Prevalence and Clinical Features of Rotavirus among Children in Eastern Mediterranean Region: A Systematic Review

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ABSTRACT

Background: Clinical features of rotavirus gastroenteritis vary from mild to severe and the prevalence of the disease is high in Eastern Mediterranean Region. The aim of this systematic review is to create solid evidence for the prevalence and clinical features of rotavirus among children under five years in Eastern Mediterranean Region.

Methods: Several databases have been searched: MEDLINE, PubMed, ScienceDirect, google scholar and the Cochrane Library. In addition, the authors searched relevant organizations websites and, they went through grey literature search. A total of 3220 articles have principally traced. After excluding the irrelevant, ineligible, duplicated and very low-quality papers, only 10 studies were included in this review.

Results: The highest prevalence rate of rotavirus in the Eastern Mediterranean Region countries was reported from Egypt by 76.9%[1] followed by Bahrain by 44.8%[2] then Jordan by 39.9%[3] and it was less prevalent in Saudi Arabia and Sudan by 10% and 16% respectively[4,5]. Diarrhea, vomiting and fever were reported in high rates in most countries[1-10], and in low rate in Saudi Arabia[1]. Dehydration was reported in Libya by 93.5%[6], Bahrain by 95.3%[2], Yemen by 59%[10] and Egypt by 56%[1].

Conclusion: The prevalence of rotavirus in Eastern Mediterranean Region countries was ranged between 10% in Saudi Arabia to 76.9% in Egypt. Diarrhea, vomiting, and fever were more prevalent in many countries of the region while dehydration was mainly reported in Libya, Bahrain, and Egypt.

Keywords: Clinical features, RV, Eastern Mediterranean Region, Under-five children.

INTRODUCTION

Based on previous reports from Eastern Mediterranean Region (EMR) countries, rotavirus (RV) is the responsible factor for gastroenteritis among young children[2]. For instance, in 2008, it represented 36% of diarrheal cases among under 5 years children annually, it accounted for approximately 453,000 deaths globally among them about 65,000 from 22 countries of the EMR[2,11]. World Health Organization (WHO) has reported that RV gastroenteritis among young children has reduced after introduction of vaccine[12]. RV represented the main leading cause of diarrhea and related deaths in the region[13].

Gastroenteritis related to RV is manifested by diarrhea, fever, and vomiting, and rarely could results in severe dehydration and could lead to death in young children specially in developing countries and developed countries[14]. Seasonal variation in the incidence of the disease has been noted, particularly in temperate climates where it peaks during the cooler months, while in tropical climates cases occur throughout the year[15].

Recent reports from EMR countries have stated that approximately 65,000 children die annually for reasons related to RV in EMR. The mortality rate in the region, is still high, especially in low-income countries, such as Pakistan, Afghanistan, Sudan, Yemen, and Somalia[16]. Furthermore, the morbidity and mortality of the RV is on the top compared to other regions, limited data is found on the burden of RV for each country of the region. The prevalence of different strains in EMR countries after introduction or RV vaccine was reported in recent systematic review by Almalki 2018, which highlighted that some RV stains have been increased after vaccination[17]. A scientific inquiry has been raised about the reported prevalence and clinical features of RV cases among children between 0-5 years in EMR countries.

METHODS

Keywords and search strategy

The authors used specific keywords about RV clinical features and the findings from searched database were presented in table 1. They restricted their search to English and the studies conducted after January 2010 and up-to date of search (September 2021). The searches were research the databases immediately before starting analysis.

The search strategy and the used keywords for this review were explained in the summary of search results (Table 1). The flowchart was used to reflect the different stages of the systematic review (identification, screening, eligibility, and inclusion), as shown in figure 1.

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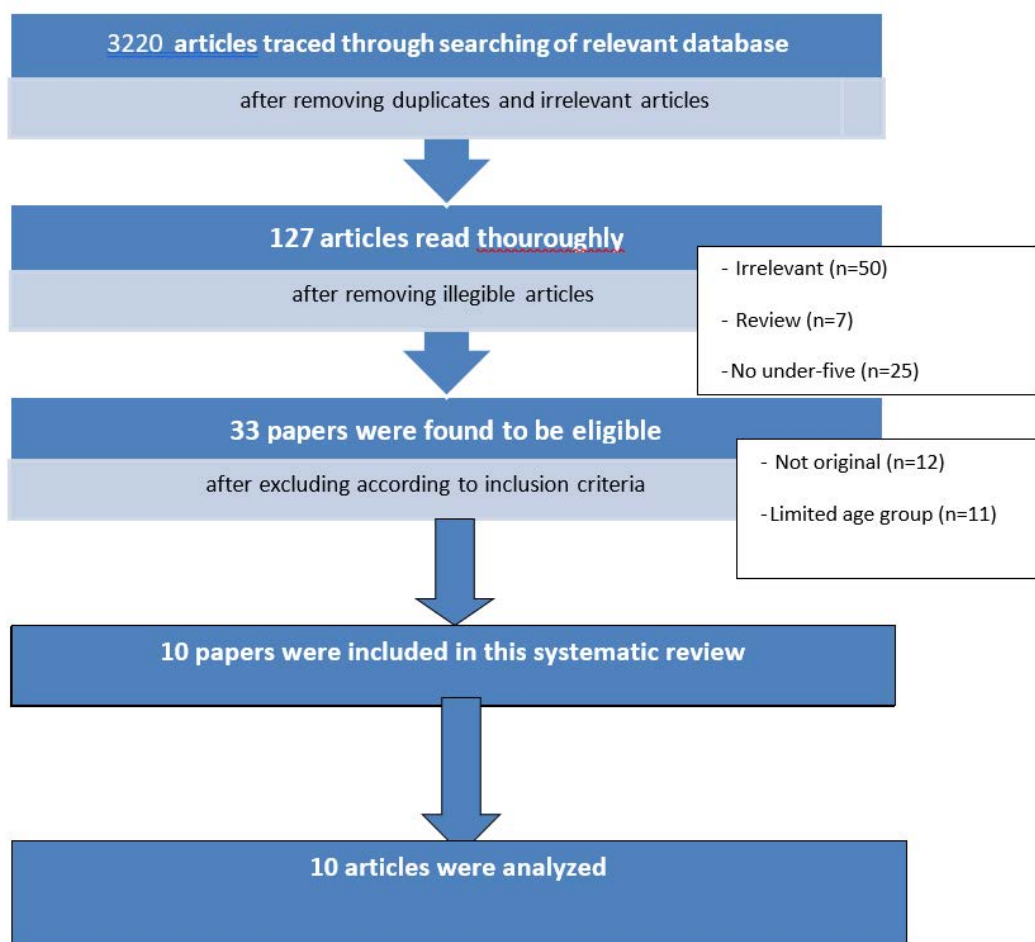**   Department of Laboratory Medicine
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Table 1: Summary of search results

Search Engine	Search Terms	Limits activated	Date searched	Papers
Cochrane	RV		23th January, 2017	6
PubMed (MEDLINE (OvidSP), and EMBASE (OvidSP)	(Clinical features OR characteristics) AND RV AND (under-five children OR CHILDREN) AND (Eastern Mediterranean OR MIDDLE EAST OR EMR)	Human	20 September, 2021	17
ScienceDirect	(EMR AND RV) OR (Afghanistan AND RV) OR (Bahrain AND RV) OR (Djibouti AND RV) OR (Egypt AND RV) OR (Iran AND RV) OR (Iraq AND RV) OR (Jordan AND RV)	Year: 2010-2021	22 September, 2021	612
	(Saudi Arabia AND RV) OR (Somalia AND RV) OR (Sudan AND RV) OR (Syrian Arab Republic AND RV) OR (Tunisia AND RV) OR (United Arab Emirates AND RV) OR (Yemen AND RV)	Year: 2010-2021	22 September, 2021	930
	(Kuwait AND RV) OR (Morocco AND RV) OR (Lebanon AND RV) OR (Oman AND RV) OR (Pakistan AND RV) OR (Qatar AND RV)	Year: 2010-2021	22 September, 2021	715
ISI Web of Science and Conference Proceedings/ Publon	RV AND Features		25 September, 2021	3
Google scholar	(Clinical features OR characteristics) AND RV AND (under-five children OR CHILDREN) AND (Eastern Mediterranean OR MIDDLE EAST OR EMR)		25 September, 2021	937
	Titles and Abstracts examined			3220
	Full texts retrieved			127
Total	**Papers included in the review**			**10**

3 Limits Activated: Years: 2000-2021, Humans, and Children < 5 years

Figure 1: Flow diagram

Eligibility criteria

All articles published in English and dated after 2010 and before October 2021, were included in this systematic review. Articles included the search terms in any fields were screened (3220 articles). The duplicated and irrelevant articles were excluded according to titles and abstracts (3126 excluded articles). Then, the full texts were retrieved for other eligible articles (94 articles) to conduct in-depth reading for the RV features. Then, the exclusion of the irrelevant studies based on the full text of articles was conducted to yield finally included studies in this systematic review (10 articles).

Data sources

The authors have searched the following websites: MEDLINE, PubMed, ScienceDirect, google scholar and Cochrane Library (Cochrane Database of Systematic Reviews). Several organizations websites were also included such as WHO and CDC in addition to the grey literature search. A total of 2198 papers have primarily found. After excluding of irrelevant, ineligible, duplicated and very low-quality papers, only 35 studies are included in this systematic review. The details of search strategy were demonstrated in table 1.

Type of studies

This systematic review included only the studies with cross-sectional, comparative and surveillance designs.

Data extraction

Three researchers independently screened the search results using inclusion criteria. They retrieved the full- text articles of all possibly relevant references selected by either screener. The full-text articles were requested and checked for eligibility. The reference manager software EndNote X8 was used to sort the retrieved articles into inclusion and exclusion folders. The search strategy and the selection process of the studies were detailed using flowchart, figure 1.

Two researchers separately extracted data on a prepared form for data extraction. The data extraction form was tested and refined based on a pilot data extraction. In case of disagreement during studies selection or data extraction, the third researcher additionally reviewed the studies and agreement was reached based on discussion and consensus. They then confirmed all data extraction and in case of discrepancies, check the original articles were conducted.

Risk of bias (quality) assessment

The selected studies were appraised using the criteria of STROBE Statement—Checklist for observational studies, the quality of studies was measured using the checklist include:
1. Setting of study
2. Sample size
3. Bias
4. Diagnostic test used
5. The outcome data

Two authors independently judged each domain for bias as 'high risk', 'low risk', or 'unclear risk'. The judgment was confirmed with the third researcher and when reaching consensus, studies were divided into "low risk"," high risk" and "unclear risk", and the studies with poor quality (high risk studies) were excluded from this systematic review (Table 2).

Statistics

The narrative analysis was conducted and guided by statistician. The findings were written as narrative summary. The clinical features were reported as frequency and percentages.

Dissemination plan

This systematic review is independent work. The researcher intends to publish the findings of this systematic review in scholarly peer-reviewed journal and circulation of final report to the faculties and institutes in the region.

This systematic review included 10 studies from nine countries (Bahrain, Jordon, Libya, Pakistan, Lebanon, Sudan, Yemen, Saudi Arabia and Egypt).

Types of outcome measures

Primary outcome(s): The main outcome was the clinical features of RV cases in EMR countries.

Secondary outcome(s): Secondary outcomes include:
1. RV prevalence
2. RV clinical features

Table 2: Quality assessment of included studies

Country	Author	Year	Sample	Design	Study area	Age	Quality
Bahrain	(Al Musawi et al., 2013)[2]	2006	239	Hospital based surveillance	Single Pediatric Hospital	Under 5	Moderate
Jordon	(Nafi, 2010)[3]	2007-08	148	Prospective Hospital-based study	Al-Karak General Teaching Hospital	Under 5	Moderate
Libya	(Abugalia et al., 2011)[6]	2007-08	1090	Cross-sectional	Inpatient outpatient	Under 5	High
Pakistan	(Kazi et al., 2014a)[7]	2006-08	6679	Cross-sectional	5 Sentinel Hospitals	Under 5	High
Lebanon	(Dbaibo et al., 2013)[8]	2007-08	491	Hospital-based surveillance	5 large hospitals	Under 5	High
Sudan	(Magzoub et al., 2014)[5]	2010	755	Hospital based study	Pediatric hospitals in states	Under 5	High
Yemen	(Banajeh and Abu-Asba, 2015)[9]	2013-14	5691	Comparative study	2 Sentinel Hospitals	Under 5	High
	(Al-Sonboli et al.)[10]	2016	400	Cross-sectional	Al-Sabeen Hospital	Under 5	High
Saudi Arabia	(Ghazi et al., 2005)[4]	2003	479`	Descriptive	3 hospitals	Under 5	High
Egypt	(Ibrahim et al., 2015)[1]	2014-15	65	Case-control	Pediatric department/ Zagazig University Hospital	Under 5	Low

Table 3: Summary of the systematic review findings

Country	Author	Year	Prevalence	Severity	Diarrhea	Vomiting	Fever	Dehydration	Hospital Stay
Bahrain	(Al Musawi et al., 2013)[2]	2006	44.8%	11.4 % sever	100%	97.2%	58.9%	95.3%	3.8 days
Jordon	(Nafi, 2010)[3]	2007-08	39.9%	-	96.6%	86.4%	75%	11.1 sever	-
Libya	(Abugalia et al., 2011)[6]	2007-08	35.8%	-	100%	97.8%	86%	Mild 93.5%	4 days
Pakistan	(Kazi et al., 2014a)[7]	2006-08	30.5%	-	100%	58.6%	52.8%	Sever	7 days
Lebanon	(Dbaibo et al., 2013)[8]	2007-08	27.7%	79.4% sever	98.5%	87.5%	81.6%	-	7-11 days
Sudan	(Magzoub et al., 2014)[5]	2010	16%	-	Diarrhea & Fever &Vomiting = 44.6% Diarrhea & Vomiting = 36.4% Diarrhea & Fever =14%			-	-
Yemen	(Banajeh and Abu-Asba, 2015)[9]	2013-14	19.9%	-	100%	93%	45%	-	-
	(Al-Sonboli et al.)[10]	2016	29.5%		100%	89.8%	80.5%	Sever& moderate =59%	-
Saudi Arabia	(Ghazi et al., 2005)[4]	2003	10%	-	62%	-	-	-	-
Egypt	(Ibrahim et al., 2015)[1]	2014-15	76.9%	-	100%	92%	84%	Sever 56%	-

RESULTS

All included studies investigated the prevalence of RV and its clinical features in all EMR countries but the data on the topic were found only in 9 countries out of 22[1-10]. The ten included studies for this review were found from nine countries (Bahrain, Jordon, Libya, Pakistan, Lebanon, Sudan, Yemen, Saudi Arabia, and Egypt)[1-10]. The highest prevalence rate of RV was reported from Egypt (76.9%)[1] among under-five children admitted to hospital with diarrhea followed by Bahrain by 44.8% among admitted children with severe diarrhea[2] then Jordan by 39.9%[3]. The studies from Saudi Arabia and Sudan reported the lowest prevalence rate of RV by 10% and 16% respectively[4,5].

Furthermore, all studies reported that more than 95% of cases have diarrhea[1-10] except the findings of Saudi Arabia studies where only 62% of children have diarrhea[1].

Another presenting features the children came to hospitals with was vomiting where it was reported from all studies[1-10] except the findings of Saudi Arabia[1].

Fever as one of the reported features among children with RV where it was reported from all studies[1-10] except the findings of Saudi Arabia study[1].

Dehydration as one of the most dangerous sign among infected children, it was ranged from sever to mild and it was commonly reported from Libya by 93.5%[6], Bahrain by 95.3%[2], Yemen by 59%[10] and Egypt by 56%[1]. It was less prevalent from study in Jordan where only 11.1% of case suffered dehydration[7]. It was not reported in the findings from other studies from Lebnon, Sudan, Saudi Arabia[4,5,8].

The hospital stay was also reported from some studies from Bahrain, Libya, Pakistan and Lebanon[2,6-8] which ranged from 3.8 to 11 days.

DISCUSSION

There is a notable shortage for recent studies on the prevalence of RV infections to cover the Eastern Mediterranean region[18]. However, the previous studies on prevalence of RV infections that were conducted in the EMR countries showed that RV infections were ranged from 19%-78.2% of all investigated diarrheal specimens[19]. There are some reports

that highlighted the fact, although the introduction of RV vaccines into the EMR countries, the RV were still responsible for about 65,000 deaths annually among children[16].

The clinical features of RV gastroenteritis among under-five children was reported in ten included studies from nine countries of EMR[1-10]; The nine countries include: Bahrain, Jordon, Libya, Pakistan, Lebanon, Sudan, Yemen, Saudi Arabia, and Egypt[1-10]. The rates of RV infections were varied from country to another in the EMR countries. Among under-five children admitted to hospital with diarrhea, the highest prevalence rate of RV infections was reported in Egypt estimated at 76.9%[1]. That was followed by 44.8% in Bahrain[2] then Jordan by 39.9%[3]. The studies from Saudi Arabia and Sudan reported the lowest prevalence rate of RV by (10% and 16% respectively)[4,5]. This review has shown that clinical features reported among under-five children from the included countries were varied from sever to mild in most of the cases. The clinical features were reported to include diarrhea, fever, vomiting and dehydration. In fact, these findings are similar to the findings of a study that was conducted in Jordan. The Jordanian study showed that gastroenteritis related to RV infections is manifested by diarrhea, fever, and vomiting, and rarely could results severe dehydration. The diarrheal manifestation of RV infections was common in both developing and developed countries[14].

The current review showed that more than 95% of cases had diarrhea[1-10] except the findings of some studies in Saudi Arabia which showed that only 62% of children had diarrhea[1]. Likewise, vomiting and fever, were reported in most studies in different EMR countries as clinical features of RV infections[1-10], except in the findings of the studies that were conducted in Saudi Arabia[1].

Dehydration as one of the most dangerous signs among infected children, it was ranged from severe to mild. It was commonly reported in Libya estimated at 93.5% of the infected children[6]. In Bahrain was about 95.3%[2], then, Yemen by 59%[10] and Egypt by 56%[1]. It was less prevalent in Jordan for about 11.1% of cases[7]. Dehydration seemed to be not significant in the findings from other studies in Lebanon, Sudan and Saudi Arabia[4,5,8]. The hospital stay was also reported from some studies including some countries i.e. Bahrain, Libya, Pakistan and Lebanon[2,6-8] which ranged from 3.8 to 11 days.

Nevertheless, this systematic review has used scientific search strategy and all traced studies were included in the review, there is still a limitation due to no appropriate statistics on the current situation. The clinical studies of the RV infections feature only covered limited number of EMR countries. This is almost covered only the half of the EMR countries due to the lack of research on this area.

CONCLUSION

The prevalence rate of RV infections in EMR countries was varied between (76.9%) in Egypt to 10% in Saudi Arabia. Diarrhea, vomiting, and fever were more prevalent in many cases in the covered studies while dehydration was reported mainly in Libya, Bahrain, and Egypt.

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