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EPIDEMIOLOGICAL FEATURES OF THE CHOLERA EPIDEMIC IN YEMEN, 2016-2017

By
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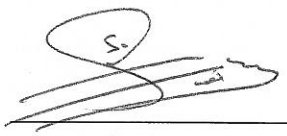

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AN ABSTRACT OF THE THESIS OF

Abdullah Ameen Salem Awash for Master of Science
Major: Epidemiology

Title: Epidemiological features of the cholera epidemic in Yemen, 2016-2017

Background: Cholera was believed to be under control in Yemen, till the eruption of full-fledged civil war and foreign interventions in 2015. Since then, the country experienced by a major epidemic, the largest in more than a century. This thesis presents the characteristics of the epidemic in the first two waves spanning the period from October 2016 to October 2017.

Objective: To describe the epidemiological characteristics of cholera incident cases and case-fatality, and to evaluate the overall quality of the control measures and gaps in surveillance within the context of the current violence.

Methods: All cases and deaths reported to the Yemen Ministry of Public Health& Population (MOPH&P) sources were retrospectively described geographically, historically and demographically (age and gender). The clinical and laboratory characteristics of reported cholera cases were also tabulated. Finally, variable-specific rates of incomplete reporting in records at the MOPH&P were studied.

Results: There were 901,191 cases reported until the end of the observation period, from twenty-twoYemenis governorates, especially in two peak outbreak waves (October 2016 n= 26028, and April 2017 n= 875163), a peak of cholera cases was observed during the epidemiological week 26 (June). Subsequently, the weekly number of cases decreased, until epidemiological week 36 (September). Of the case-load, 50% were males and the mean age was19 years. Eight governorates in the northern part of Yemen reported more than 73% of cholera suspected cases. In particular, Al-Hudaidah and Hajjah governorates reported 14.5% and 10.9% of cholera cases respectively. The overall case fatality rate was 0.26 %. (1st wave CFR=0.46%and 2^{nd} wave = 0.25%). Outbreak case-loads continued decreasing trend, starting from week 37, with a shortage of Vibrio laboratory culture results (0.7%), 0.2% tested positive for *V. cholerae*, 1.3% cases tested by RDTs, 1.0% tested positive. The classical cholera clinical presentation (AWD) was present in 93% of cases. In addition, 66.5% of cases had vomiting, and 25% of them received a treatment with antibiotics. The lowest completeness rate among all reported variables was found for laboratory data (<2%).

Conclusions: This recent cholera outbreakis characterized by high incidence and relative severity, with low fatality rate. The high case-load found in Al-Hudaidah and Hajjah governorates are directly attributable to the fact that these cities received a bulk

of refugees from neighboring areas affected by violent conflicts, bringing their local capacity for clean water, adequate sanitation, and health services provision to the brink of collapse. Continued chlorination of drinking/cooking water efforts are recommended, especially at the water stations and household levels. Community health workers activities are strongly recommended especially in the remote areas that are no yet fully affected by the epidemic.

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LIST OF ABBREVIATIONS

AB	Anti-biotic
AWD	Acute Watery Diarrhea
CFR	Case Fatality Rate
CTC	Cholera Treatment Center
DTC	Diarrhea Treatment Centers
eDEWS	Electronic Disease Early Warning System
EMR	Eastern Mediterranean Region
IDPs	Internally displaced persons
IV	Intravenous
MOPH&P	Ministry of Public health and population
OCV	Oral cholera vaccine
ORCs	Oral Rehydration Corners
ORS	Oral Rehydration Salt
RDT	Rapid Diagnostic Test
UN	United Nation
UNICEF	United Nations Children's Fund
WASH	Water, Sanitation and Hygiene
WHO	World Health Organization

CHAPTER I

INTRODUCTION

1.1. Background

Cholera remains a serious public health problem when numbers of cases clearly surpass the capacity for control and management in any given country, causing an epidemic (WHO, 2016). It is an acute enteric infection caused by the ingestion of bacterium *Vibrio cholerae* present in contaminated water or food. *V. cholerae* is a Gram –negative bacterium. The structure of the cell surface lipopolysaccharide O antigen is used to categorize *V. cholerae* into more than 200 serogroups, of which only two, O1 and O139, possess the ability to cause epidemic or pandemic cholera. The O1 serogroup is further divided into two biotypes, classical and El Tor, which evolved from independent lineages and they display genotypic and phenotypic variation the latter being the most predominant worldwide. (Karaolis, et al. 1995). Each of these serotypes occurs as three biotypes: Inaba, Ogawa, and (rarely) Hikojima. In any epidemic, one specific serogroup and biotype is usually dominant (Finkelstein, 1996). Only vibrios that secrete cholera toxin can cause epidemics (Clemens et.al., 2017)

Typically, the incubation period of *V. cholerae* is two to three days, but it can be anywhere from a few hours to five days. In its severe form, it is characterized by sudden onset, profuse painless watery stools, nausea, and profuse vomiting (WHO, 2017). If left untreated, cholera may cause rapid dehydration, acidosis, circulatory collapse, hypoglycemia (in children), and renal failure, rapidly leading to death (Heymann, 2005). Most cases, however, are asymptomatic or present with mild diarrhea. Asymptomatic carriers can transmit the infection. The main reservoir of this

bacterium is humans, but studies have found environmental reservoirs as well, in copepods or other zooplankton in brackish water or estuaries. The case-fatality rate without treatment is around 50%, while with treatment it is less than 1% (WHO, 2017).

According to the World Health Organization (WHO, 2017), cholera is on the rise with an estimated 1.4 billion people at risk in endemic countries and an estimated 3 million to 5 million cases and 100,000-120,000 deaths per year worldwide. Currently, sub-Saharan Africa and South-East Asia account for the majority of cholera burden (Appendix 1) (Ali et al., 2015). Cholera has been eliminated in the developed world, aside from an isolated outbreak in the Americas in 2010. Cases are regularly imported to the developed world (Heymann, 2005). Since the XVIIth century, seven cholera pandemics have been reported of which three strongly linked to conflicts or economic crises (Mengel et al., 2014)

The persistence of the disease is most enduring in populations with limited or insufficient access to clean water and proper sanitation as well as a poor understanding of the hygienic practices that can limit the disease's ability to spread. (Anbarci, Escaleras, & Register, 2012). Thus, cholera is most commonly found in relatively poorer countries or those experiencing wars and conflicts, with great mass movement, decline in sanitaryconditions and in effective public health programs. Mass population movements associated with war have the effect of speeding up the geographical propagation of cholera (Smallman-Raynor& Cliff, 2000; Ganin, 2009).

1.2. Cholera in the Eastern Mediterranean Region (EMR)

Over the past few decades, the EMR has experienced many wars and political instability, making it a convenient area for the epidemic re-emergence of communicable

diseases such as cholera (Raslan et al., 2017). During the past two decades, 9 out of 22 countries in the Region have reported cholera cases, often in epidemic proportions. The persistence of the disease is most enduring in populations with limited or insufficient access to clean water and proper sanitation as well as a poor understanding of hygienic toilet practices (Anbarci, Escaleras, & Register, 2012). Explosive outbreaks have been reported from Afghanistan, Djibouti, Iraq, Pakistan, Somalia, Sudan, Syria and Yemen. (WHO, 2017a).

In 2015, 172,454 cholera cases were reported in the EMR, with 1304 deaths (CFR= 7.6 per 1000). However, the true burden of cholera is very likely under-estimated due to lack of lab equipment necessary for case confirmation in rural/hard-to-reach areas, as well as social, political, and economic disincentives (Ali et al., 2015). Poor surveillance systems, inadequate preparedness and response strategies and unsustainability of well-trained health cadres are also challenges for the adequate reporting, confirmation and control of cholera in the EMR (WHO, 2016).

1.3. Cholera in Yemen

The Republic of Yemen is located in the southwestern part of the Arabian Peninsula, with an area of about 555,000 km^2 and a coastline of 2,000 km along the Red Sea and the Arabian Sea. The country is bordered by Saudi Arabia to the north, the Sultanate of Oman to the east, the Arabian Sea & the Indian Ocean to the south and by the Red Sea to the West. It is administratively divided into 23 governorates including the capital city Sana'a. Large areas in the Eastern part of the country are desert with very dry and harsh climate. The Western part is hot and humid along the coast, and temperate in the mountains. (Appendix 2).

Yemen had the highest level of poverty in the Middle East, prior to the onset of a full-fledged civil war, which started in 2015. As the civil war, complicated by foreign interventions entered its third year, it resulted in a catastrophic humanitarian crisis, following the near-total collapse of the infrastructure, and basic health care services. By 2017, about 30,000 dedicated health workers had not been paid their salaries for almost two years (Chotani & Khan, 2017; EOC, 2017). As of March 2017, 7 million persons were already severely suffering from food insecurity, which threatened an additional 17 million (about 60 percent of the total population). Chronic drug shortages and conflict-related destructions restricted around 14 million Yemenis, including 8.3 million children, from accessing health care services (World Bank, 2017).

Before the start of the current round of civil war, cholera has traditionally been endemic in the Yemen, with occasional outbreaks, which have been coming under increasingly better control since re-unification in 1990. Cholera is a mandatory, notifiable disease. All suspected cases of cholera must be reported immediately to the appropriate authority. In 1971, Yemen experienced a large cholera outbreak, which started mainly in Aden city through travels between Somalia and Jeddah city in Saudi Arabia during Hajj season (Barua, 1992). In the early 1980s, cholera outbreaks were recorded in periodically in Yemen (Mukhopadhyay et al, 2014). In 2011, more than 31,789 cases of acute watery diarrhea/cholera cases, with 134 related deaths (0.4%) occurred mainly in the southern governorates of Abyan, Lahj, Aldhalae and Aden governorates (WHO, 2012). Yemen was also known by the spatial modeling technique as a cholera endemic country with an average annual case of 17546 and CFR of 3.2% (Ali et al., 2015)

A cholera epidemic started in Yemen in 2016, which has gone way beyond the epidemiological modeling predictions. This major outbreak occurred in conjunction with the current civil war, and has now evolved to affect most of the country, adding hardship and death on an already exhausted population (Chotani &Khan, 2017). This cholera outbreak hit Yemen in two initial waves. The first one began on October 6, 2016, when 11 out of 25 suspected cases were confirmed in one neighborhood of the capital Sanaa. By October 23, 31 cases had been confirmed in other governorates: in Aden, as well as the mountainous governorates of Lahj, Al Bayda and Hajjah. By January 2017, 15,658 suspected cholera cases were reported in 156 districts. "A total of 180 out of 841 cases tested positive for Vibrio Cholera, serotype Ogawa." (UNICEF, 2016). The epidemic seemed to come under control in the following months, starting in February 2017.

On April 27, 2017, a second wave of cholera started simultaneously in several Yemeni governorates. The number of suspected cholera cases increased dramatically in a very short period and the outbreak expanded to 18 out of 23 governorates. Sana'a City, which by that time had been receiving a steady flow of internally displaced persons in dire living conditions, was the most affected area. By mid-May, more than 7,000 cholera cases had been suspected, 131 confirmed and 36 resulted in death. A peak of cholera cases was observed during the epidemiological week 26 (June). Subsequently, the weekly number of cases decreased, until epidemiological week 32 (September). Between 27 April 2017 and 4 October 2017, 791,551 suspected cholera cases and 2,142 associated deaths were reported across the country. In total, all governorates except the island of Socotra and 305 out of 333 districts (92%) were affected by the outbreak. UNICEF and WHO released a statement in June 2017

declaring that "Yemen is facing the worst cholera outbreak in the world" (Lake& Chan, 2017). At the time of writing this thesis, the epidemic was still raging on and the number of cases had been estimated at one million and one hundred thousand cases.

In April 2017, the Yemeni Ministry of Public Health and Population (MOPH&P), in cooperation with United Nation (UN) agencies such as WHO and UNICEF, prepared an "Integrated Cholera Response, Prevention and System Strengthening Plan". The plan aims to reduce the occurrence of Acute Watery Diarrhea (AWD) including cholera, and to minimize the associated morbidity and fatality, through effective prevention and timely response through local "Health Clusters". Up to October 2017, Health Cluster partners were operating 4,295 beds in 259 Diarrhea Treatment Centers (DTC), and 1,155 Oral Rehydration Corners (ORCs) in 19 governorates and 149 affected districts in Yemen (EOC, 2017).

Three treatment modalities depend on the dehydration level at presentation. Plan A is applied to patients with mild dehydration who are given oral rehydration salt (ORS) sachets to take home after two hours observation. Plan B applied with those with moderate dehydration level, includes ORS at the health center. Plan C applied on patients with severe dehydration includes ORS, Intravenous (IV) fluid Ringer's lactate solution and antibiotics (AB) all administered at the health center.

In August 2017, the MOPH&P implemented a national cholera awareness campaign in collaboration with UNICEF and WHO, as part of the Cholera Responseprogram. Youth volunteers carried out national and local social media campaigns, mainly through Facebook, Twitter and WhatsApp groups. Community

engagement partners together with the health, information, religious affairs and education authorities supported these social media campaigns.

1.4. Aims of the Study and Significance on Policies

This study identifies the epidemiological features and trends in the current cholera epidemic over the one-year period from October 2016 until October 2017. It uses data already available through MOPH&P sources to evaluate the overall quality of the control measures in Yemen. Geographical differences in outcome severity and gaps in surveillance are discussed within the context of the current violence. Avenues for improving the validity and reliability of outbreak surveillance and response under extreme conditions are suggested. Findings may prove important for countries worldwide with similar socio-economic and political conditions facing similar epidemics.

1.5. Objectives

The objectives of this analysis are:

1. To describe the historical trends in the occurrence of the cholera epidemic
2. To describe the geographical and demographic distribution of cases and deaths
3. To calculate and describe the Case Fatality Rates (CFR)
4. To measure gaps in case surveillance, confirmation and completeness of reporting in different areas and by various demographic groups.

CHAPTER II

METHODS

2.1. Study Design and Sources of Data

This is a descriptive study used data reported to the Electronic Disease Early Warning System (eDEWS) in Yemen. We analyzed daily and weekly data starting from the first wave of the cholera epidemic on October 1, 2016 until October 2017. Data from (eDEWS) were reported from all districts and governorates in Yemen. Reports generated by the WHO National Office in Yemen were also included as sources of data. The analysis covered only the two first waves of the epidemic, occurring over a 56-week period from October 2016 to October 2017.

2.2. Subjects

In this analysis, cases were classified according to the WHO guidelines in a cholera outbreak (2004): (Nair & Takeda, 2014)

- A case is suspected when reported in an area where the disease is not known to be present, when a patient aged 5 years or more develops severe dehydration or dies from acute watery diarrhea. In an area where cholera is endemic, a case is suspected when a patient aged five years or over develops an acute watery diarrhea with or without vomiting.
- A case is confirmed when "*V. cholerae* O1 or O139 is isolated from any patient with diarrhea". Cases are confirmed by sending samples to reference laboratories in main cities. A minimum of 1 in 10 patients in an outbreak situation should be tested with

the Rapid Diagnostic Test (RDT). All RDT positive cases should be sent to culture to control the quality of the test.

All suspected cases reported to the Yemeni health authorities during the 12-month period were included in the analysis, with special consideration to the existence of confirmatory test or not.

2.3. Study Variables

For each case, the following variables were extracted for this analysis:

1. Demographical characteristics of cases: age and gender. Age was subsequently categorized into 5 age-group levels of particular public health significance: 1 year and less (infants), 2-5 years (children less than 5 years), 6-15 years (young adults), 16-45 years (reproductive age) and more than 45 years (older adults).
2. Geographical distribution by governorate and districts:
3. A detailed list of localities by governorates is provided as Appendix 3.
4. Clinical characteristics (outcome variables):
5. Disease outcomes (dead or recovered); laboratory results (Rapid Diagnostic Test (RDT), stool culture), and clinical manifestation (vomiting and/or acute watery diarrhea; degrees of dehydration; type of treatment received).

2.4. Plan of Analysis

All variables were presented in frequency tables with percentages for categorical variables, or with means and standard deviations (SD) calculated when needed for quantitative variables. The epidemiological curve of the epidemic was plotted. Outcome variables were cross-tabulated by demographic and geographical

variables. The CFR were computed using the total number of deaths over the total number of cases reported, and described by demographic variables. When needed, differences were tested using appropriate statistical procedures, which yield a probability of type 1 error (p-value). A difference with a p-value ≤ 0.05 was considered statistically significant. Data missing rates were calculated per each variable. All computations were performed using SPSS 20 and/or STATA 12. The analysis results were presented in form of tables, figures, narrative illustration, and maps.

2.5. Ethical Considerations and Protecting Human Subjects

This study is limited to the secondary analysis of surveillance data, with no direct interaction with any human subject. Permission to analyze the data was received from the Yemeni MOPHP, which provided open access to de-identified data for the purposes of this analysis, with the understanding that our results and recommendations will be communicated back to improve the general control performance. The study received an IRB clearance at the American University of Beirut (AUB).

CHAPTER III

RESULTS

3.1. Geographic and demographic profiles of cholera cases and deaths

Peaks of cholera outbreak incidence were reported in two successive waves in 22 out of 23 governorates in Yemen between October 2016 and October 2017. More than 900,000 cases and 2301 deaths were reported over the entire period in a population estimated at 30 million. The first wave started in October 2016 (N= 26,028) and after an apparent pause in March, a second emerged in April 2017 (N= 875,163). Geographically, more than 73% of cases were reported from eight governorates in the northern part of Yemen. The highest relative proportions of cases were reported in the largest cities, especially in governorates bordering areas of open conflicts: Al Hudaydah (14.5%), Hajjah (10.9%), Amran (9.5%), Amanat Al Asimah (9.4%), Dhamar (8.9%), Sanaa (7.3%), Ibb (6.4%), and Taiz (6.2%). Ultimately, of all the 23 governorates, only the island of Socotra was fully spared. However, the five governorates with the highest death cases were Hajjah (18.6%), Ibb (12.6%), Al Hudaydah (12.6%), Taiz (8.5%), and Amran (7.5%). Despite the huge case-load during that period, the overall case-fatality was less than 1%. Details on the geographic distribution of reported cases and deaths during the study period are presented in detail in Table 1. The peak of cholera cases reported in the 1st wavewas observed during the epidemiological week 50 (December), while in the 2nd wave of the epidemic, it was observed during the epidemiological week 26 (June). Thereafter, the weekly number of cases decreased, until epidemiological week 36 (September). The distribution of cholera cases by weekly date of onset are detailed in figures1&2.

Men and women were equally affected by the epidemic. All ages were affected, especially children 15 or less (about 30% of the entire case-load). The mean age of cases was 19.1 years. The demographic characteristic of cases is detailed in Table 2.

3.2. Case-Fatality Rates (CFRs) of cholera in Various Governorates

During the study period, 2301 patients died for a total CFR of 0.26%. (0.46% in the 1st wave and 0.25% in the second wave). The highest proportion of deaths (41%) occurred in the age-group older than 45 years, with a mean age at death of 37.8 years. The CFR surpassed 1% only in the older age-groups. There were no significant gender differences. Raymah governorate had the highest overall CFR (0.84%), while no fatalities were reported in Say'on governorate. Details on CFRs by age, sex and governorates are presented in Table 3.

3.3. Clinical Manifestations and Test Outcomes

Most cases (93%) were suspected based on the classical clinical presentation of acute watery diarrhea (AWD), although 7% presented with no diarrhea initially, suggesting an extreme status of dehydration. Over 37% of the suspected cases were moderately dehydrated at presentation, while18% were already severely dehydrated. No gender or age differences were found in the clinical presentation. Less than 1% of suspected cases obtained a confirmation culture, of which 43% returned negative. The RDT was obtained for 1.3% of cases, and returned positive for cholera in 1% of cases. Details can be found in figure 3. Various treatment combinations were applied of which

the most frequent were ORS (46%) and IV fluid compensation almost (30%) not mutually exclusive. Details can be found in Table 4.

CHAPTER IV

DISCUSSION

4.1. Dynamics and Epidemiological Profile of Cholera in Yemen

Cholera has been endemic in Yemen since the 1960s, and was slowly coming under full control. Episodic re-emergence episodes had been occurring in the Western and Southern governorates nearer to the Red Sea and African horn where the number of cases of cholera had been increasing in recent years (ECDC, 2017). Most significantly, across the Gulf of Aden, an outbreak was reported in Somalia in 2016, with 15619 suspected cholera cases and 531 deaths (CFR: 3.4%). In Ethiopia, 32689 acute watery diarrhea cases and 776 deaths (CFR: 2.4%) were reported in 2015 (Green, 2017). The success of cholera control in Yemen prior to the civil war was indicated by low annual case-loads, adequate management and limited case-fatality rates. The skills acquired by the entire healthcare system practitioners provided a large degree of resilience to the country when a massive breakdown of civil stability and destruction of the infrastructure occurred, leading to the largest epidemic recorded in a century. Up to the date of writing, cases amounted to one million and one hundred thousand cases (WHO, 2018a).

The UN authorities have already acknowledged that an unknown proportion of cases have gone undetected and unreported in the overall context of instability and continued movement of internal displacement to/from most governorates in Yemen.

Despite initial delays in detecting and responding to the epidemic, the surveillance and control system was able to gather enough momentum and to channel help through several ways. Most cases were reported in the north region of Yemen largely under the Houthis' control, and subjected to land, sea and air blockade. This is also where the majority of the population, about 70 percent of Yemen's population lives. Heightened active surveillance and case finding have come in place in those districts and much less rapidly in low reporting districts. As a consequence, the epidemic seems to have entered a phase of continuous decline in numbers of reported cases since October 2017, very likely affected by the end of the summer months. Nevertheless, the amount of suffering, especially among infants and the elderly was staggering and is very likely one of the darkest consequences of a war which seems to have lost its direction.

Prior to this national analysis, a limited description was published by Action Contre la Faim (ACF), a French NGO operating in Al-Hodaidah city and other Yemenis governorates (Altmann et al., 2017). The demographic features were similar, and did not differ from previous outbreaks in 1971 (Barua, 1992), in the early 1980s (Mukhopadhyay et al, 2014), 2010 and 2011(WHO, 2012). Nor did the recent epidemic differ from outbreaks occurring in less developed countries at the same period: South Sudan (Bekolo et al, 2016), Zimbabwe (Maponga et al., 2015), and Bangladesh (Saha et al., 2017). Overall, both genders were represented equally, the bulk of cases occurred in children and adolescents, and the bulk of deceased in the older age-groups. Children and adolescents are more likely to be exposed to the bacteria for the first time and therefore lacked adequate immunity. Studying the situation in some low-endemic areas

in Iran, Masoumi et al., (2008), mentioned the increase in younger age-groups as a significant demographic variable associated with periodic cholera epidemics every 5-6 years because of lowered levels of herd immunity. Same arguments were presented from Uganda (Bwire et al., 2017) and South Sudan (Bekolo et al., 2016).

The circumstances of the civil war have strained the resources in all parts of Yemen and revealed the fragility of control measures under stressful conditions. Al-Hodaidah governorate has reported the highest relative case-load in this analysis, a situation similar to numerous cholera outbreaks since the 1970s. Al- Hodeidah is a port city which normally provides a large population mixing in non-sanitary conditions which may not be ideal. However, the health care system is familiar with cholera signs and symptoms, and is usually well provided to face small outbreaks. Now the city is harboring huge waves of internally displaced people from bordering hot spots. The refugee influx to Hodeidah, as well as to other urban centers, has resulted in sudden increased pressure on the water, sanitation and health and infrastructure systems, surpassing the coping resources there. Cities like Hajjah and Amran have also reported record numbers, in parallel to the blockade of land, sea and air ports of the northern part of Yemen. In contrast, lower case-loads have been reported in Say'on, Mokalla and Al Maharah governorates, which are not affected by the war and have retained easy access to international medical care and medical supplies through airport and ports. Socotra is the only governorate in Yemen spared by the epidemic because its island situation isolated it from the chaos of civil war. However, flights to the island from Say'on have started last month in April 2017, following a decision to use the island as a backup area for humanitarian and health relief. The new traffic pattern may lead to the transmission

of cases of cholera on the island for the first time. Prevention requires heightened control of all entrants and enhanced provision of safe drinking water.

Interestingly, in urban areas with the greatest recorded number of cases are also areas where fatality rates remained relatively low. In fact, the CFRs under the current very adverse circumstances are actually at lower levels than previously registered before the civil war. In fact, the UN agencies have reported a CFR in more peaceful conditions in Somalia (2016) to be five times more than what was reported in in the same time in Yemen (WHO, 2018b). All this is a testimony to the resilience of the pre-existing control systems despite the lack of usual supplies and manpower.

Elsewhere in the countryside, the situation is different. In more rural/remote areas, the original control status was already problematic due to difficult geographic access, lack of paved roads, lack of medical supplies and personnel, and limited capacity of health facilities. The uncertainties of communications with the central procurement in the capital, along with the influx of refugees carrying the epidemic, added on a previously fragile situation, have resulted in a much more catastrophic outbreak marked by higher CFRs, like for example in Raymah governorate, despite the limited number of cases. The geographic inequity in health care resources and response capacity is a constant reality in large, mountainous and low-income countries such as Yemen. The approach to solving such inequities is possible in peace time through a planned vision for regional economic development. Under a situation of dramatic civil war, those inequities unfortunately become an unsurmountable obstacle to health and well-being.

Vaccines may add an important boost to the control efforts. Inactivated oral cholera vaccine (OCV) can play an important role as a supplementary measure in endemic, epidemic and in large emergency situations, either pre-emptively or reactively. A few epidemic countries with civil disruptions have initiated vaccine campaigns targeting those residing in informal settlements and refugee camps, such as in Rohinga camps in Bangladesh (UNICEF, 2017). OCV vaccination is cost-effective when targeted at a population with high-risk of cholera and poor access to health care facilities when herd protection effect is incorporated and OCV price is low (Teoh et al., 2018). Recent evidence for herd protection presented by oral cholera vaccinations suggests that immunizing a fraction of a community reduces the transmission of cholera sufficiently for the unvaccinated members of the community to benefit from reduced risk of disease (Ali et al., 2005). One million doses of cholera vaccines were procured for Yemen, but the distribution was suspended by the Yemeni government and its UN partners for logistical and security reasons. Should massive vaccination ever take place the Yemeni MOH&P decided to conduct a vaccination campaign, it should target first children and adolescents, and very likely older persons.

4.2. Gaps Defined

Reports on persons with suspected cholera are routinely made by clinicians or public health authorities. These reports are sent to the local health surveillance unit at the governorates level, and then forwarded to the central level. Gaps may exist at each level preceding the central one. The reporting case investigation form should include basic demographic information, dates of symptom onset, the residence district, sample collection, laboratory investigations information, water and sanitation resources types,

and the outcome of the disease. In the records examined for this analysis, information related to onset time and demographic characteristics of patients, as well as the overall clinical classification of the disease were almost totally complete. When cases were reported, forms tended to be complete, except for laboratory confirmation and epidemiology section data: water exposure and source, food consumption, patient transportation and severe acute malnutrition. Within the current design for cases reporting, WHO strongly recommended that at least 1 in 10 patients should be tested with RDT, and all RDT positive cases should be tested for culture. It is not clear whether laboratory data, when not entered, mean that results were negative or that they were not reported or that they were not done. This situation may generate confusion which affects the completeness and accuracy of the data, and will lead to increasing in number of "suspected" cases not due to cholera. In addition to the incompleteness of some laboratory report, the reporting system should use the line list register only for those cases that meet the case definition of suspected cholera (WHO, 2017c).

With few variations, the presenting clinical sign was the classical acute watery diarrhea (93%), which under the existing conditions were rarely confirmed through laboratory testing (2%). Previous experience in cholera affected the rate of laboratory confirmation: in non-endemic areas, samples were more likely to be collected when new cases of severe watery diarrhea were diagnosed. As a consequence, the case-load of "suspected" cases may have been inflated by including all sorts of acute diarrheas which abound in times of hardships, but are not caused by *V. cholerae*, such as rotavirus, shigella and other enteric bacteria. Nevertheless, from the patient point of view, all these diarrheas, regardless of etiology, would have benefited from the treatment

protocol established by the Yemeni authorities working in conjunction with WHO and other international NGOs. The protocol rests first and foremost on oral hydro-ionic compensation, and only rarely resorts to IV fluids or antibiotics.

CHAPTER V

CONCLUSIONS & PRACTICAL RECOMMENDATIONS

The cornerstone for cholera control are ensuring access to safe water, water and sanitation interventions, such as water chlorination whether at the public or individual levels, to treat water with chlorine, use one of the locally available treatment products and follow the instructions. In addition, strengthening the surveillance system, educating the at-risk population about the need to seek treatment immediately and community mobilization, and providing effective treatment facilities with early detection and optimal management of cases are fundamental for cholera control.

At an individual level, the simplest form of protection is to wash hands before handling food or drinks. For people travelling to cholera endemic areas, the oral vaccine can be taken. For Yemen, the future course of the cholera epidemic is difficult to predict, especially given the on-going degradation of water and sanitation infrastructure and the lack of and logistical difficulties in moving supplies and personnel to areas in need, this makes us expect a third wave of a cholera epidemic during the rainy season. Training community health workers in remote areas on cholera-related first aid and providing medically-equipped transportation means especially in areas of difficult geographical nature and unpaved roads such as Raymah governorate, will help to reduce the severity of cases. Additional water and sanitation facilities have to be provided in the temporary IDPs camps, such as schools or governmental buildings not initially equipped to those ends. This is especially crucial in cities that are constantly receiving displaced people, such as Al Hudaydah, Hajjah, Amran and Sanaa.

In times of peace or war, an accurate surveillance system providing valid, timely and complete data is important for interventions, research, policies and strategies. The incompleteness of reporting data is a gap in the surveillance system in Yemen, indicating the need for urgent revision of reporting processes, quality of data collection and training for surveillance personnel, especially in governorates with little previous experience with cholera. Nevertheless, it is clear that such a goal cannot be targeting before the end of the current cholera crisis, which requires all priority efforts.

Vigilance is still needed to intensify the humanitarian response efforts throughout the country, particularly health and water, sanitation and hygiene (WASH) interventions, to sustain the decreasing incidence of cholera and preventing new waves. In this context, it is important to note the crucial role of international help in providing support to the Yemeni population. However, this help, faced with continued violence and destruction, and may have reached a plateau of sustainability and effectiveness. Resilience based on previous control measures and acquired experience among health personnel can be eroded beyond repair. A tragic situation may again start to escalate into more morbidity and even more mortality. As of today, the best control strategy for the cholera epidemic in Yemen remains the return of civil peace and a negotiated solution of the country's internal problems.

Table 1: Geographic distribution of cholera cases in the Yemen epidemic (October 2016-October 2017)

VARIABLES	WAVE 1 (October 2016-March 2017)		WAVE 2 (April 2017-October 2017) *		TOTAL (October 2016-October 2017)	
	Cases	Death	Cases	Death	Cases	Death
N (valid %)	**26028**	**121**	**875163**	**2180**	**901191**	**2301**
Governorate						
Abyan	815 (3.1)	0 (0)	27740 (3.2)	35 (1.6)	28555 (3.2)	35 (1.5)
Aden	1654 (6.4)	19 (15.7)	19284 (2.2)	62 (2.8)	20938 (2.3)	81 (3.5)
Al Bayda	**2905 (11.2)**	10 (8.3)	**25148 (2.9)**	29 (1.3)	28053 (3.1)	39 (1.7)
Al Dhale'e	1592 (6.1)	5 (4.1)	46019 (5.3)	80 (3.7)	47611 (5.3)	85 (3.7)
Al Hudaydah	**5822 (22.4)**	18 (14.9)	**125214 (14.3)**	267 (12.2)	**131037 (14.5)**	285 (12.4)
Al Jawf	9 (0)	-	12990 (1.5)	21 (1.0)	12999 (1.4)	21 (0.9)
Al Maharah	-	-	1164 (0.1)	1 (0)	1164 (0.1)	1 (0)
Al Mahwit	35 (0.1)	2 (1.7)	50199 (5.7)	143 (6.6)	50234 (5.6)	145 (6.3)
Amanat Al Asimah**	299 (1.1)	2 (1.7)	83971 (9.6)	68 (3.1)	84270 (9.4)	70 (3.0)
Amran	54 (0.2)	2 (1.7)	85477 (9.8)	170 (7.8)	85531 (9.5)	172 (7.5)
Dhamar	189 (0.7)	5 (4.1)	79598 (9.1)	156 (7.2)	79787 (8.9)	161 (7.0)
Hajjah	2350 (9.0)	20 (16.5)	96070 (11.0)	409 (18.8)	98420 (10.9)	429 (18.6)
Ibb	2354 (9.0)	10 (8.3)	55465 (6.3)	280 (12.8)	57819 (6.4)	290 (12.6)
Lahj	1104 (4.2)	1(0.8)	22473 (2.6)	21 (1.0)	23577 (2.6)	22 (1.0)
Marib	-	-	5741 (6.3)	7 (0.3)	5741 (0.6)	7 (0.3)
Mokalla	-	-	568 (0.1)	2 (0.1)	568 (0.1)	2 (0.1)
Raymah	722 (2.8)	3 (2.5)	13405 (1.5)	116 (5.3)	14127 (1.6)	119 (5.2)
Sa'ada	-	-	7626 (0.9)	5 (0.2)	7626 (0.8)	5 (0.2)
Sana'a***	1659 (6.4)	12 (9.9)	63893 (7.3)	122 (5.6)	65552 (7.3)	134 (5.8)
Say'on	-	-	18 (0)	0	18 (0)	0
Shabwah	85 (0.3)	-	1384 (0.2)	3 (0.1)	1469 (0.2)	3 (0.1)
Taiz	**4379 (16.8)**	12 (9.9)	**51716 (5.9)**	183 (8.4)	56095 (6.2	195 (8.5)

The analysis stopped on October 2017, but unfortunately the epidemic is still going on and becoming even more serious

** The city of Sanaa'

*** The suburbs of Sanaa'

Table 2: Demographic characteristics of cholera cases in the Yemen epidemic (October 2016-October 2017)

VARIABLES	WAVE 1 (October 2016-March 2017)		WAVE 2 (April 2017-October 2017) *		TOTAL (October 2016-October 2017)	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
N (valid %)	**26028**	**121**	**875163**	**2180**	**901191**	**2301**
Age-groups (years)						
≤1	3709 (14.3)	**24 (19.8)**	94849 (10.8)	**199 (9.12)**	98558 (10.9)	223 (9.7)
2-5	5969 (22.9)	27 (22.3)	172446 (19.7)	247 (11.3)	178415 (19.8)	274 (11.9)
6-15	6678 (25.7)	18 (14.9)	201485 (23.0)	302 (13.9)	208163 (23.1)	320 (13.9)
16-45	8087 (31.1)	30 (24.8)	321795 (36.8)	513 (23.5)	329882 (36.6)	543 (23.6)
>45	1585 (6.1)	**22 (18.2)**	84588 (9.7)	**919 (42.2)**	86173 (9.6)	941 (40.9)
Mean age (SD)	**15.6 (16.1)**		**19.2 (18.2)**		**19.1 (18.2)**	
Sex						
Males	13547 (52.0)	64 (52.9)	437756 (50)	1104 (50.6)	451303 (50.1)	1168 (50.8)
Females	12478 (47.9)	57 (47.1)	437406 (50)	1076 (49.4	449884 (49.9)	1133 (49.2)

* The analysis stopped on October 2017, but unfortunately the epidemic is still going on and becoming even more serious
** The city of Sanaa'
*** The suburbs of Sanaa'
All governorates reported cases except the island of Socotra.

Table 3: Case fatality rates (CFR) by demographic characteristics in the Yemen epidemic (October 2016- October 2017)

VARIABLES	WAVE 1 (October 2016-March 2017)	WAVE 2 (April 2017-October 2017) *	TOTAL
CFR (Valid%)	**0.46**	**0.25**	**0.26**
Age-groups (years)			
≤1	0.65	0.21	0.23
2-5	0.45	0.14	0.15
6-15	0.27	0.15	0.15
16-45	0.37	0.16	0.16
>45	1.39	1.09	1.09
Sex			
Males	0.47	0.25	0.26
Females	0.46	0.25	0.25
Governorates			
Abyan	0	0.13	0.12
Aden	1.15	0.32	0.39
Al Bayda	0.34	0.12	0.14
Al Dhale'e	0.31	0.17	0.18
Al Hudaydah	0.31	0.21	0.22
Al Jawf	0	0.16	0.16
Al Maharah	-	0.09	0.09
Al Mahwit	**5.71**	**0.28**	**0.29**
Amanat Al Asimah**	0.67	0.08	0.08
Amran	**3.70**	**0.20**	0.20
Dhamar	**2.65**	**0.20**	0.20
Hajjah	0.85	0.43	0.44
Ibb	0.42	0.50	0.50
Lahj	0.09	0.09	0.09
Marib	-	0.12	0.12
Mokalla	-	0.35	0.35
Raymah	0.42	0.87	0.84
Sa'ada	-	0.07	0.07
Sana'a***	0.72	0.19	0.20
Say'on	-	0.00	0.00
Shabwah	0	0.22	0.20
Taiz	0.27	0.35	0.35

* The analysis stopped on October 2017, but unfortunately the epidemic is still going on and becoming even more serious

** The city of Sanaa'

*** The suburbs of Sanaa'

All governorates reported cases except the island of Socotra

Table 4: Clinical manifestations of cholera cases in the Yemen epidemic (October 2016-October 2017)

1. Presenting symptoms	
Acute watery diarrhea	93%
Vomiting	66.5%
2. Levels of dehydration	
No dehydration	11%
Mild dehydration	34%
Moderate dehydration	37%
Severe dehydration	18%
3. Type of treatment applied*	
ORS	46%
IV Fluid	30%
Antibiotics	24%

* Not mutually exclusive

Figure 1: Distribution of cholera cases by date of onset reported in 1st wave of epidemic (October 2016-March 2017) (N=26,028)

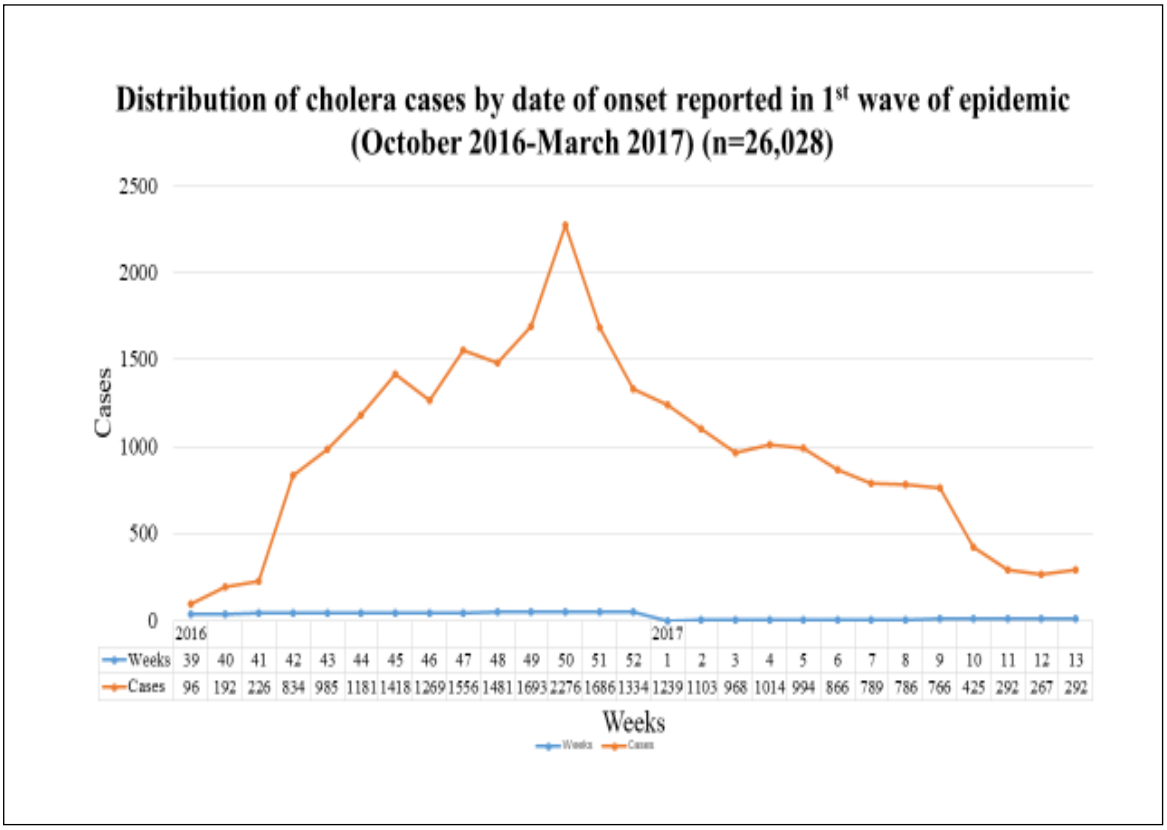


Figure 2: Distribution of cholera cases by date of onset reported in 2nd wave of epidemic (April 2017-October 2017) (n=875,677)

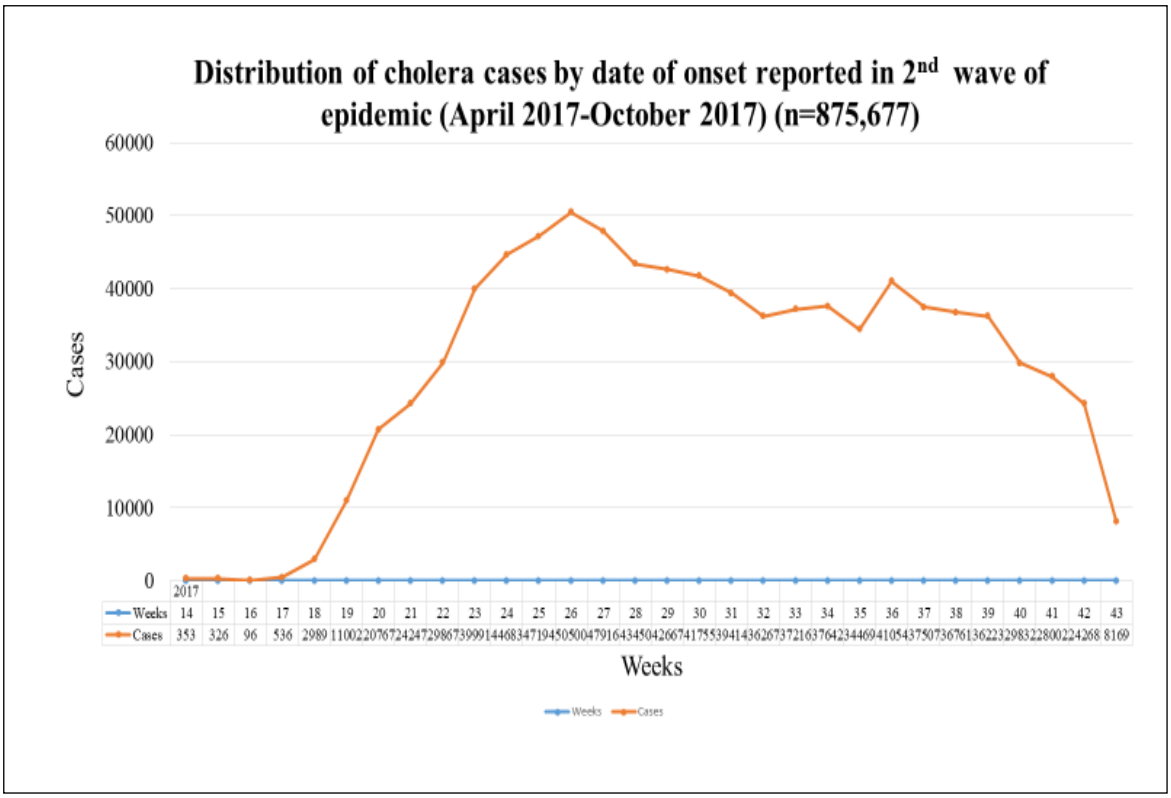


Figure 3: Laboratory Confirmation of cholera cases

Vibrio laboratory culture result (2nd wave)

	Frequency	Valid Percent
Not done	403494	99.4
Positive	913	0.2
Negative	1045	0.3
Pending	656	0.2
Total	406108	100.0
Missing	469059	
Total	875167	

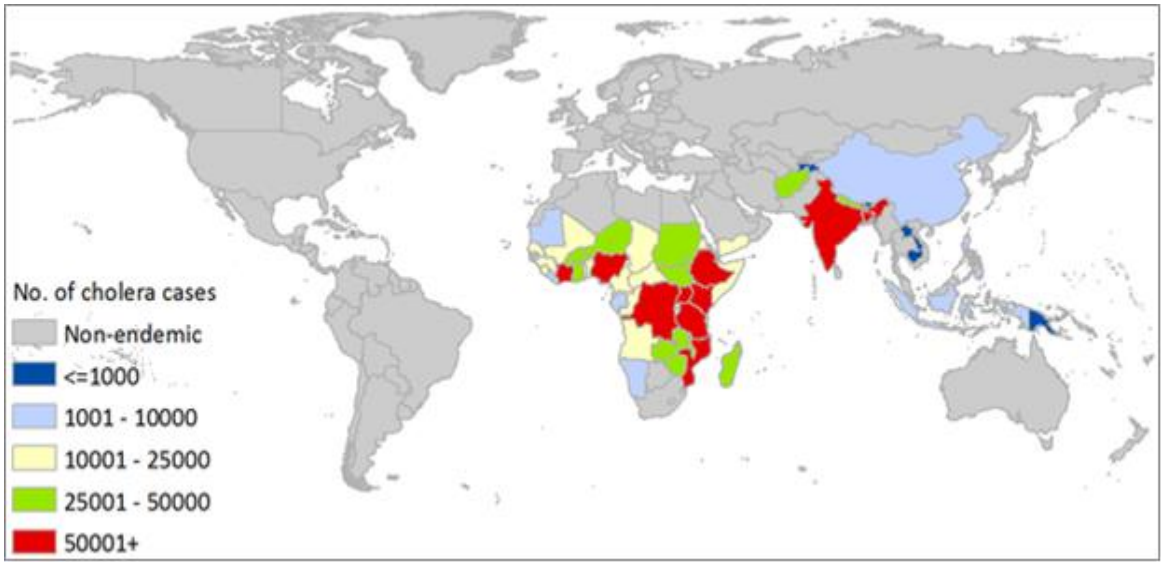
Rapid Diagnosis Test (RDT) result (2nd wave)

	Frequency	Valid Percent
Not done	491198	98.6
Positive	5117	1.0
Negative	1700	0.3
Total	498015	100.0
Missing	377152	
Total	875167	

APPENDICES

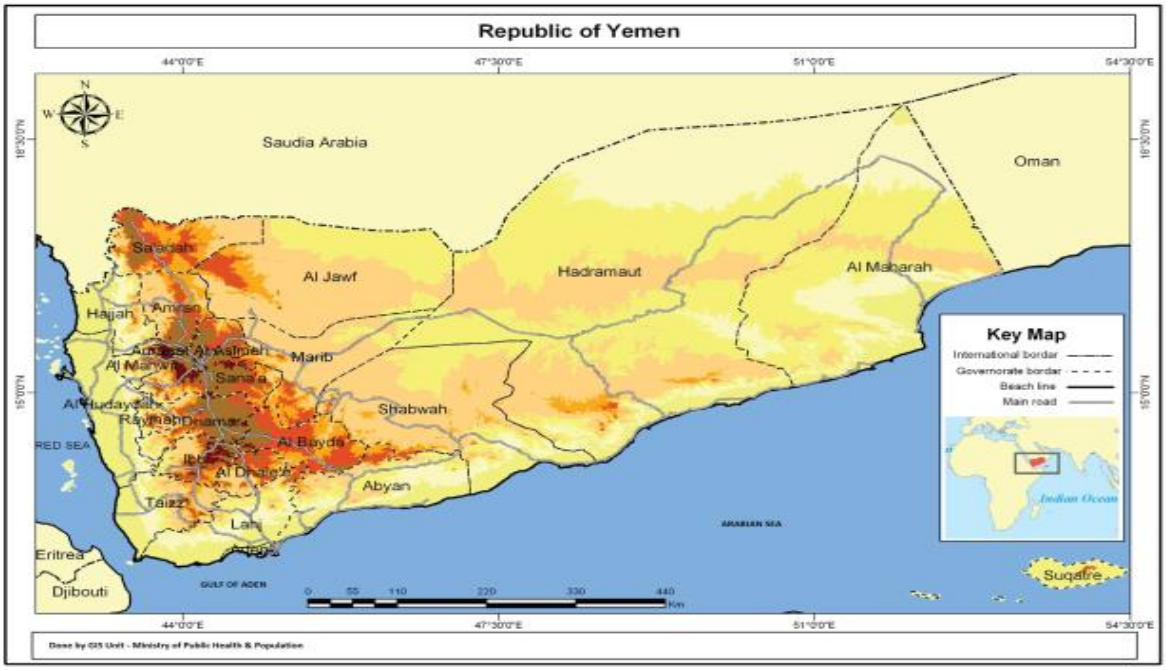
APPENDIX 1

ANNUAL NUMBER OF CHOLERA CASES IN ENDEMIC COUNTRIES (ALI .ET.AL, 2015)



APPENDIX 2

REPUBLIC OF YEMEN MAP



APPENDIX 3

DETAILED GEOGRAPHICAL DISTRIBUTION OF CHOLERA CASES IN YEMEN BY GOVERNORATES,1ST WAVE (OCTOBER 2016- MARCH 2017) (N=26029)

Governorate	Frequency	%
Abyan	815	3.1
Aden	1654	6.4
Al Bayda	2905	11.2
Al Dhale'e	1592	6.1
Al Hudaydah	5822	22.4
Al Jawf	9	0
Al-Mahweet	35	0.1
Amanat Al Asimah*	299	1.1
Amran	54	0.2
Dhamar	189	0.7
Hajjah	2350	9
Ibb	2354	9
Lahj	1104	4.2
Raymah	722	2.8
Sana'a**	1659	6.4
Shabwah	85	0.3
Taiz	4379	16.8
Total	26029	100

* The city of Sanaa'
** The suburbs of Sanaa'
Governorates with no reported cases were not listed (n= 6)

APPENDIX 4

DETAILED GEOGRAPHICAL DISTRIBUTION OF CHOLERA CASES IN YEMEN BY GOVERNORATES, 2ND WAVE (APRIL 2017-OCTOBER 2017) (N=875,167)

Governorate	Frequency	%
Abyan	27740	3.2
Aden	19284	2.2
Al Bayda	25148	2.9
Al Dhale'e	46019	5.3
Al Hudaydah	125214	14.3
Al Jawf	12990	1.5
Al Maharah	1164	0.1
Al Mahwit	50199	5.7
Amanat Al Asimah*	83971	9.6
Amran	85477	9.8
Dhamar	79598	9.1
Hajjah	96070	11
Ibb	55465	6.3
Lahj	22473	2.6
Marib	5741	0.7
Mokalla	568	0.1
Raymah	13405	1.5
Sa'ada	7626	0.9
Sana'a**	63893	7.3
Say'on	18	0
Shabwah	1384	0.2
Taiz	51716	5.9
Total	875167	100

* The city of Sanaa'

** The suburbs of Sanaa'

All governorates reported cases except the island of Socotra.

APPENDIX 5

DETAILED GEOGRAPHICAL DISTRIBUTION OF CHOLERA CASES IN YEMEN BY GOVERNORATES, (OCTOBER 2016-OCTOBER 2017) (N=901,191)

Governorate	Frequency	%
Abyan	28555	3.2
Aden	20938	2.3
Al Bayda	28053	3.1
Al Dhale'e	47611	5.3
Al Hudaydah	131036	14.5
Al Jawf	12999	1.4
Al Maharah	1164	0.1
Al Mahwit	50234	5.6
Amanat Al Asimah*	84270	9.4
Amran	85531	9.5
Dhamar	79787	8.9
Hajjah	98421	10.9
Ibb	57819	6.4
Lahj	23577	2.6
Marib	5741	0.6
Mokalla	568	0.1
Raymah	14127	1.6
Sa'ada	7626	0.8
Sana'a**	65552	7.3
Say'on	18	0.0
Shabwah	1469	0.2
Taiz	56095	6.2
Total	901191	100

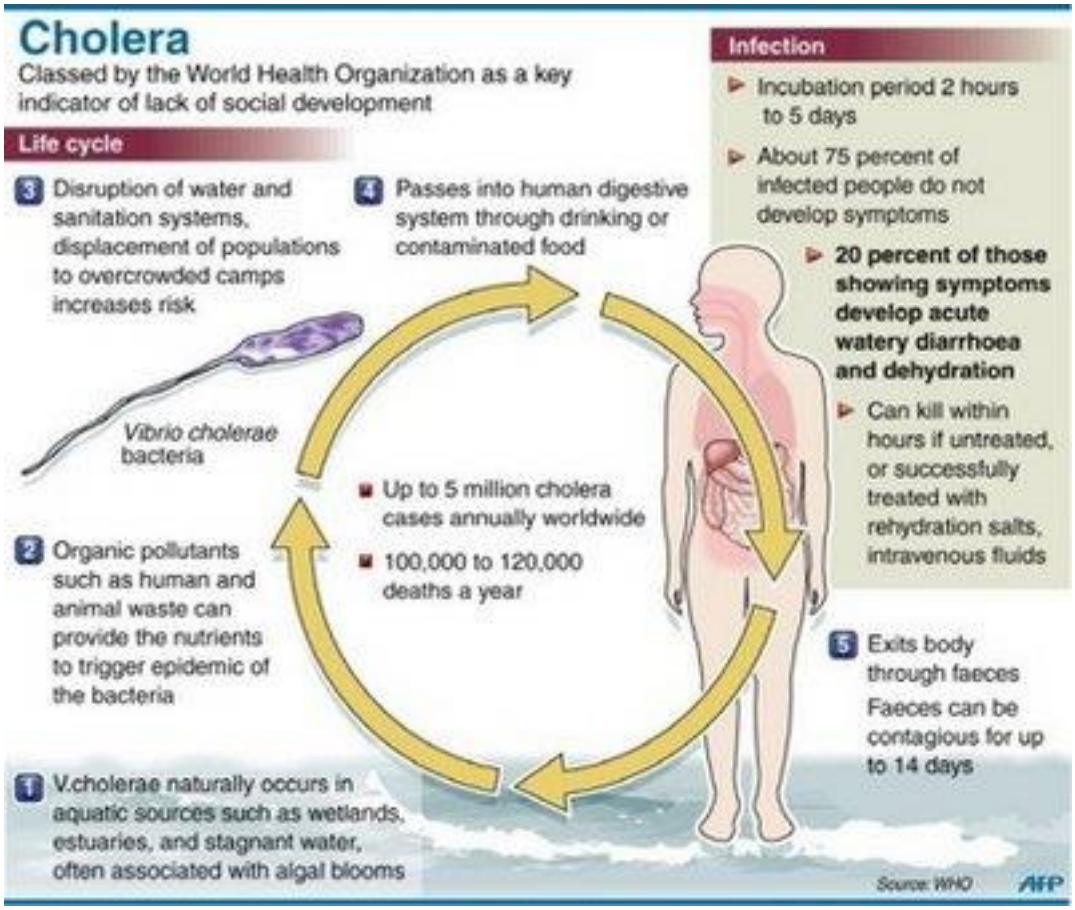
* The city of Sanaa'

** The suburbs of Sanaa'

All governorates reported cases except the island of Socotra

APPENDIX 6

FACT FILE ON CHOLERA



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