A REVIEW OF RESPIRATORY AND ENTERIC VIRAL DISEASES

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Abstract: Enteric infections cause acute gastroenteritis rank along with respiratory tract infections which affect animals and humans of all age groups worldwide. Annually there are 1.7 million deaths from diarrheal diseases and 1.5 million deaths from respiratory infections worldwide. Viruses are a significant cause of morbidity and mortality around the world. The outbreaks occur often in hospitals, nursing homes, health care centers as well as in individual homes. Due to the high number of outbreaks and frequency of infection, the burden of disease is high. They can enter the body through various sites including the respiratory and enteric tracts by aerosolized droplets, droplet nuclei, or the fecal–oral route. They cause an estimated 60% of human infections, and most common illnesses are produced by respiratory and enteric viruses. Unlike bacterial disease, viral illness cannot be resolved with the use of antibiotics. To date there are no vaccines or antiviral drugs for most common enteric and respiratory viruses with the exception of influenza virus and hepatitis A virus (HAV).

***IndexTerms* – Enteric infections, gastroenteritis, fecal-oral route.**

1. INTRODUCTION

Respiratory viral infections are a leading cause of severe illness and mortality in immunocompromised and non immunocompromised hosts [1]. The severity of these illnesses can vary markedly from mild or asymptomatic upper airway infections to severe wheezing, bronchiolitis or pneumonia [2]. In most cases, respiratory viral infections are self-limiting and confined to the upper airways, where they evoke relatively mild symptoms such as sneezing and a runny nose [3]. However, in susceptible individuals, such as newborns and the elderly, the symptoms can impact on the lower airways, resulting in wheeze, shortness of breath, bronchiolitis or pneumonia [4]. Common respiratory viral pathogens include adenovirus, enterovirus, human coronavirus, human metapneumovirus, rhinovirus (RV), influenza, parainfluenza and respiratory syncytial virus (RSV). Transmission can occur by air through aerosolization, by drops of respiratory secretions or by inoculation after touching contaminated surfaces [5]. Healthcare-associated viral infections cause an increase in morbidity and mortality among hospitalized patients and also in healthcare-associated costs. Each virus has a different mechanism of transmission; therefore, early detection and prompt implementation of infection control measures are very important in order to avoid their transmission in the hospital setting [6].

Enteric viruses can cause many significant diseases and their effects may range from asymptomatic infections or mild symptoms to serious or life-threatening illnesses [7]. They can affect both human and animal's health by causing diseases such as gastrointestinal and respiratory infections. Enteric viral pathogens recognized since 1970 include viruses mainly belonging to the four families *Reoviridae* (rotavirus), *Caliciviridae* (calicivirus), *Astroviridae* (astrovirus) and *Adenoviridae* (adenovirus) and are known to cause billions of cases of enteric viral infections every year. The clinical illness caused by enteric pathogens varies but usually involves diarrhea, vomiting and fever, of differing length and severity. The possible transmissibility of such viruses between animals and humans should be assessed as a number of known and emerging viruses have been associated with enteric infections in animals [8]. These viruses spread via fecal- oral transmission; they are conveyed by fecal contaminated food or water, and thus dependent on control through public health hygienic measures. To better understand and tackle such existing and emerging enteric viral infections there is an urgent need to acquire more scientific knowledge of these pathogens including their reservoir hosts.

2. RESPIRATORY AND ENTERIC DISEASE CAUSING VIRUSES

2.1. ROTAVIRUS

Rotaviruses (RVs), a member of the reovirus family, are distributed across the world in humans and animals as the leading enteric pathogen. Rotavirus is common, accounting for 35–60% of acute severe diarrhoea in children < 5 years of age in countries without rotavirus vaccine, with the highest attributable percentage in infants [9, 10]. Rotavirus gastroenteritis inflicts a devastating impact on infants and young children, particularly in developing countries. It is estimated that the disease is associated with the deaths of more than 600,000 children per year worldwide, with the majority of deaths occurring in Africa and Asia. Despite the global introduction of vaccinations for rotavirus, rotavirus infections still result in >200,000 deaths worldwide per year. Rotavirus symptoms include profuse diarrhea, vomiting, fever, malaise, and rarely neurologic features such as convulsions, encephalitis, or encephalopathy [11]. Since its discovery in 1973 rotavirus has been well documented as a causative agent of infantile gastroenteritis [12, 13]. Occasionally rotaviruses are encountered with other enteropathogens, but their significance in such dual infections is unknown [14]. Also uncertain is the role of rotaviruses in the aetiology of respiratory symptoms often associated with rotavirus diarrhea [15,16,17].

Rotavirus is highly communicable; it is shed in the stool at high concentration and transmission is through faecal-oral route, either person-to-person or through fomites in the environment. Rotavirus diarrhoea is ubiquitous and is not more prevalent in settings with poor water, sanitation and hygiene [18]. Diarrhoea caused by rotavirus infection is of more than average severity; the proportion of diarrhoea episodes that are caused by rotavirus is lowest in patients in the community who require only home care (5–10%) compared with those who require outpatient care (15–20%) or inpatient care (30–50%). Although the prevalence of rotavirus infection in children hospitalized with diarrhoea is similar worldwide (~30–50%), >90% of children with fatal rotavirus infections live in low-income countries [19], which is likely because of limited access to health care, lack of available hydration therapy and a greater prevalence of comorbid conditions (such as malnutrition), among other factors. In contrast to gastroenteritis caused by

bacterial pathogens, rotavirus infections cause non-bloody diarrhoea that lasts for a relatively short duration and is associated with a limited inflammatory response [20, 21].

2.2. ADENOVIRUS

Human adenoviruses (HAdVs), which are members of the family *Adenoviridae* and genus *Mastadenovirus*, are non-enveloped, icosahedral, double-stranded DNA viruses. They are most commonly associated with pediatric illnesses of the upper respiratory tract, including the common cold. Young children, close-quartered populations such as crowded communities, schools, and military training camps [22], along with immunocompromised individuals are susceptible populations. Adenoviral infections can also manifest with gastrointestinal, ophthalmologic, genitourinary, and neurologic symptoms [23]. They can infect and replicate in epithelial cells of the gastrointestinal (GI) tract, respiratory tract, eyes, and urinary bladder.

Infection may be airborne or waterborne. Transmission occurs from an infected person to other individuals via respiratory routes, fecal-oral contamination, contaminated fomites, and/or direct contact. Respiratory transmission via a cough or a sneeze is the most common mode of transmission. Fecal-oral transmission occurs through contaminated food or water, and transmission via water can occur in public swimming pools due to ineffective chlorine treatment. They are commonly acquired by contact with secretions (including those on fingers of infected people) from an infected person or by contact with a contaminated object (eg, towel, instrument). Therefore, the infection can occur through an individual's lack of proper hygiene. The virus can survive for extended periods on environmental surfaces and is resistant to lipid disinfectants because it is nonenveloped, however, it is inactivated by heat, formaldehyde, and bleach.

HAdV infections are readily spread in human populations. There are 7 human adenovirus species (A to G) and 57 serotypes which are classified according to 3 major capsid antigens (hexon, penton, and fiber) [24]. A person infected with HAdV is extremely contagious during the incubation period, which typically ranges from 4–8 days, but can last up to 24 days, depending on the HAdV serotype [25]. Asymptomatic respiratory or gastrointestinal viral shedding may continue for months, or even years. Outbreaks often occur in crowded populations, such as nosocomial facilities (e.g., hospitals and nursing homes), military bases, and schools [26, 27]. HAdVs may cause outbreaks of diarrheal and gastroenteritis illness, pharyngoconjunctival fever, febrile respiratory illness, and/or keratoconjunctivitis [28].

2.3. CORONAVIRUS

The coronaviruses are a diverse group of large, enveloped, positive-stranded RNA viruses. SARS-CoV-2 is the seventh coronavirus (CoVs) that is known to have infected humans after HKU1, NL63, OC43 and 229E, associated with common cold symptoms, and bat-SL-CoVZC45, MG772933 [29,30], commonly known as SARS-CoV, and Middle East respiratory syndrome coronavirus (MERS-CoV) that cause severe respiratory illnesses. The modern world is facing a major public health crisis due to this novel corona virus SARS-CoV-2 which has caused a pandemic involving at least 210 countries. In humans, there are 2 forms of coronavirus, HCoV-229E and HCoV-OC43 that are associated with about 30% of mild upper respiratory tract infections. Moreover, human coronaviruses or coronavirus-like particles have been linked to diarrheal disease in susceptible hosts, including patients with acquired immunodeficiency syndrome and children from developing countries [31, 32].

This SARS-CoV-2 virus primarily transmits through fomites, air droplets, and aerosols from human to human. Transmission may be possible during the incubation period which has been estimated to be 5 days. The main symptomatology of COVID-19 pertains to respiratory system, with patients presenting predominantly with fever, cough, sore throat, and shortness of breath, and in serious cases, leading to ARDS, necessitating intensive care unit (ICU) admission, and sometimes death [33]. Available data have shown that patients with COVID-2019 present respiratory symptoms and fever; however, approximately 8.8–60.6% of patients suffer from gastrointestinal symptoms, such as decreased appetite, nausea, vomiting, and diarrhea, as well as possible abnormal liver function [34,35,36].

The effects of coronaviruses on the respiratory system are of great concern, but their effects on the digestive system receive much less attention [37]. Gastrointestinal tract (GIT) involvement has been well documented by previous corona viral infections both in animals and human beings. Although earlier reports of COVID-19 reported a low 1 to 3.8% [38, 39, 40] prevalence of diarrhea, these figures kept on surging as more focused GI symptomatology–related studies came to forefront.

2.4. NOROVIRUS

Norovirus, an RNA virus of the family *Caliciviridae*, is a human enteric pathogen that causes substantial morbidity across both health care and community settings [41]. Humans are believed to be the only host for human norovirus. Human norovirus, previously known as Norwalk virus, was first identified in stool specimens collected during an outbreak of gastroenteritis in Norwalk, OH, and was the first viral agent shown to cause gastroenteritis [42].

Noroviruses are the leading cause of gastroenteritis outbreaks around the world, and are responsible for severe diarrhea and foodborne disease outbreaks. Fecal–oral spread is the primary mode of transmission, although infectious vomitus can play a role as well. Several characteristics of noroviruses facilitate their spread. During the acute phase of infection, norovirus causes vomiting and diarrhea which typically resolves within 1–2 days. Viral shedding into the stool, however, can continue for weeks to months in asymptomatic patients. Several factors enhance the transmissibility of norovirus, including the small inoculum required to produce infection (<100 viral particles), prolonged viral shedding, and its ability to survive in the environment [43].

2.5. RESPIRATORY SYNCYTIAL VIRUS (RSV)

RSV is a single-stranded RNA virus, which represents the most frequent viral cause of acute lower respiratory tract infection (ALRTI) in infants, with a worldwide distribution and seasonal occurrence [44,45,46,47]. RSV is a global infection, but 99% of related mortality is in low/middle-income countries. It was discovered more than 50 years ago, and it has since been identified as the most common cause of acute respiratory tract infections in infants. It was first isolated in 1956 from nasal secretions of chimpanzees with rhinorrhea and coryza; the novel virus was initially named 'Chimpanzee coryza agent' (CCA) [48,49]. Human respiratory syncytial virus is one of the most common viruses to infect children worldwide and increasingly is recognized as an

important pathogen in adults, especially the elderly [50]. The majority of patients with RSV will have an upper respiratory illness, but a significant minority will develop lower respiratory tract illness, predominantly in the form of bronchiolitis. Children under the age of one year are especially likely to develop lower respiratory involvement, with up to 40% of primary infections resulting in bronchiolitis.

RSV is a widespread pathogen of humans, due in part to the lack of long-term immunity after infection, making reinfection frequent. It infects 90% of children within the first 2 years of life and frequently reinfects older children and adults. RSV is spread from person to person via respiratory droplet, and the incubation period after inoculation with RSV ranges from 2 to 8 days, with a mean incubation of 4 to 6 days, depending on host factors such as the age of the patient and whether it is the patient's primary infection with RSV [51].

2.6. ENTEROVIRUS

Enteroviruses are a group of single-stranded sense RNA viruses that commonly cause infections, especially in infants and children [52]. Most human enterovirus infections are either asymptomatic or result in mild disease. Periodically, enteroviruses are associated with outbreaks of more serious disease, resulting in considerable morbidity and occasionally in significant mortality [53]. EV can induce nonspecific respiratory illnesses in infants or adults, including upper respiratory tract infections but also lower respiratory tract infections (LRTIs), resulting in bronchitis, bronchiolitis [54], and pneumonia [55]. These viruses are transmitted from person to person via direct contact with virus shed from the gastrointestinal or upper respiratory tract. They are most commonly spread either by coming into contact with secretions, like saliva, sputum or mucus, from an infected person or with their faeces. People most likely to develop more severe disease are those with underlying health conditions, pregnant women, newborns or premature babies, and people who have cold stress or malnutrition [56].

2.7. INFLUNZA VIRUS

Influenza viruses are member of Orthomyxoviridae family of viruses, and are negative strand RNA viruses. Influenza viruses can be classified as A, B or C. Influenza A is found in humans, other mammals, and birds, and is the only influenza virus, which has historically caused pandemics. Influenza A and B are more common than type C, and cause more severe disease [57]. Influenza C is a significant cause of respiratory infections in children younger than 6 years of age. Symptoms associated with influenza virus infection vary from a mild respiratory disease confined to the upper respiratory tract and characterized by fever, sore throat, runny nose, cough, headache, muscle pain and fatigue to severe and in some cases lethal pneumonia. Influenza virus infection can also lead to a wide range of non-respiratory complications in some cases — affecting the heart, central nervous system and other organ systems [58,59].

3. CONCLUSION

Enteric and respiratory viruses represent an important public health issue both in developed and in developing countries. Increases in population growth and mobility have enhanced pathogen transmission and intensified the difficulty of interrupting disease spread. Prevention and management of viral disease heavily relies upon vaccines and antiviral medications. Control of viral disease spread requires a clear understanding of how viruses are transmitted in the environment. Moreover, understanding the epidemiology and pathogenesis of viral infections, and the hosts' immune response to such infections are key to the control and prevention of viral diseases and to the development of vaccines.

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