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Original Article

Cholera Outbreak in Hadhramout, Yemen: The Epidemiological Weeks 2019

Eidha Ali Bin-Hameed[1*], **Huda Ameen Joban**[2]

[1]Hadhramout University, Hadhramout, Yemen
[2]The National Center of Public Health Laboratories, Hadhramout Coast Branch, Yemen

***Corresponding Author:**
Eidha Ali Bin-Hameed,
Email: eidha6@gmail.com

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Abstract

Background and aims: Cholera is a disease of acute watery diarrhea caused by *Vibrio cholerae* usually transmitted through contaminated water. In this study, we collected and analyzed the related epidemiological data to determine cholera outbreak in Hadhramout, Yemen during the disease epidemic in 2019.

Methods: A cross-sectional study was conducted according to screening rapid diagnostic and confirmatory laboratory culture testing methods for diagnosing clinically cholera cases.

Results: Suspected cholera cases were tested by rapid diagnostic test (RDT) and 399 (50.5%) out of 794 cases were determined positive, and 76(9.6%) of them were confirmed by laboratory culture test (LCT) with statistically significant difference. Serotype *V. cholerae* O1 was also detected in patients' diarrhea. Females were the most affected by the disease manifested in 201 (25.3%) and 43 (5.4%) when tested by RDT and LCT, respectively, with no statistically significant difference. The highest proportion of cholera cases (224) were reported in the age group less than 15 years (56.1%) with statistically significant difference when tested by RDT, and 45(13.3%) when tested by LCT with insignificant statistics difference. Hajr directorate was revealed to be the most affected with 242 (30.47%) followed by Mukalla city directorate with 108 (13.60%) when the cases were tested by RDT; while Hajr and Mukalla city directorates reported 55 (7.0%) and 15 (2.0%), respectively, when it was confirmed by LCT with a statistically significant difference.

Conclusion: Severe cholera outbreak occurred during the epidemiological weeks in 2019 in Hadhramout coast. *V. cholerae* O1 serotype was the causative agent of cholera. Females and age group less than 15 years were the most affected by the disease. Hajr and Mukalla city directorates reported serious outbreak cholera cases.

Keywords: Cholera, Epidemiological data, Outbreak, *Vibrio cholerae*

Introduction

Cholera is considered a significant public health disease in many developing countries. It is an acute fatal watery diarrheal disease caused by the bacterium *Vibrio cholerae*. *V. cholerae* is a highly motile Gram-negative and non-invasive bacteria which colonizes the small intestine,[1] and includes pathogenic and non-pathogenic strains. *V. cholerae* O1 and O139 serotypes are the sole factors responsible for the disease which is clinically and epidemiologically defined as cholera.[2-4] Serotype *V. cholerae* O1 is divided into classical and El Tor biotypes, and into three sero-subtypes; that is, Ogawa, Inaba and Hikojima. Serotype *V. cholerae* O139 has several characteristics in common with El Tor biotype, but it differs from serotype O1 regarding polysaccharide surface antigen.[5] Other serovars of *V. cholerae* are generally termed as non-O1 and non-O139 strains, and these are non-choleragenic, usually causing a milder form of gastroenteritis than serotypes O1 and O139.[6] *V. cholerae* (including both serogroups O1 and O139) is a natural inhabitant of the aquatic environment, particularly brackish, riverine, estuarine, and coastal waters.[7]

Vibrio cholerae produces a major virulence factor enterotoxin (cholera toxin) that is primarily responsible for the diarrheal disease and is characterized by profuse water and ion loss.[1] Cholera is spread either directly from person to person or indirectly through contaminated fluids from an environmental reservoir of varying duration, food, and potentially flies and fomites.[8,9] The occurrence of epidemics cholera is an obvious sign of the disruption of basic services.[10] Therefore, cholera disease is closely related to overcrowded settings, poor hygienic status, and environmental conditions in typical at-risk areas like urban slums with precarious basic infrastructures and internally displaced or refugee camps. Also, the most affected populations are those living in insalubrious conditions where environmental safety is not ensured.[11]

Yemen is situated in southwest Asia on the Arabian Peninsula and has diverse topography with mountainous areas in the north, desert in the east, a coastal landscape in the south and the west. Cholera disease outbreaks was reported as early as the 1980s.[12] Outbreak of cholera in Yemen is the largest in the recent history of the disease, and the magnitude of this outbreak may be explained by the overall breakdown of public services like hygienic and sanitation conditions.[13] During 2008-2012, the estimated annual number cases of cholera in Yemen were 17.546, and the estimated annual number of deaths were 561.[14] Several outbreaks of cholera occurred during the last 10 years in Yemen with 3 smaller outbreaks in 2009, 2010 and 2011, and with case fatality rate (CFR) of 5.5%, 1.3% and 0.4%, respectively.[15-17] The most severe outbreak occurred in October 2016 with 1 423 700 suspected cases.[18] Following Spatial modelling technique, Yemen is defined as an endemic country for cholera with around 17 546 cases per year, and a CFR of 3.20%.[14] In 2017, Yemen was the first country to report more than one million suspected cases in a single year when 41% of cholera attributed fatalities and 2261 deaths were recorded, which was evidence of the severity of the epidemic sweeping the country.[19] In 2018, the outbreak of cholera became a major public health issue in Yemen. A total of 1 111 653 cases and 2,400 deaths were reported up to March 2018.[20] Also, a total of 4510 laboratory confirmed cases were reported from 306 districts for January 2019, resulting in 2767 deaths corresponding to a CFR of 0.6%.[18]

Hadhramout governorate – Southern Yemen – recorded the first outbreak of cholera during the years 2017 and 2018.[21] So far, several studies have been conducted to investigate the cholera outbreak in Yemen, but none has been ever carried out to explore Hadhramout governorate since the first cholera outbreak in 2017. Therefore, this study aimed to examine and analyze the epidemiological data concerning cholera outbreak in Hadhramout coast governorate from January to December 2019. This study may help the healthcare system to epidemiological develop prevention and control activities supported by medical surveillance.

Materials and Methods

Study Area and Location

The geographical area of the study was Hadhramout coast district, the first division of Hadhramout governorate with a population of around 706, 070 people, spread over approximately 26 852.25 km^2 and separated into 12 directorates (Figure 1). Topographically, the district includes hills, valleys, and coast.[21]

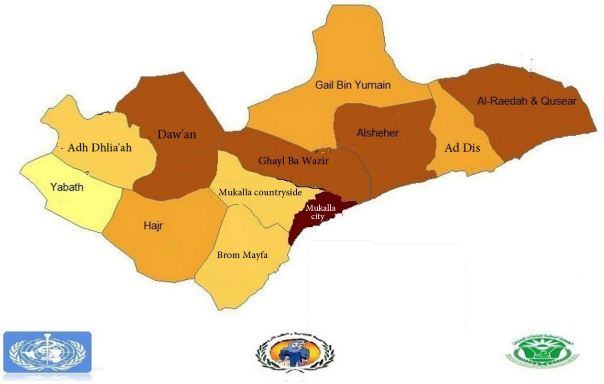

Figure 1. Map of Hadhramout Coast Directorates.[21]

Study Design and Study Population

This study is a cross-sectional study aimed to examine the epidemiological data of cholera outbreak in 2019 in Hadhramout coast governorate. We reviewed the data on cholera epidemic reported by the epidemiological surveillance department at the ministry of health and population office in Hadhramout coast, Yemen, and the national center of public health laboratories, Hadhramout coast branch, from January to December 2019. Variables recorded in the line list included name, age, sex, residence, and rapid diagnostic test (RDT) result. The suspected cholera cases were also confirmed by culture test and the CFR as well as attack rate (AR) were calculated.

Among the study population, 388 (48.9%) were males and 406 (51.1%) were females. The age groups were classified into less than 15 years 468 (58.9%), 15-30 years 140 (17.6%), 31-45 years 103 (13.0%), 46-60 years 50 (6.3%) and over 60 years 33 (4.2%). The total cases of districts were as the following; Hajr 555 (69.9%), Mukalla city 141 (17.8%), Brom Mayfa 42 (5.3%), Daw'an 40 (5.0%), Ad Dis 5 (0.6%), Ghayl Ba Wazir 4 (0.5%), Mukalla countryside 3 (0.4%), Adh Dhlia'ah 3 (0.4%), and Huraidhah 1(0.1%) case.

Inclusion and Exclusion Criteria

All clinically suspected cholera cases were included in the study, whereas non-clinically suspected cholera cases were excluded.

Rapid Diagnostic Test

RDT was performed according to the kit manufactured by ARKRAY Health care Pvt. Ltd., India. Serotyping of *V. cholerae* O1 and O139 was detected by lateral flow immunochromatographic one step rapid visual dipstick test. The test is a simple *in vitro* qualitative screening test for detecting lipopolysaccharide (LPS) antigen of *V. cholerae* O1 and O139 in human stool, in order to diagnose cholera through using monoclonal antibodies specific to *V. cholerae* O1 and O139 LPS.

Bacteriology and Serotyping

The clinical diagnosis of cholera is based on the WHO case definition; it is confirmed in a laboratory when *V. cholera* O1 or O139 is detected in a patient's diarrhea or vomitus.[22] In this study, the standard laboratory culture test (LCT) method was used to examine the positive RDT cholera cases. Bacterial culture isolates were grown on an enrichment alkaline peptone water broth (Deben Diagnostics Ltd., England), then were sub-cultured on thiosulphate citrate bile salt sucrose (TCBS) agar (Oxoid, England) at 37°C for 18–24 hours. Typical sucrose fermenting yellow colonies were subsequently used in routine identification, and presumptive identified *V. cholerae* isolates were examined by oxidase test. Confirmed identification was employed using O1 and O139 antisera for slide agglutination testing with polyvalent O1 or O139 antisera kit (Denka Seiken Co., Ltd. Japan) for fresh growth of suspected *V. cholerae*.

Data Analysis

The data were analyzed by Statistical Package for Social Sciences (SPSS) software, version 19.0. Descriptive statistics was adopted to measure the frequencies and percentages. Comparison between variables was performed using F-test and one-way ANOVA. The association between different categories was measured and compared using Pearson chi-square test. Statistical significance was defined at *P* values less than 0.05.

Results

The study showed outbreak of cholera cases in some districts of Hadhramout coast during the epidemiological weeks in 2019. A total of 794 suspected cholera cases were screened by RDT and confirmed by LCT with statistically significant differences for positive cases (*P* value = 0.001) (see Table 1). Using bacteriology and serotyping test, *V. cholerae* O1 serotype was detected in patient's diarrhea 76 (9.6%).

According to RDT and LCT results, females were more affected by the disease than males. The highest proportion of cholera cases was reported to belong to the age group less than 15 years. High cholera cases were reported by Hajr and Mukalla city, as shown in Tables 2 and 3. According to the indicators of cholera cases outbreak in Hadhramout coast during 2019, CFRs was 0.9 and attack rate (AR)/10000 people was 7.0 (see Table 4).[21]

Time distribution of cholera exhibited a marked difference in epidemic. An association was discovered between outbreak of disease and seasons in districts from March to June, as the highest number of cases was recorded from July to October, and the lowest number was observed from November to February (Figure 2).

Table 1. Cholera Outbreak According to RDT and LCT

Type of Test	Result	Frequency	Percent	Mean	F- Statistic	*P* Value
RDT	Positive	399	50.2	0.478	3.429	0.001
	Negative	229	28.8			
	Not done	166	21.0			
	Total	794	100.0			
LCT	Positive	76	9.6	0.574	16.399	0.001
	Negative	164	20.6			
	Not done	554	69.8			
	Total	794	100.0			

Abbreviations: RDT, rapid diagnostic test; LCT, laboratory culture test.

Discussion

This study aimed to study and analyze the related epidemiological data on cholera outbreak in Hadhramout, Yemen during the disease epidemic in 2019. Adopting bacteriological examination of stool samples, *V. cholerae* O1 serotype was detected. Several other studies investigating cholera outbreak in different countries have shown that the same agent is responsible for cholera. Countries involved in the given studies are: India, *V. cholerae* O1 biotype El Tor serotype Ogawa[23] and *V. cholerae* O1,[24] Bangladesh *V. cholerae* O1/O139,[25] Nigeria *V. cholerae* O1 biotype El Tor,[26,27] Guinea *V. cholerae* El Tor,[28] Kenya *Vibrio cholerae* O1 El Tor variant,[29] and Indonesia *V. cholerae* O1 ST69 strains.[30]

Subjects affected by the disease were found in all age groups for males and females from less than 15 years to 60 years. The most affected ones were found to be under 15 years of age. This is consistent with the results from other study reporting the infection in individuals aged between 1 to 70 years.[31] Following another study, the majority of the cases diagnosed with the disease was reported to be under 18 years of age.[32] A different study showed that more than half of the suspected cases were within the age group 3 to 10 years.[23] In children aged <5 years, incidence of severe diarrhea was found during May 2012 due to cholera attack rate ranged from 1.0 to 11.0/1000 children.[31] Also, females were the most affected with cholera disease in this study with no statistically significant difference, and this is inconsistent with the result of another study introducing males as the most affected ones.[23]

The present study revealed that CFRs was 0.9; therefore, great majority of cholera deaths occurred during the first weeks after the beginning of outbreak. This result may have been generated due to delay in care-seeking or accessing traditional healers instead of referring to health clinics at

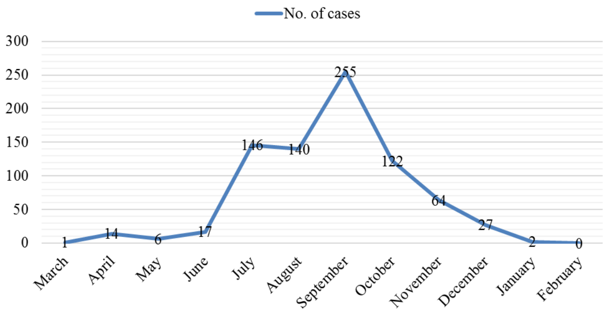

Figure 2. Time Distribution of Cholera Cases During 2019.

Table 2. Cholera Outbreak in Relation to Demographic Variables According to RDT

Variables	Categories	RDT Results				χ2 Test	*P* Value
		Total Cases	Positive No. (%)	Negative No. (%)	Not Done No. (%)		
Gender	Male	388	198 (25.0)	113 (14.2)	77 (9.7)	0.418	0.518
	Female	406	201 (25.3)	116 (14.6)	89 (11.2)		
Age groups (y)	<15	468	224 (28.2)	130 (16.4)	114 (14.3)	8.953	0.003
	15-30	140	75 (9.4)	37 (4.7)	29 (3.7)		
	31-45	103	56 (7.0)	32 (4.0)	14 (1.8)		
	46-60	50	26 (3.3)	18 (2.3)	6 (0.8)		
	> 60 years	33	18 (2.2)	12 (1.5)	3 (0.4)		
District	Hajr	555	242 (30.47)	184 (23.17)	129 (16.24)	1.701	0.192
	Mukalla city	141	108 (13.60)	16 (2.01)	17 (2.14)		
	Mukalla countryside	3	3 (0.37)	0 (0)	0 (0)		
	Brom Mayfa	42	21 (2.64)	20 (2.51)	1 (0.12)		
	Ad Dis	5	4 (0.50)	0 (0)	1 (0.12)		
	Adh Dhlia'ah	3	2 (0.25)	0 (0)	1 (0.12)		
	Daw'an	40	16 (2.01)	7 (0.98)	17 (2.14)		
	Ghayl Ba Wazir	4	3 (0.37)	1 (0.12)	0 (0)		
	Huraidhah	1	0 (0)	1 (0.12)	0 (0)		

Abbreviation: RDT, rapid diagnostic test.

Table 3. Cholera Outbreak in Relation to Demographic Variables According to LCT

Variables	Categories	LCT Results				χ2 Test	*P* Value
		Total Cases	Positive No. (%)	Negative No. (%)	Not Done No. (%)		
Gender	Male	388	33 (4.2)	86 (10.8)	269 (33.9)	0.532	0.466
	Female	406	43 (5.4)	78 (9.8)	285 (35.9)		
Age groups (y)	<15	468	45 (5.66)	90 (11.33)	333 (41.93)	0.112	0.738
	15-30	140	12 (1.51)	39 (4.91)	89 (11.29)		
	31-45	103	11 (1.38)	20 (2.51)	72 (9.06)		
	46-60	50	4 (0.50)	6 (0.75)	40 (5.03)		
	> 60 years	33	4 (0.50)	9 (1.13)	20 (2.51)		
District	Hajr	555	55 (7.0)	70 (8.8)	430 (54.1)	9.325	0.002
	Mukalla city	141	15 (2.0)	71 (8.9)	55 (6.9)		
	Mukalla countryside	3	1 (0.1)	1 (0.1)	1 (0.1)		
	Brom Mayfa	42	4 (0.5)	14 (1.8)	24 (3.0)		
	Ad Dis	5	0 (0.0)	3 (0.4)	2 (0.3)		
	Adh Dhlia'ah	3	0 (0.0)	0 (0.0)	3 (0.4)		
	Daw'an	40	1 (0.1)	5 (0.6)	34 (4.3)		
	Ghayl Ba Wazir	4	0 (0.0)	0 (0.0)	4 (0.5)		
	Huraidhah	1	0 (0.0)	0 (0.0)	1 (0.1)		

Abbreviation: LCT, laboratory culture test.

the beginning of outbreak, and also may have reflected differing case severity or improved case management as an outbreak progress.[33] Identification and case management of cholera outbreak are important because mortality can be rapidly reduced by early and aggressive intervention. The majority of areas in the world have achieved CFRs of <1% even with limited resources.[34] A study carried out in India in 2009 showed that diarrheal deaths caused by cholera were most common among 18.5/100 000 of the population.[31] Other studies reported CFR of 0.87% in Mozambique during 2009–2011,[33] 2.2% in Congo during 2000-2007,[35] and 0 in India 2018.[23]

Contaminated water was determined as the main sources of infection during cholera outbreak in Hadhramout. This finding confirms the results from several other studies.[23,36,37] Socioeconomic status and urban/rural geography play a more important role in cholera outbreak risk factor than nationality.[38] Also, cholera outbreak exhibited different

Table 4. Indicators of Cholera Cases in Hadhramout Coast During 2019

Suspected cases	Deaths	CFR%	AR	RDT	LCT	Affected Districts
			/10000	Positive	Positive	
794	7	0.9	7.0	399	76	8(67%)

Abbreviations: CFR, case fatality rate; AR, attack rate; RDT, rapid diagnostic test; LCT, laboratory culture test

seasonal climate patterns in Hadhramout coast district. Coastal climate varies, and it is often warm in summer and mild in winter. There is semi-monsoon rain in Mukalla city district, and there are desert and valley with hot, dry climate throughout the year in Hajr district. Thus endemic area with cholera was found to be associated with tidal seawater intrusions and seasonal climate patterns, whereas epidemic cholera often occurs near waterways when weather conditions are favorable for the bacteria to growth.[39]

In this study, epidemic of cholera was considered as an alarming sign of absence or shortage of safe water and sanitation infrastructures, poor hygiene, unhealthy social practices, and a weak public health system. Rapid spread of cholera disease through contaminated fluids may be facilitated by a transient hyperinfective state of *V. cholerae* present in fresh stool.[40,41] *V. cholerae* hyperinfectivity for a few hours after dissemination may have implications for transmission, especially in densely populated areas.[42] In addition, direct exposure to households contributes significantly to transmission of cholera [43], and nearness to cholera patients increases the risk of disease development.[44] Cholera disease outbreak in Yemen is directly associated with damage to infrastructure. It is possible to control such an outbreak through public health measures including early detection, immediate reporting, as well as timely and effective responses.[45,46] Considering the actual context of Yemen and its water infrastructure, much more efforts are needed to control the cholera outbreak resurgence.[47] Cholera outbreak in Yemen highlights the importance of holding a continuing discussion by international humanitarian health organizations discussing whether, and to what extent, they should increase their focus on environmental determinants of communicable diseases in humanitarian emergencies.[48]

Conclusion

High cases of cholera were detected during the epidemiological weeks in 2019 in Hadhramout coast. *V. cholerae* O1 serotype was the causative agent of cholera. Females and age group less than 15 years were the most affected with cholera. Hajr and Mukalla city directorates reported serious cholera outbreak cases. As indicators of cholera cases, CFRs was found to be 0.9 and AR was revealed to be 7.0. For combating cholera in Hadhramout effectively, there is a need to strengthen and provide proper laboratory support in future. We recommended that safe water and food supplies should be provided over the year. The health facility infrastructures, training of the rapid response teams for outbreak investigation, and report writing should be improved.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests, financial interest, or such like.

Ethical Approval

This research was authorized by the ministry of health and population office/Hadhramout coast governorate, Yemen.

Author's Contributions

HJ conceptualized the study and interpreted all of the data. EH wrote, edited and reviewed the manuscript. All authors read and approved the final manuscript.

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