



INFECTIOUS DISEASES

The insidious return of cholera in the Eastern Mediterranean Region, Lebanon and Syria: a worrying signal!

Past, present, and future forthcoming

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Summary

Introduction. War, hunger, and disease continue to decimate the populations of many countries in the world. Owing to conflicts, environmental instability and natural disasters, many people, especially the poorest, fall victim to epidemic diseases. One such disease, cholera, began to spread again in 2022, striking Lebanon and Syria, countries that have experienced serious social troubles for years. The return of cholera immediately alarmed the scientific community, which is now making every effort, most notably by implementing a major vaccination campaign, to prevent this disease from becoming endemic in these two countries, thus making them a reservoir for its potential spread in the Eastern Mediterranean Region.

Discussion. Cholera is a disease that draws its strength from poor hygiene, primitive sanitation and the consumption of contami-

nated water and food. From the 19th Century onwards, its spread was facilitated by overcrowded housing and lack of hygiene, which became commonplace features of urban life.

Method. In outlining the spread of cholera in Lebanon and Syria, the authors raise the question of the possible resurgence of epidemic cholera, especially in the light of the consequences of the devastating earthquake that hit the border area between Turkey and Syria last February.

Conclusion. These events have had a devastating effect on the population, destroying, among other things, the few existing health facilities and aggravating the already difficult living conditions of millions of people who, owing to the ongoing war, have been living for years in makeshift settlements, bereft of water, sanitation and any form of health care.

Introduction

Last autumn, on 6 October 2022, the Lebanese Ministry of Public Health reported a cholera epidemic to the World Health Organization; within a few weeks, significant numbers of people had been affected, especially children under the age of 5 years [1]. In the same period, cholera also reappeared in Syria.

This situation is in line with data showing that the global number of cholera outbreaks in the last 5 years has increased significantly, from an average of 20 per year in the period 2017-2021 to 29 in 2022 [2].

The epidemic is also particularly serious in the WHO African Region. "Between 1 January and 13 March 2023, 40 563 suspected cholera cases were reported from 13 countries, with 818 deaths (case fatality ratio [CFR] = 2.0%). Malawi accounts for 57.5% (23308) of all reported cases in 2023, followed by Mozambique with 15% (6082) and the Democratic Republic of the Congo with 13% (5284). Of the deaths reported in 2023, Malawi accounts for 78% (638), followed by Mozambique at 5% (45) and Kenya with 5.1% (42) [3]".

Among the countries where cholera is endemic there are also Yemen and Haiti, which is experiencing a resurgence of cholera, with the outbreak initially reported on 2 October 2022 [4, 5].

Before 2022, the cholera epidemic hit Haiti from October 2010 to February 2019: it was the world's deadliest of the last 25 years.

In October 2010, cholera occurred in Haiti for the first time in a century, ten months after a devastating earthquake. This earthquake destroyed the fragile buildings of local population and the main infrastructures, people and children stranded in the camps or overcrowded in refugee camps [6].

The number of the population in these poor conditions was really very high, hundreds of thousands of people. It was really a terrible and devastating earthquake and one of the worst of recent history with more than 700,000 cases (820,000) and 9,000 deaths (reported deaths 9,792) [7].

The last cholera case in Haiti was recorded in January 2019, and in February 2022 [8].

The recent outbreak in Lebanon and Syria has greatly

alarmed the scientific community, as cholera is not endemic in these two countries, which last experienced an epidemic 30 and 20 years ago, respectively. The severe economic and political crisis afflicting Lebanon and the war in Syria [9] have impoverished the population and displaced masses of people, disrupting sanitation and waste management systems. The vulnerability of the Lebanese population is compounded by the difficult economic conditions and limited access to clean water and adequate sanitation. The Syrian people, after 12 years of war, destruction, displacement, and hunger, are now faced with a new horror: cholera; owing to the consumption of contaminated food and water, the disease has spread to several parts of the country in recent months and has already claimed lives.

The WHO risk assessments have noted that the re-emergence of cholera in Syria and Lebanon is alarming, as it increases the risk of cholera outbreaks in other countries in the WHO Eastern Mediterranean Region (EMR) [10].

Cholera, a disease carried by contaminated water

Cholera is an acute enteric infection caused by the bacterium *Vibrio cholera* (Fig. 1). It was identified for the first time in 1854 by the Italian anatomist Filippo Pacini (1812-1883), who during the cholera epidemic broke out in Florence demonstrated the presence, in the intestinal mucosa of people died of cholera, of millions of elements that he called vibrios. He argued that the contagion was due to the human-to-human transmission of this microorganism, laying the foundations of infectiology [11, 12].

The bacterium was subsequently isolated in culture and studied in detail in 1884 in Egypt by the German physician Robert Koch (1843-1910).

Transmission of the bacterium is closely linked to the unavailability of clean water, the consumption of

contaminated food and, in general, poor sanitation and the deficient management of sewage and drinking water systems.

The incubation period of the disease usually ranges from 24 to 72 hours; in exceptional cases, however, it may vary between 2 hours and 5 days, depending on the number of bacteria ingested. In 75% of cases, infected subjects do not experience any symptoms, and of those who do, only a small proportion develop a severe form of the disease [13]. The main symptom is acute watery diarrhea, causing severe dehydration; if untreated, this can lead to shock, which in severe cases can rapidly be fatal.

The treatment of cholera is relatively simple; in 90% of cases, oral rehydration is enough to reintegrate the fluids and salts lost through diarrhea and vomiting. In severe cases, however, intravenous fluid replacement is required. With adequate rehydration, only 1% of patients die, and the disease usually resolves spontaneously. In order to shorten the course of the disease, and especially in the most severe forms and in at-risk patients, antibiotics are used, usually tetracyclines or ciprofloxacin.

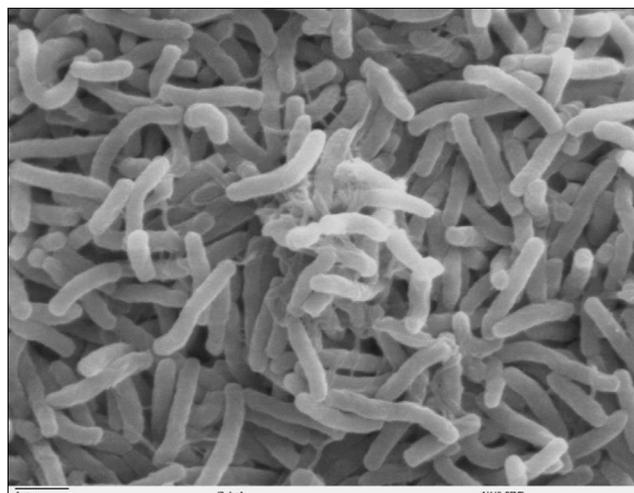
To prevent cholera, it is essential to guarantee the safety of food and water and improve hygiene. This also involves educating people to respect hygiene measures during the preparation and consumption of food, such as washing hands with soap before starting to cook or eat; indeed, cholera vibrios are sensitive to the action of common detergents and disinfectants. Vaccines are also available.

The "new disease" that appeared in the 19th Century

Cholera was localized in Asia until 1817, when a first pandemic spread from India to several other regions of the world [14]. It appeared in Europe in the first half of the 19th Century (Tab. I). Endemic in Asia, and particularly in the delta of the Ganges (India), it remained confined to that geographical area until the beginning of the 1800s. It first emerged from the Sundarbans Forest of the Bay of Bengal, in the Ganges delta, where the bacterium *Vibrio cholera* had probably been mutating for millennia. The organism is found naturally in the environment in some coastal area, wastewater, and brackish waters, where shellfish often carry the infection [15].

It subsequently reached the Mediterranean and Europe as new trade routes were opened up between East and West. In the early 1800s in fact the British were opening up new trade routes in India and moving troops across the subcontinent, did cholera begin to move out of its home territory. At the beginning across India and then across the world in a devastation and massive pandemics. Its migration began in India in 1817, a very difficult period for the Indian subcontinent, which was hit by floods and frequent famines. Indeed, it was precisely the movement of large numbers of people from the affected areas that upset the environmental balance, leading to the spread of the cholera bacterium outside its natural

Fig. 1. Scanning electron microscope image of *Vibrio cholera* (Public domain photo).



habitat. It is also very likely that the situation was exacerbated by the appearance of a more virulent variant of the disease, which inexorably struck the multitudes of fugitives who hoped to leave hunger behind; instead, increasingly malnourished and in poor conditions of health and hygiene, these refugees fell victim to cholera. Just in the summer of 1817 there were some really alarming and worrying dates: in August the British Government received a report of a “*malignant disorder*” in the Sundarbans. It killed 20/30 people a day and only after a few weeks, ten thousand people died. From then the disease spread through the countries and regions both in the east and west to: Nepal, Afghanistan, Iran, Iraq, Oman, Thailand, Burma, China and Japan. While this first pandemic (1817-1823) affected Europe only partially, being limited to the eastern Mediterranean and the disease began to decrease and to regress, the second pandemic, which broke out in 1826, involved the whole continent, taking a heavy toll among the poorest and most defenseless sectors of the population [16]. Its exotic origin, the rapidity of its spread and its almost instantaneous lethal impact seared the collective imagination, fueling anxiety and terror, not completely unlike the psychological effect [17] of the COVID-19 pandemic on many people [18]. Again, the origin was the river Ganges Delta area, and again the disease spread with a particular speed, hitting places to hang out and meeting places but also even further, to United States, Europe, and Egypt. It was estimated that only in Cairo and Alexandria died 33,000 people and just a few years later a cholera epidemic hit Moscow; it had heavily decreased the population of the big and crucial commercial city of Astrakhan. It reached St Peterburg, crossing the borders of Asia and headed towards Poland, Bulgaria, Latvia and Germany. When cholera first appeared in Europe at the end of the 1820s, the advanced world began to realize and understand better the importance of the disease. Scientists and doctors of the largest developed countries

such as Russia, France, Britain began to study the disease with strong priority and the Russian government offered a prize for the best essay on the subject. Faced with the disconcerting spread of the disease, scholars of the time took two different positions: for and against the transmissibility of cholera. The English physician John Snow (1813-1858), pioneer in hygiene studies, not only firmly stated that cholera was a communicable disease, but identified water as the main vehicle through which it spread [19].

Various waves of cholera also scourged Asia and Europe in the 20th Century.

The pandemic that persisted from 1902 to 1926 also severely affected troops during the First World War [20]. In Italy, it made its return in 1909. The government of the day immediately commissioned the hygienist Achille Sclavo to coordinate all necessary actions to stamp out cholera, or at least curb the spread of the disease, which had hit southern Italy, particularly Puglia and Sicily [21, 22].

In 1961, a pandemic broke out in southern Asia, spreading to Africa in 1971 and reaching America in 1991; it is still ongoing (moreover, the disease remains endemic in many countries and the bacterium that causes it has not yet been eliminated from the environment).

During the 1990s, the pattern of spread of cholera changed markedly; the disease reappeared in Central and South America, where it had been absent for over 100 years.

- In the period 1991-1994, an extensive epidemic (*V. cholerae* O1, toxigenic, Inaba serotype, El Tor biotype) hit many Latin American countries, from Peru to Mexico, wreaking devastating consequences: 1,400,000 people were infected and over 10,000 died [23].
- In the same period (1993-94) an epidemic strain (*V. cholerae* O139 Bengal) appeared in the Indian subcontinent and other Asian countries [24], and in Madras (India) 13,275 were hospitalized and 437 died. The O139 serotype has a greater potential for diffusion, as it is endowed with greater transmissibility (secondary infection).
- A severe epidemic of El Tor biotype cholera broke out among refugees in Ghana and Zaire, causing 70,000 cases of disease and 12,000 deaths, a much higher lethality rate (15%) than that recorded in Central and South America (1%) and there was also a revival of *V. cholerae* O139 in Bangladesh [25].
- In the United States, 61 cases of cholera were reported between 1995 and 2000, all caused by *V. cholerae* O1 [26]. One death was recorded, and 35 patients were hospitalized (57%); 37 (61%) infections had been acquired outside the United States; 14 (23%) had been acquired through uncooked foods consumed in the USA; 2 (3%) through the consumption of slices watermelon contaminated by the hands of an asymptomatic infected subject, and in 8 (13%) cases the source of infection was not identified. (Figs. 2-4).

Tab. I. The historical cholera pandemics between the Nineteenth and Mid-Twentieth Centuries.

The historical cholera pandemics between the Nineteenth and Mid-Twentieth Centuries with regions and countries where it has hit the most in order of time
1817-1823: The first major pandemic India, Tibet, Middle East Asia.
1828-1838: The second pandemic Bengal, Europe, Canada, US
1841-1856: The third pandemic India, Russia, Europe
1864-1874: The fourth pandemic Singapore, Sumatra, Afghanistan, Persia, Arabia, Egypt, Turkey, Italy
1884-1886: The fifth pandemic Vietnam, China, France, Italy, South America
1892-93: The sixth pandemic Russia, Europe
1902-1926: The seventh pandemic Far East Asia, Persia, Arabia, Russia, Europe

Fig. 2. Gun syringe cholera vaccination, 1973 (Public domain photo).



The road map toward ending cholera

Today, as in the past, “the risk factors for cholera are inadequate or poor water and sanitation infrastructure, the impact of climate change, natural disasters, the effects of humanitarian emergencies which precipitate population movements, overcrowding, and inadequate access to healthcare services, clean water, sanitation and hygiene (WASH) facilities” [1, 27].

The severe floods in Pakistan [28], the earthquakes and drought that have hit Afghanistan and the severe drought in Somalia are significantly increasing the number of cholera cases in these countries (Fig. 5). For this reason, every effort must be made to comply with the provisions of the 2017 “Ending Cholera Road Map”. “Ending Cholera-A Global Roadmap to 2030 operationalizes the new global strategy for cholera control at the country level and provides a concrete path toward a world in which cholera is no longer a threat to public health.

By implementing the strategy between now and 2030, the Global Task Force on Cholera Control (GTFCC) partners will support countries to reduce cholera deaths by 90 percent. With the commitment of cholera-affected countries, technical partners, and donors, as many as 20 countries could eliminate disease transmission by 2030” [29].

Efforts must focus on improving access to clean water and adequate sanitation, raising public awareness, strengthening surveillance systems for the early detection of cases, and supporting coordinated and timely responses. Moreover, in 2022, the World Health Organization (WHO) also supported the rollout of the oral cholera vaccine (OCV) in Lebanon, Pakistan, Somalia and Syria in 2022.

Indeed, it is essential that the disease does not become endemic in countries such as Lebanon and Syria, despite the difficult conditions they are experiencing.

Several factors could be linked to the recent cholera outbreak in Lebanon. Indeed, as cholera is a sign of a country’s state of development, this outbreak can be ascribed, at least in part, to the consequences of the country’s humanitarian crisis. This has resulted in the disruption of water and sanitation systems and the displacement of populations to overcrowded camps with inadequate access to clean water and sanitation, with a subsequent increased risk of cholera transmission. In addition, the Lebanese healthcare system has been hard hit by a three-year financial crisis and an explosion at the port of Beirut in August 2020, which destroyed essential medical infrastructure in the capital. In this context, a cholera outbreak may overwhelm the response capability of the country’s already fragile health system [30].

Fig. 3. Number of cholera cases in the world reported to WHO (2012-2021).

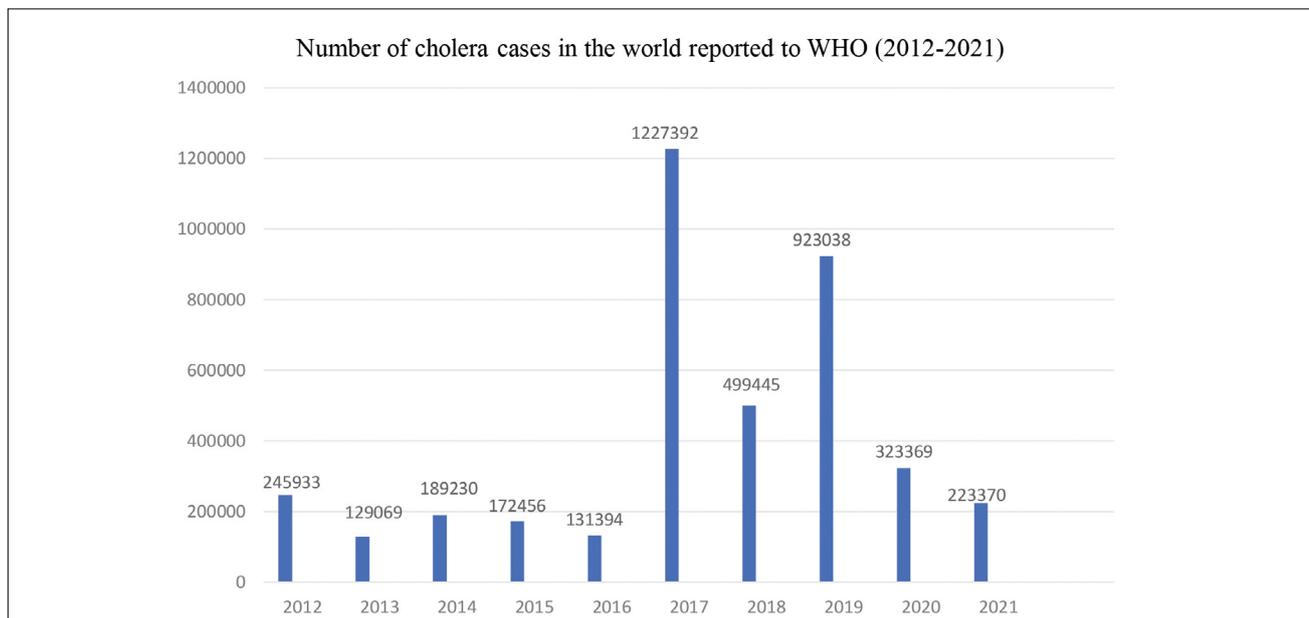
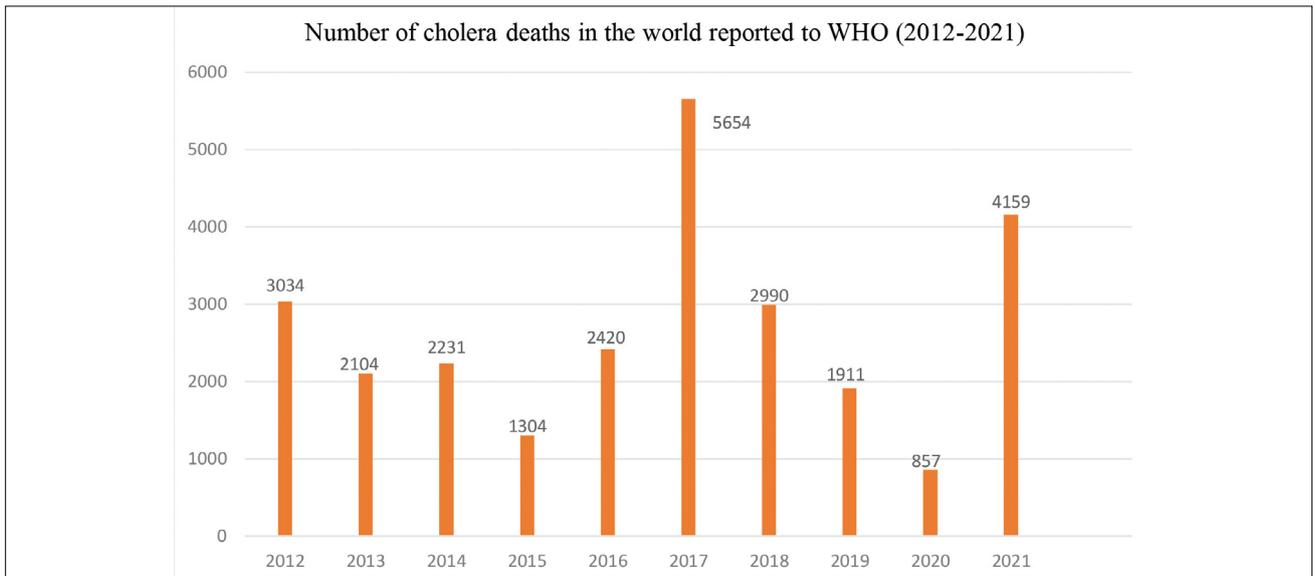


Fig. 4. Number of cholera deaths in the world reported to WHO (2012-2021).

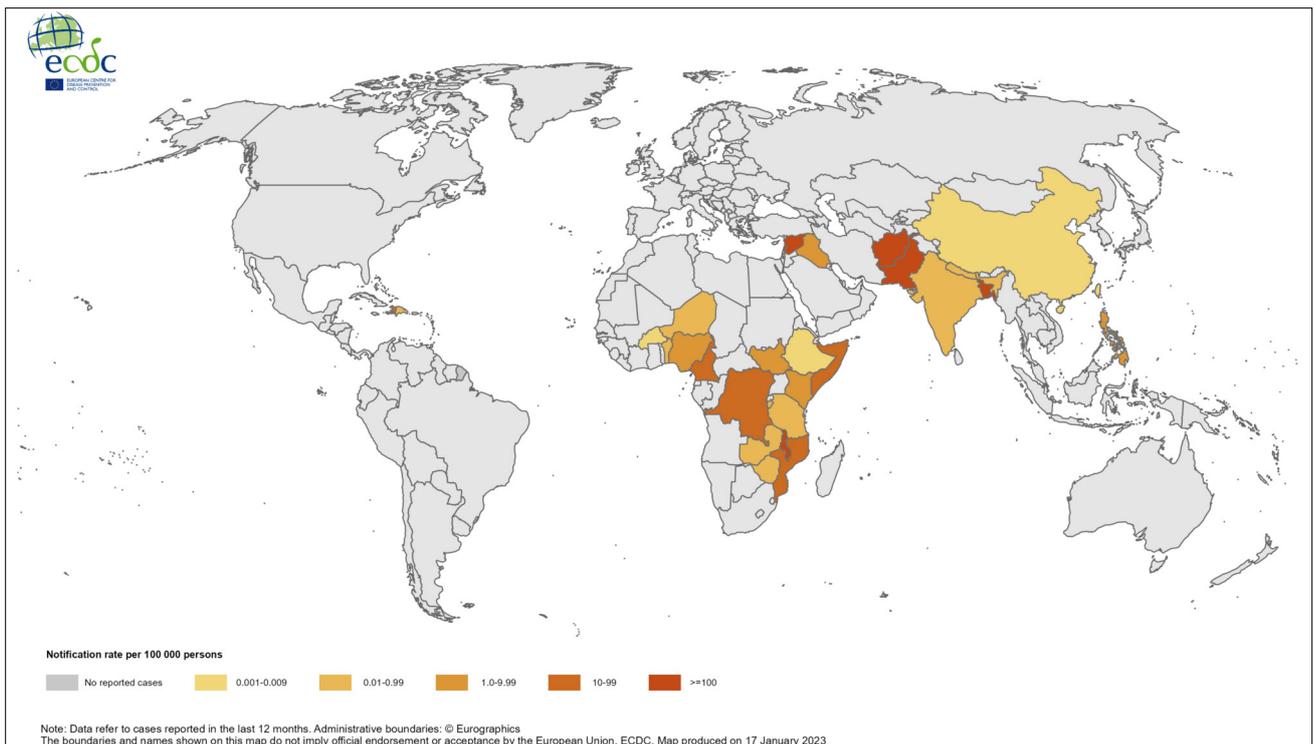


Can the nightmare of a cholera epidemic come from a Syria devastated by war and earthquake?

For 12 years, Syria has been in the throes of a bloody war. This has displaced large masses of the population, who now live in refugee camps where the hygiene situation is totally out of control [31]. Added to this are poverty and hunger, the return of the wild polio virus [32] and

several cases of cholera [33, 34]. In this context, we can only speculate as to the current and future impact of the consequences of the devastating earthquake that struck the territory on the border between Turkey and Syria on 6 February, causing thousands of deaths, injuries and displaced persons. The most dramatic situation can be seen in north-western Syria, where the earthquake hit both government-controlled areas and areas controlled by the rebels fighting the regime of President Bashar al

Fig. 5. Geographical distribution of cholera cases reported worldwide from January 2022 to January 2023 (Data: ECDC - European Centre for Disease Prevention and Control - © ECDC [2005-2022]. <https://www.ecdc.europa.eu/en/all-topics-z/cholera/surveillance-and-disease-data/cholera-monthly>).



Assad. Owing to the civil war, which has been going on since 2011, these regions are inhabited by about 4 million people, including refugees from other parts of the country, who often live in makeshift settlements without any kind of health care. “The healthcare system was already overwhelmed and, after the earthquakes, is at risk of complete collapse in some affected areas, as are certain life-saving departments and services. Disease surveillance teams detect in shelters suspected cases of cholera, diarrhea, scabies, lice, hepatitis A, COVID-19, measles and leishmaniasis” [35].

The earthquake has therefore further strained the Syrian health system, with at least 55 healthcare facilities in north-western Syria having been partially or completely damaged. All this is happening at the same time as Syrian communities are suffering an ongoing cholera epidemic. “As of 24 February 2023, more than 50,000 suspected cholera cases, and 21 associated deaths have been reported in northwest Syria. Forty-four percent of suspected cases are children aged four years old or younger” [36].

Starting March 7, an anti-cholera vaccination campaign was launched in the earthquake-stricken north-western area of Syria, led by the World Health Organization and UNICEF, in coordination with health authorities, the Syria Immunization Group (SIG) and the Global Alliance for Vaccines (GAVI). In the space of 10 days about 1.7 million people were vaccinated in northwest Syria. As of 27 March 2023, 584 cholera cases have been lab-confirmed [37].

It is therefore essential, in a land devastated by a seemingly endless war and a catastrophic earthquake, to make every effort quickly and in a coordinated manner to prevent further victims of a disease which can be prevented through the contribution of all concerned.

Conclusion and future forth coming

The World Health Organization (WHO) aims to reduce cholera deaths: a global roadmap to 2030, with a target to reduce cholera deaths by 90% was launched in 2017. Researchers have estimated that each year there are 1.3 to 4.0 million cases of cholera, and 21 000 to 143 000 deaths worldwide due to cholera [38].

The main approach to controlling the disease is still decent sanitation and the strategy includes, first of all specialist treatment centers and better access to clean water, then effective sanitation and waste management, good hygiene and food safety practices and counselling.

Oral cholera vaccines should be used in conjunction with improvements in water and sanitation to control cholera outbreaks and for prevention in areas known to be high risk for cholera [39].

Meanwhile, the WHO classifies cholera not only a global threat to public health but also as a crucial indicator of lack of social development.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

DO and MM designed the study, conceived, and drafted the manuscript; the authors revised the manuscript, performed a search of the literature. All authors critically revised the manuscript. All authors have read and approved the latest version of the paper for publication.

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