of tracheal aspirate CMV PCR of 70 versus 62% using blood CMV PCR<sup>66</sup>. As in adult studies, CMV replication in blood is apparently to be the best measure of uncontrolled systemic viral infection in critically ill children. Although CMV in BAL fluid may simply represent shedding, high viral loads are predictive of CMV pneumonitis in transplant recipients and, perhaps, in critically ill children. Thus, pediatric ICU studies should incorporate CMV testing of BAL fluid<sup>67-69</sup>.

Narvaez et al. worked on a study to determine the incidence of congenital CMV infection and the frequency of postnatal infection in a neonatal intensive care unit (NICU). They collected Urine samples of 135 infants who were admitted to the NICU during a 6-month period to detect CMV and they used nested PCR assay. A breast milk sample was obtained to determine viral excretion. CMV was diagnosed in two infants (1.48%). Post-natal infection was documented in four of 36 (11.1%) infants. Therefore, CMV excretion in breast milk is frequent and is associated to congenital and postnatal infection<sup>70</sup>.

## Human Adenoviruses (HAdVs)

Since first isolation from adenoid tissue over 60

years ago human adenoviruses (HAdVs) (*adénos, gland*) have contributed many challenges in clinical settings<sup>71</sup>. HAdVs are non-enveloped, double-stranded DNA viruses, pervasive in the environment. HAdV pneumonia mostly is limited to newborns, immunocompromised patients, and military camp populations. Adenoviruses cause mild infections including the upper or lower respiratory tract, gastrointestinal (GI) tract, or conjunctiva. Rare demonstrations of AdV infections include hemorrhagic cystitis, hepatitis, hemorrhagic colitis, pancreatitis, nephritis, and encephalitis<sup>72</sup>.

The 57 identified types of HAdVs have been classified into 7 species, A to G, on the basis of their serological, biochemical and genetic criteria<sup>73</sup>. HAdV-3 of species B is among the most common types implicated in endemic and epidemic HAdV infections in children and adults in the world<sup>74-78</sup>.

Over the last few years of HAdV-3 has become the main agent of acute respiratory infection worldwide and including 15 to 87% of adenoviral respiratory infections<sup>74,76,78-81</sup>.

Cassir et al. described the first outbreak of severe pneumonia caused by human adenovirus type 1, which included immunocompetent patients in an ICU of France, and occurred between September and October 2012. Seven successive patients were diagnosed by HAdV specific real-time PCR with a positive bronchoalveolar lavage. Their findings submitted that HAdV-1 could be considered as possible cause of severe pneumonia even in immunocompetent patients with potential to cause outbreak in ICU<sup>82</sup>.

Ganime AC et al. studied on viability and distribution of a hAdv on fomites in an Intensive Care Unit of a private hospital in Rio de Janeiro, Brazil. In this study 141 samples were collected and screened by quantitative PCR (qPCR) using TaqMan System. Among them 63 samples (44.7%) were positive. The viability was indicated by integrated cell culture/nested-PCR in 5 out of 10 samples. Nucleotide sequencing confirmed all samples as HAdV and characterized one of them as specie B, serotype 3 (HAdV-3). The results determined the risk of nosocomial transmission via contaminated fomites<sup>83</sup>.

In another study Dingyu et al. 2012-2014 in Northern China, 15 immunocompetent patients who had severe



community-acquired pneumonia (CAP) were evaluated for Adv infection. A total 15 cases were confirmed with HAdV as the only pathogen of pneumonia. And the HAdV-55 sub-type play an important role among viral pneumonia pathogens in hospitalized immunocompetent adults. Two patients with HAdV positive samples were excluded due to coinfection with *Legionella pneumophila* and *S. pneumonia* respectively<sup>84</sup>.

Ersoy et al. described an outbreak of adenovirus conjunctivitis, which occurred between 15 January and 25 February at a neonatal intensive care unit of a university hospital in Turkey. Adenovirus type 8 was identified in 14 samples by PCR analysis<sup>85</sup>.

## Discussion

Viral infections are 5 to 10 times more likely in ICU. This review real tht these infections in the ICU often involve the respiratory or the central nervous system and include different types of viruses such as Human rhinoviruses (HRV), Influenza virus, Human parainfluenza virus (HPIV), Human Respiratory Syncytial Virus (HRSV) (RNA viruses) and Herpes simplex viruses (HSV), Epstein–Barr virus (EBV), Cytomegalovirus (CMV) and Human Adenoviruses (HAdVs) (DNA viruses).

## Conclusion

Due to the significant outbreak of viruses in the ICU and the presence of effective treatments against some viruses, knowing the important viruses in this area and rapid diagnosing and treatment can be important.

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None.

## Conflict of interest

The authors further declare that, they have no conflict of interest.

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