Epidemiology of Human Bocavirus in the Middle East and North Africa: Systematic Review

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Abstract: The emergence of the COVID-19 pandemic highlighted the importance of studying newly emerging viruses that cause respiratory illnesses. Human bocavirus (HBoV) is one of the relatively newly discovered viruses that has been detected worldwide and causes respiratory and gastrointestinal infections, mainly in pediatric patients. However, little is known about the pathogenicity and evolution of HBoV. This systematic review was initiated to clarify the prevalence and circulating genotypes of HBoV in both respiratory and stool samples from patients of all age groups in the Middle East and North Africa (MENA) from 2005 to February 2021. We performed an electronic search through Science Direct, Scopus, PubMed, Mendeley and Cochrane Library databases. We included all studies reporting the detection rate of HBoV in the MENA region. Data were extracted, and the quality of the included articles was assessed. We included articles containing data on HBoV only or with other respiratory or gastrointestinal viral infections. Review articles, case studies, and animal and environmental studies were excluded. The final number of articles included in this study was 65 articles. The results showed that the HBoV prevalence in children was the lowest in Iran (0%) and the highest in Egypt (56.8%). In adults, the lowest and the highest prevalence were reported in Iran, with values of 0% and 6.6%, respectively. Regarding the respiratory cases, our findings revealed no significant difference between HBoV prevalence among the tested categories (p-value = 0.998). The present study has shown that HBoV is common in children and adults in the MENA region. This systematic review highlights the need for more data on the role of coinfection of HBoV and other viruses, for instance, SARS-CoV-2 in children with acute bronchiolitis.

Keywords: human bocavirus (HBoV); MENA; epidemiology

1. Introduction

Human bocavirus (HBoV) is a parvovirus reported for the first time in 2005 [1]. Since then, an increasing number of reports have emerged indicating the common presence of the virus in the respiratory and gastrointestinal samples. HBoV is known to cause viral respiratory and gastrointestinal tract infections [1,2]. However, the pathogenicity of the virus is not fully understood [3,4]. As with other viruses that cause respiratory tract infections, HBoV can occur during any time of the year, with the highest incidence rate during winter and spring [5,6]. Although HBoV has been found in individuals of all ages, it was mainly reported in infants aged 6–24 months [4,5].

HBoV is a small non-enveloped single-stranded DNA virus with a genome size of 5300 nucleotides. The name Bocavirus was derived after the phylogenetic analysis of the HBoV genome, which showed a close relation to bovine parvovirus (BPV1) and minute virus of canines (MVC). HBoV belongs to the family Parvoviridae, subfamily Parvovirinae and genus Bocavirus. There are four genotypes that belong to the Bocavirus genus. The first
genotype was named HBoV1, and was predominantly reported in respiratory samples [7]. The others, named HBoV2, 3 and 4, were reported in the stool samples of gastroenteritis patients [8].

Globally, the total prevalence of HBoV was estimated at around 6.0% [3]. Death cases due to HBoV infections have been reported [9–11]. However, there is no definite death rate. The Middle East and North Africa (MENA) region is a term that represents a group of twenty-one countries found in Asia (Bahrain, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syria, Turkey, United Arab Emirates, Palestine and Yemen) and Africa (Algeria, Egypt, Libya, Morocco, Sudan and Tunisia) (https://istizada.com/mena-region/, accessed on 16 January 2021) (Figure 1). Only 14 countries reported the prevalence of HBoV in the MENA region. On the other hand, a lack of reported data was noticed in several countries (Bahrain, Syria, Palestine, Yemen, Algeria, Libya and Morocco) due to lack of knowledge, awareness and attitude of physicians, wars, conflicts, civil revolutions and low scientific research output. The aim of this systematic review was to investigate the prevalence of HBoV and its distribution in the MENA region. Data included patients of all age groups, mainly children, with acute respiratory and gastrointestinal infections, including pilgrims returning from Hajj and Umrah and suffering from acquired acute respiratory tract illness (ARI).

Figure 1. The Middle East and North Africa region (MENA) (https://istizada.com/mena-region/) (assessed on 16 January 2021).

2. Methods

2.1. Search Strategy and Selection Criteria

This systematic literature review involves all published journal articles and preprints that reported HBoV prevalence and genotypes in the Middle East and North Africa (MENA) region between 2005 and February 2021. Five databases were searched (Science Direct, Scopus, PubMed, Mendeley and Cochrane Library) by using (“boca*” OR “bocavirus” OR “boca virus”) AND (“gastro*” OR “genotype” OR “epidemiology” OR “resp*” OR “prevalence” OR “type”) AND (“The Middle East” OR “North Africa” OR “The Middle East and North Africa” OR “The Middle East & North Africa” OR “MENA” OR “Algeria” OR “Bahrain” OR “Djibouti” OR “Egypt” OR “Iran” OR “Iraq” OR “Jordan” OR “Kuwait” OR “Lebanon” OR “Libya” OR “Morocco” OR “Occupied Palestinian Territories” OR “Oman” OR “Palestine” OR “Qatar” OR “Saudi Arabia” OR “KSA” OR “Somalia” OR “Sudan” OR
“Syria” OR “Tunisia” OR “UAE” OR “The United Arab Emirates” OR “Yemen”) as a search strategy. The eligible articles were screened for both the titles and abstracts. The studies involved in this systematic review were selected based on the following criteria: (1) the published articles contain data on HBoV only or with other respiratory or gastrointestinal viral infections from 2005 to February 2021, (2) the studied population in the article is patients residing in, or having acquired infection from, the MENA region. Review articles, case studies, and animal and environmental studies were excluded.

2.2. Data Collection and Data Adjustment

Following the research strategy, a total of 265 articles were identified as follows: 117 articles from PubMed, 73 from Mendeley, 60 from Scopus, eight from Science Direct and seven articles from Cochran. The number of records after deduplication was 175, 88 articles were excluded due to their titles, 11 articles were excluded due to their abstracts and 12 articles were excluded after full-text article screening. The final number of articles included in this study was 65 articles (Figure 2).

Figure 2. Flow chart of the study selection protocol.

The data collection sheet was designed to extract data from the selected articles at a 95% confidence interval. The prevalence data were extracted and arranged according to the country and year of sample collection and were reported as percentages. Data of respiratory records were compared by Fisher’s exact test, and p-values were calculated in IBM SPSS statistics version 28 by using the Chi-square test to identify associations.

The summary of individual study parameters was prepared using Microsoft Excel. A mean percentage prevalence was taken if more than one prevalence study was reported from the same country. Prevalence charts were produced for both respiratory and gastrointestinal samples.
3. Results

In total, 142,748 patients were reported in sixty-five studies, and 5622 (3.94%) were positive for infection. All those studies reported the prevalence of HBoV in the MENA from 2005 to February 2021 (Table 1). A mean percentage prevalence was calculated for each country for both respiratory and gastrointestinal samples. The prevalence charts were constructed for both respiratory (Figure 3) and gastrointestinal samples (Figure 4).

![Figure 3. The prevalence of HBoV in respiratory samples in the MENA.](image1)

![Figure 4. The prevalence of HBoV in gastrointestinal samples in the MENA.](image2)
| Country | First Author, Year | Study Period | Age Group | HBoV Positive | Sample Size | Prevalence | Type of Specimen | HBoV Genotypes | Study Design |
|---------|--------------------|--------------|-----------|---------------|-------------|------------|-----------------|----------------|-------------|
| Egypt   | Zaghloul (2011) [12] | 2009–2010 (8 months) | Children (<5 years) | 22 | 100 | 22.0% | NPAs | ND | Case-control |
|         | Tabl et al. (2012) [13] | 2010–2011 (10 months) | Children (<12 years) | 18 | 100 | 18.0% | Serum | ND | Cross section |
|         | EL-Mosallamy et al. (2015) [14] | 2013–2015 (18 months) | Children (<2 years) | 20 | 200 | 10.0% | NPAs | ND | Cross section |
|         | Abdel-Moneim et al. (2016) [15] | 2011–2015 | Aged between 30 and 75 years | 24 | 101 | 23.8% | Colorectal cancer biopsy | Genotype 1 | Cross section |
|         | Abdel-Moneim et al. (2016) [16] | 2013–2014 (2 months) | Children (<3 years) | 54 | 95 | 56.8% | NP | Genotype 1 | Cross section |
|         | Meligy et al. (2016) [17] | 2013–2014 (5 months) | Children (<3 years) | 8 | 51 | 18.2% | NP and NPA | ND | Cross section |
|         | Amr et al. (2017) [18] | 2015–2016 (11 months) | Children (<5 years) | 19 | 123 | 15.4% | NPAs | ND | Cross section |
|         | Hatem et al. (2019) [19] | 2010–2014 (48 months) | All age groups with viral infection | 1075 | 11 | 1.0% | NP and OP | ND | Cross section |
|         | Abozahra et al. (2020) [20] | 2018–2019 (5 months) | Children (<5 years) | 7 | 75 | 9.3% | NP | Genotype 1 | Cross section |
|         | Rosshdy et al. (2020) [21] | 2013–2014 (11 months) | All age groups | 2 | 200 | 10.0% | NPAs | ND | Cross section |
| Iran    | Naghipour et al. (2007) [22] | 2003–2004 (4 months) | Children (<5 years) | 21 | 261 | 8% | NPAs or NP | Genotype 1 | Cross section |
|         | Nadji et al. (2010) [23] | 2007–2008 (11 months) | Children (<17 years) | 9 | 133 | 6.8% | NPAs | Genotype 1 | Cross section |
|         | Monavari et al. (2013) [24] | 2010–2011 (12 months) | Children (<5 years) | 6 | 47 | 12.8% | Stool | ND | Cross section |
|         | Romani et al. (2013) [25] | 2008–2010 (24 months) | All age groups | 16 | 200 | 8.0% | Stool | Genotype 1, 2 and 3 | Cross section |
|         | Shokrollahi et al. (2014) [26] | 2009–2011 (24 months) | Children (<9 years) | 6 | 80 | 8.0% | Stool | ND | Cross section |
| Country | First Author, Year | Study Period | Age Group | HBoV Positive | Sample Size | Prevalence | Type of Specimen | HBoV Genotypes | Study Design |
|---------|--------------------|--------------|-----------|---------------|-------------|------------|------------------|----------------|--------------|
| Iran    | Mortazavi et al. (2015) [27] | 2014 (5 months) | Age group between 29 and 91 years | 6 | 91 | 6.6% | Throat swabs | ND | Cross section |
|         | Tabasi et al. (2016) [28] | 2012–2013 (6 months) | Children (<2 years) | 15 | 140 | 10.7% | Throat swabs | Genotype 1 | Cross section |
|         | Moradi et al. (2017) [29] | 2015–2016 (10 months) | Age group between 56 and 80 years | 0 | 30 | 0.0% | BAL and NP | ND | Cross section |
|         | Malekshahi et al. (2017) [30] | 2013–2014 (8 months) | Children (<5 years) | 0 | 71 | 0.0% | Throat swabs and nasal washes | ND | Cross section |
|         | Niya et al. (2018) [31] | 2011–2016 (12 months) | All age groups | 1 | 66 | 1.5% | Colorectal cancer biopsy | Genotype 1 | Case-control |
|         | Mohammadi et al. (2019) [32] | 2016–2017 (12 months) | Children (<3 years) | 10 | 75 | 13.3% | NP | Genotype 1 | Cross section |
|         | Mohammadi et al. (2020) [33] | 2017–2018 (12 months) | Children (<3 years) | 67 | 500 | 13.4% | NP | ND | Cross section |
|         | Hashemi et al. (2021) [34] | NA | Confirmed COVID-19 cases from all age groups | 10 | 105 | 9.7% | Throat swabs and NP | ND | Cross section |
| Iraq    | Atyah et al. (2017) [35] | 2015–2016 (8 months) | Children (<15 years) | 48 | 195 | 24.6% | NP | ND | Cross section |
|         | Al-Mayah et al. (2018) [36] | 2017–2018 (2 months) | Children (<5 years) | 8 | 122 | 6.6% | NP | Genotype 1 | Cross section |
|         | Shamiran et al. (2019) [37] | 2017 (3 months) | Children (<3 years) | 18 | 50 | 36.0% | NP and blood | ND | Cross section |
|         | Hasan et al. (2020) [38] | 2017–2018 (2 months) | Children (<5 years) | 8 | 122 | 6.6% | NP | Genotype 1 | Cross section |
|         | Yaseen et al. (2020) [39] | 2018–2019 (7 months) | Children (<10 years) | 31 | 80 | 38.8% | Pharynx swab | ND | Cross section |
| Israel  | Hindiyeh et al. (2008) [40] | 2006 (11 months) | Children (<10 years) | 26 | 231 | 11.3% | Nasal suction, NP, BAL, throat swab, sputum, pleural fluid | ND | Cross section |
| Country     | First Author, Year | Study Period | Age Group               | HBoV Positive | Sample Size | Prevalence | Type of Specimen | HBoV Genotypes | Study Design |
|-------------|--------------------|--------------|--------------------------|---------------|-------------|------------|------------------|----------------|--------------|
| Jordan      | Kaplan et al. (2006) [41] | 2003–2004 (5 months) | Children (<5 years) | 57            | 312         | 18.3%      | NPA              | Genotype 1   | Cross section |
|             | AL-Rousan et al. (2011) [42] | 2007 (11 months) | Children (<13 years) | 20            | 220         | 9.1%       | NPA              | Genotype 1   | Cross section |
|             | Awad et al. (2020) [43] | 2016 (3 months) | Children (<5 years) | 12            | 479         | 2.5%       | NP              | ND            | Cross section |
| Kuwait      | Essa et al. (2015) [44] | 2010–2013 (31 months) | All age groups | 14            | 735         | 4.9%       | BAL, TA, NPAs and NP | ND | Cross section |
|             | Madi and A. AL-Adwani (2020) [45] | 2018–2020 (24 months) | All age groups | 111           | 5941        | 1.9%       | NPAs and throat swabs | Genotype 1 | Cross section |
|             | Mohammad et al. (2020) [46] | 2017 (11 months) | Children (<10 years) | 2             | 84          | 2.3%       | Stool            | Genotype 1   | Cross section |
| Lebanon     | Finianos et al. (2016) [47] | 2013–2014 (11 months) | Children (<16 years) | 36            | 236         | 15.0%      | NPAs             | ND            | Cross section |
| Oman        | Khamis et al. (2012) [48] | 2007–2008 (12 months) | Children (<5 years) | 8             | 259         | 3.0%       | NPAs             | ND            | Cross section |
| Qatar       | Janahi et al. (2017) [49] | 2010–2011 (24 months) | Children (<2 years) | 15            | 369         | 4.1%       | NP              | ND            | Cross section |
|             | Al-Romaihi et al. (2019) [50] | 2012–2017 (71 months) | Adult (>15 years) | 286           | 37929       | 0.7%       | OP, NP and NPAs | ND            | Cross section |
|             | Al-Romaihi et al. (2020) [51] | 2012–2017 (71 months) | Children (<15 years) | 1920          | 30946       | 6.2%       | Throat swabs, NP and NPAs | ND | Cross section |
|             | Nadeem et al. (2020) [52] | 2013–2016 | All age groups with respiratory illness | 874           | 43106       | 2.0%       | OP and NP | ND            | Cross section |
| Saudi Arabia| Memish et al. (2012) [53] | 2009 (6 days) | HCP age between 31 and 49 years | 0             | 184         | 0.0%       | Throat swabs and NP | ND | Cross section |
|             | Abdel-Moneim et al. (2013) [54] | 2012 (4 months) | Children (<10 years) | 18            | 80          | 22.5%      | NP              | Genotype 1   | Cross section |
|             | Al-Ayed et al. (2014) [55] | 2012–2013 (9 months) | Children (<5 years) | 1             | 135         | 0.74%      | NP              | ND            | Cross section |
|             | Bubshait et al. (2015) [56] | 2010–2011 (12 months) | Children with viremia (<5 years) | 5             | 47          | 10.6%      | Serum           | ND            | Cross section |
Table 1. Cont.

| Country     | First Author, Year | Study Period | Age Group | HBoV Positive | Sample Size | Prevalence | Type of Specimen | HBoV Genotypes | Study Design |
|-------------|--------------------|--------------|-----------|---------------|-------------|------------|------------------|----------------|--------------|
| Saudi Arabia | Memish et al (2015) [57] | 2013 (22 day) | Pilgrims came from worldwide to do hajj or Umrah (>18 years) | 2 | 1676 | 0.1% | Nasal swabs | ND | Cohort |
|             | Eifan et al (2017) [58] | 2014–2015 (11 months) | Children (<5 years) | 171 | 2266 | 7.5% | NP, NPAs and BAL | ND | Cohort |
|             | Abdel-Moneim et al. (2018) [59] | 2016 (11 months) | Blood donors (adult) (20–48 years) | 21 | 300 | 7.0% | Whole blood sample | Genotype 1 | Cross section |
|             | Koul et al. (2018) [60] | 2014–2015 (6 MONTHS) | Pilgrims returning from Saudi Arabia, adults between 26 and 60 years | 2 | 300 | 0.7% | Throat swabs and NP | ND | Cross section |
| Sudan       | Adam et al. (2018) [61] | 2014 (8 months) | Children (<5 years) | 5 | 437 | 1.1% | Stool | Genotype 1 | Cross section |
| Tunisia     | Kapoor et al. (2010) [62] | NA | Children (<15 years) | 32 | 96 | 33% | Stool | Genotype 1, 2, 3 and 4 | Case-control |
|             | Khalifa et al. (2019) [63] | 2013–2014 (15 months) | Children (<1 years) | 37 | 515 | 7.2% | NPAs | ND | Cross section |
| Turkey      | Midilli et al. (2010) [64] | NA | All age groups | 7 | 155 | 4.5% | NPAs and throat swab | Genotype 1 | Cross section |
|             | Azkur et al. (2014) [65] | 2011–2012 (6 months) | Children (<2 years) | 3 | 55 | 5.4% | NP | ND | Cross section |
|             | UYAR et al. (2014) [66] | 2010 (6 months) | Children (<2 years) | 3 | 62 | 4.8% | NPAs | ND | Case-control |
|             | Akturk et al. (2015) [67] | 2013–2014 (7 months) | Children (<7 years) | 30 | 1143 | 2.6% | NP | ND | Cross section |
|             | ÇİÇEK et al. (2015) [68] | 2002–2014 (151 months) | All age groups | 18 | 5102 | 4% | NP, BAL and NPAs | ND | Cross section |
|             | Demirci et al. (2016) [69] | 2009 (3 months) | Children (<5 years) | 8 | 120 | 6.7% | NP | ND | Cross section |
|             | Erdem et al. (2016) [70] | 2013–2014 (26 months) | Pilgrims (adult) (>15 years) | 1 | 97 | 1% | NP | ND | Cross section |
|             | Goktas et al. (2016) [71] | 2014–2015 (11 months) | All age groups | 91 | 845 | 10.76% | NP | ND | Cross section |
|             | Bakir et al. (2020) [72] | 2015–2017 (32 months) | Children (<18 years) | 105 | 2310 | 4.5% | NP | ND | Cross section |
Table 1. Cont.

| Country                  | First Author, Year | Study Period       | Age Group                          | HBoV Positive | Sample Size | Prevalence | Type of Specimen | HBoV Genotypes | Study Design   |
|--------------------------|--------------------|--------------------|------------------------------------|---------------|-------------|------------|------------------|----------------|---------------|
| United Arab Emirates     | Alsuwaidi et al. (2018) [73] | 2016-2017 (3 months) | Children (3-6 years)                | 0             | 18          | 0.0%       | NP               | ND             | A pilot study |
|                          |                    |                    | Children (<15 years)                | 0             | 198         | 0.0%       | Sputum, NP and BAL | ND             |               |
|                          | Jeon et al. (2019) [74] | 2015–2018 (27 months) | Adults aged between 15 and 64 years | 2             | 718         | 0.3%       | Sputum, NP and BAL | ND             | Cross section |
|                          |                    |                    | Elderly (≥65 years)                 | 0             | 446         | 0.0%       | Sputum, NP and BAL |                |               |

NA: Not available, ND: Not detected, NPAs: Nasopharyngeal aspirates, NP: Nasopharyngeal swabs, OP: Oropharyngeal Swab, BAL: Broncho Alveolar Lavage, TA: tracheal aspirate, HCP: Health Care Provider.
This systematic review reports the prevalence of HBoV in the MENA region among different tested categories including various age groups (pediatric, children, adults and elderly), COVID-19 cases, pilgrims, health care providers, blood donors and patients with colorectal cancer. Concerning the respiratory cases, our findings revealed no significant differences between HBoV prevalence values among the tested categories ($p$-value = 0.998).

The study design for almost all of the included studies was a cross-sectional study that aligns with the prevalence determination. In addition, a pilot study, case-control and cohort studies were included in this systematic review. The different study designs can explain the heterogeneity of the sample size.

All included studies used valid assay procedures for the detection of HBoV. The most commonly used method is real-time polymerase chain reaction (RT-PCR). Samples from the upper (nasopharyngeal aspirates, nasopharyngeal swabs or oropharyngeal swab), middle (tracheal aspirate) and lower respiratory tract (Bronchoalveolar lavage) were examined for patients with respiratory tract infection. Stool was the specimen of choice for patients with gastroenteritis.

Surgically excised specimens were used to screen human bocavirus in colorectal cancer patients. Whole blood samples from blood donors were screened for HBoV to investigate the possibility of parenteral transmission.

4. Discussion

In the MENA Region, several reports studied the prevalence of HBoV among hospitalized children and adults suffering respiratory tract infections and whether HBoV was the causal agent [27,41]. At the same time, others investigated the HBoV prevalence in patients with gastroenteritis [14,24].

The results showed that the prevalence of HBoV varied from one country to another. The HBoV prevalence, in cases of respiratory tract infection in children, ranged from 0% in Iran to 56.8% in Egypt [16,30]. In adults, the highest prevalence (6.6%) was observed in Iran [27]. Few studies have focused on HBoV isolated from stool specimens to recognize the role of HBoV in gastroenteritis. Only nine studies were found in the MENA, five of them from Iran, and the others were conducted on populations in Egypt, Kuwait, Sudan and Tunisia. Among these studies, the lowest prevalence was reported in Sudan in 2018 (1.10%) [61], while the highest prevalence (33%) was reported in Tunisia [62]. Several factors affect the variations in the prevalence of the virus in these populations, including the geographical location of the country, the clinical diagnosis of the studied population, the type of sample, the method used for detection of the virus, the age group of the examined population and the outbreak season of the virus.

Abdel-Moneim et al. (2016) used newly developed primers to increase the sensitivity of the PCR test for HBoV detection. Using these novel primers, the prevalence of HBoV was 56.8%, which significantly differs from previous and further studies conducted in Egypt, which found prevalence values of 22%, 10% and 18.2% respectively [12,13,17]. Abdel-Moneim et al. explained that the high rate of prevalence of HBoV-1 was reported because of a potential nosocomial pathogen among pediatric care units. This explanation was verified by Cabral et al. in (2021) after he demonstrated that bocavirus is one of the airborne respiratory conditions transmitted during the analysis of the air in pediatric emergency department waiting rooms [75]. Therefore, early diagnosis of HBoV infection in the initial hospitalization time may decrease the spread of the viral infection, especially in pediatric units [47]. Moreover, unlike other respiratory viruses, HBoV can be detected in the serum and whole blood samples of patients suffering from viremia [56].

In Egypt, Abdel-Moneim et al. (2016) studied the presence of HBoV in colorectal cancer patients and found that among one hundred and one patients, twenty-four of them (23.8%) were positive for HBoV [15]. Moreover, Niya et al. (2018) used a case versus control population to detect the presence of the HBoV genome in colorectal cancer patients’ tissue and compared the result with matched healthy control group tissue; HBoV was detected in one patient from each group, with a total prevalence of 1.3% [31].
Several studies have reported the spreading of HBoV among pilgrims during Hajj and Umrah, as mass gathering aids in the transmission of respiratory diseases. The studies concluded that raising awareness among pilgrims of the importance of following public health precautions, such as wearing masks and undergoing vaccination, significantly reduces the transmission of respiratory pathogens [57,60,70].

Currently, four genotypes have been identified worldwide (HBoV1, HBoV2, HBoV3 and HBoV4). In the MENA Region, HBoV1 is the most prominent reported genotype and is mainly associated with respiratory diseases [20,28]. However, HBoV1 was rarely detected in stool samples [25]. Genotypes 2, 3 and 4 were reported in cases of acute gastroenteritis [25,62].

HBoV is detected more frequently with other viruses in the respiratory and gastrointestinal tract (Table 2). HBoV co-infection is present at a high rate among the tested samples, especially with respiratory syncytial virus (RSV) [13,32,41], which is the most prominent virus that causes respiratory illness.

**Table 2.** HBoV and other viruses detected in patients with viral co-infection.

| Country | First Author, Year | Viral Coinfection Rate | Coinfected Viruses                  |
|---------|--------------------|------------------------|------------------------------------|
| Egypt   | Tabl et al. (2012) [13] | 66.7%                  | Respiratory syncytial virus        |
|         |                    | 13.3%                  | Parainfluenza                      |
|         |                    | 6.7%                   | Influenza-B viruses                |
|         |                    | 6.7%                   | Influenza-A viruses                |
|         |                    | 6.7%                   | Adenovirus                         |
| Iran    | Naghipour et al. (2007) [22] | 14.0%                  | Adenovirus                         |
|         |                    | 15%                    | Respiratory syncytial virus        |
|         |                    | 4.0%                   | Influenza A virus                  |
|         | Tabasi et al. (2016) [28] | 13.3%                  | Respiratory syncytial virus        |
|         |                    | 40%                    | Respiratory syncytial virus        |
|         | Mohammad et al. (2019) [32] | 65.6%                  | Respiratory syncytial virus        |
|         | Mohammad et al. (2020) [33] | 62.5%                  | Respiratory syncytial virus        |
|         | Hashemi et al. (2021) [34] | 100.0%                 | Severe acute respiratory syndrome coronavirus 2 |
| Iraq    | Atyah et al. (2017) [35] | 4.6%                   | Respiratory syncytial virus        |
|         |                    | 3.6%                   | Human metapneumovirus              |
| Israel  | Hindiyeh et al. (2008) [40] | 69.2%                  | Adenovirus                         |
|         |                    | 7.1%                   | Respiratory syncytial virus        |
|         |                    | 10%                    | Parainfluenza virus 3              |
| Jordan  | Kaplan et al. (2006) [41] | 72%                    | Respiratory syncytial virus        |
|         | AL-Rousan et al. (2011) [42] | 20%                    | Respiratory syncytial virus        |
| Kuwait  | Madi and A. AL-Adwani (2020) [45] | 10.8%                  | Respiratory syncytial virus        |
|         |                    | 9.9%                   | Human rhinoviruses                 |
|         | Mohammad et al. (2020) [46] | 3.6%                   | Influenza A virus                  |
|         | Mohammad et al. (2020) [46] | 50%                    | Adenovirus                         |
| Lebanon | Finianos et al. (2016) [47] | 47.2%                  | Adenovirus                         |
|         |                    | 36.1%                  | Human rhinoviruses                 |
| Oman    | Khamis et al. (2012) [48] | 62.5%                  | Respiratory syncytial virus        |
| Qatar   | Janahi et al. (2017) [49] | 51.2%                  | Respiratory syncytial virus        |
|         |                    | 25.5%                  | Rhinovirus                         |
| Turkey  | Azkur et al. (2014) [65] | 33.3%                  | Respiratory syncytial virus        |
|         |                    | 33.3%                  | Rhinovirus                         |
|         |                    | 33.3%                  | Influenza A virus                  |

However, there is a conflict regarding the role of HBoV in cases of co-infection. Some studies reported no differences in clinical severity between patients hospitalized with a single infection (sole virus) and those with viral co-infection [13,47]. Others proved
that more disease severity was associated with a high viral load detected in a single infection [18,76].

5. Conclusions

This systematic review provides a clear summary of the existing knowledge about the prevalence of HBoV infection in the MENA region. The data presented show that HBoV infection is common in children admitted to hospitals and should be screened for as a part of the standard diagnostic panels. This systematic review also highlights the importance of studying the presence of this virus alone or in association with other viruses and stresses the need for further research on the pathogenicity and genomic variation of HBoV.

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