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Review article

Cholera prevention, control strategies, challenges and World Health Organization initiatives in the Eastern Mediterranean Region: A narrative review

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ABSTRACT

The resurgence of cholera is presenting unusual challenges in the Eastern Mediterranean Region (EMR), where it is considered endemic in nine-member states. The risk of a cholera outbreak spreading to non-endemic countries remains high. We discuss the regional trends of cholera, regional burden, and challenges with a focus on World Health Organization (WHO) initiatives in the region that could be useful in preventing and controlling the disease in similar contexts. Despite significant progress in the control of cholera worldwide, the disease continues to be a major public health problem across the region, where it constitutes both an emerging and re-emerging threat. Recurring cholera outbreaks are an indication of deprived water and sanitation conditions as well as weak health systems, contributing to the transmission and spread of the cholera infection. We note that despite the challenges in eliminating cholera in the region, effective implementation of the proposed WHO EMR Strategic framework, among other measures, could sustain the region's cholera prevention, preparedness, and response needs.

1. Introduction

Cholera remains a significant public health threat in many countries worldwide. In resource-constrained settings, it disproportionately affects thousands of poor and vulnerable populations [1,2]. Although significant advances have been made in our knowledge of cholera transmission and its control, the seventh cholera pandemic continues to afflict many countries in the EMR and thus presents a challenge to achieving the Global Task Force on Cholera Control (GTFCC) goals [2–4]. GTFCC is a network of governmental and non-governmental organizations, UN agencies, and scientific partner institutions that help coordinate activities for cholera control [4,5].

A multifaceted approach involving the combination of water, sanitation and hygiene (WaSH), rapid surveillance, social mobilization, treatment, and oral cholera vaccines (OCV) is key to controlling cholera and reducing deaths in a humanitarian environment [2,6–8]. OCV programmes should, however, be used as a short-term measure to reduce disease burden and mortality in the interim pending long-term solutions that must include sustainable WaSH infrastructure and strengthened health systems able to anticipate epidemics and robust community engagement plans required to stop transmission [4,5,9–11]. These solutions must be built on solid

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operational support, local and global resourcing, as well as technical expertise [5]. However, in a regional environment characterized by multiple ongoing conflicts, recurrent natural disasters, gross inequities in access to healthcare, and limited WaSH [2,6,12], it is critical to periodically review the strategies used to prevent and control the re-emerging cholera episodes if we have to achieve the GTFCC target of eliminating cholera by 2030 [4]. We sought to review the regional cholera burden, current prevention and control measures, challenges, and the WHO initiatives that could potentially reverse the trends.

2. Regional trend of cholera outbreaks, 2015–2020

Over the period 2015 to 2020, five countries in EMR, including Somalia, Iraq, Yemen, Afghanistan, and Sudan, reported over 20 cholera outbreaks with an estimated 2,746,513 suspected and laboratory-confirmed cases and 6878 deaths (case fatality ratio (CFR) of 0.40%), [7,13–17]. Although the region experienced outbreaks every year within the reporting period, 2017 was the most affected, with nine outbreaks reported in the three EMR countries of Yemen, Somalia, and Afghanistan [18]. In addition to these outbreaks, 12 cases of imported cholera were reported in the UAE and another five each in Qatar and Saudi Arabia [18]. The wider-geographical spread could be attributed to the spillover effects from Yemen, whose cholera outbreaks remain one of the worst cholera epidemics in recent history [6,19]. For the most part, cases reported in Yemen have been exacerbated by heavy rainfall, poor sanitation, famine, and the protracted political conflict that has affected the country for years [6,19,20].

Within the reporting period, 2016 recorded the highest CFR (1.59%), considered above the emergency threshold of less than 1% [21] (see Fig. 1), with 24% (32,055) of all cholera cases and 30% (717) of cholera-related deaths coming from five countries, including Afghanistan, Iraq, Iran, Somalia, and Yemen (see Fig. 2) [22]. Despite the increase in reported fatalities, the figures represent a 55% reduction in the number of cases reported in EMR in 2016 compared to 2015 (see Fig. 1) [22].

Over the period 2015–2020, the year 2020 saw the region report the lowest CFR (0.05%), ostensibly due to the effect of the COVID-19 pandemic [57]. Faced with the impact of the COVID-19 pandemic, national Ministries of Health and public health institutions, as well as country and other regional partners, had to re-purpose part of their capacities for cholera epidemic detection and response, to the surveillance and control of COVID-19 [23]. In retrospect and considering the period just before the onset of the COVID-19 pandemic and specifically in 2019, a total of 923,037 cholera cases and 1911 cholera deaths were reported globally, for a CFR of 0.2% [23], with about 92% of these cases and 54% deaths occurring in Yemen alone, and the remaining 61,941 cases and 886 deaths occurring in Sudan and Somalia, among other countries outside EMR [23].

Although the number of cholera cases and deaths reported globally were significantly lower in 2020 compared to 2019, experts opine that the number of cholera cases and deaths was more than the number recorded by EMR member states due to challenges of reporting cholera data and difficulties of countries to comply with the International Health Regulations (IHR) 2005 obligations of officially declaring cholera outbreaks and reporting outbreaks as 'cholera' specifically, rather than Acute Watery Diarrhoea (AWD) [24].

3. Regional cholera burden and the WHO initiatives

The EMR has reported explosive cholera outbreaks in 9 out of 22 member-states in the past five years [25], with outbreaks reported during both rainy and drought seasons [2,20,26]. Cholera remains a significant contributor to the regional disease burden and accounted for 85.3% of reported outbreaks in 2019 [25]. Afghanistan, Iran, Iraq, Pakistan, Somalia, Sudan, Djibouti, Syria, and Yemen are endemic to cholera in this region.

A country is defined as endemic when confirmed cholera cases resulting from local transmission have been detected in the last three

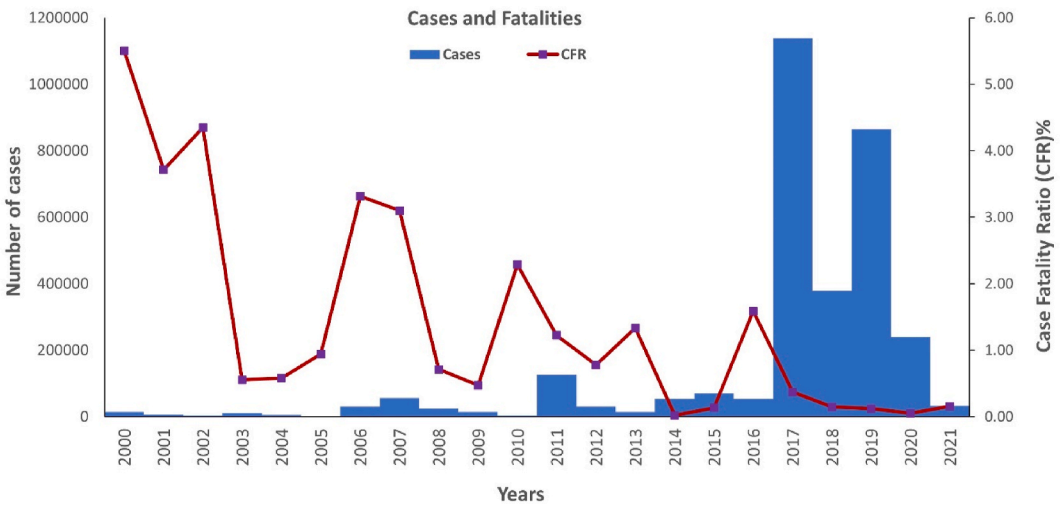

Fig. 1. Trend of cholera cases and deaths in Eastern Mediterranean Region, 2000–Oct 2021.

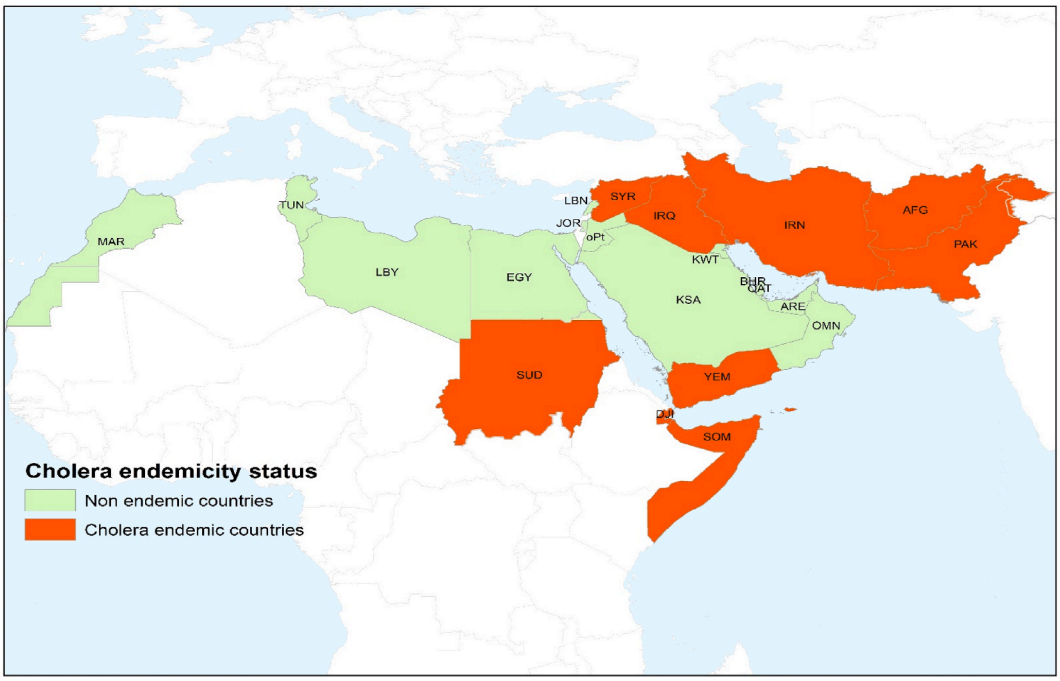

Fig. 2. Cholera endemic countries in the Eastern Mediterranean region.

years [27]. Cholera endemicity in the EMR is largely driven by inadequate WaSH infrastructure, conflict and political instability, and failure to fulfil IHR (2005) reporting obligations for surveillance, detection and reporting of cholera - and not as AWD [24].

Following internal conflicts in 2015, Iraq reported approximately 3.2 million Internally Displaced Persons (IDPs) living in camps, informal settlements, and temporary shelters with limited access to health and WaSH services [7,28]. Subsequently, on August 30, 2015, cholera was confirmed in Diwaniya Governorate, and on September 15, the Iraq Ministry of Health (MoH) declared an outbreak [7]. The response to the Iraq outbreak included implementing an OCV campaign to complement WaSH and other control measures. More than 510,000 doses of OCV were deployed in two campaign rounds that targeted approximately 255,000 persons living in selected settlements, IDP, and refugee camps [7].

The cholera outbreak reported in Yemen in October 2016 continues to date [20, 31]). The year 2017 saw Yemen record the highest number of cholera cases in the region, with an average of 5000 suspected cholera cases reported per day, in what the UNICEF and WHO described as the "world's worst cholera outbreak amid the world's largest humanitarian crisis" [22,29]. Severe malnutrition, low immunization coverage, and concurrent outbreaks of other diseases, such as diphtheria, dengue, chikungunya, and others, further complicated the situation [2,12,19,30].

WHO supported the Ministry of Health to enhance disease surveillance through the Early Warning Alert and Response Network (EWARN), provided rapid diagnostic and laboratory test kits, and mapped hotspot areas (WHO, 2018, [31]. In addition, WHO has supported and implemented WaSH activities, administered OCV to high-risk populations, provided supportive drugs, and conducted case management training [31]. During the 2017 cholera outbreak in Yemen, WHO deployed experts to support cholera case management, laboratory investigation, OCV campaigns, and the electronic Disease Early Warning System (eDEWS) surveillance upgrade. Several OCV campaigns have been conducted in Yemen from 2018 to 2021 [32]. The campaigns targeted 2,917,307 persons in both North and South of Yemen, with 2,273,157 (78%) reached at 80% for the North and 75% for the South, with a total of 4,238,614 doses of OCV administered. However, despite significant gains, the outbreak is still not contained, and this is due to the prevailing complex emergency situation, including a lack of WaSH infrastructure, limited resources, and inadequate staffing, which have led to a weakened health system [2,12,33].

The cholera situation in Somalia mirrors that of Yemen. It should be noted that both Somalia and Yemen have suffered from protracted complex emergencies that challenge efforts to eliminate cholera [6,12,17,34]. Persistent drought, shortage of safe water, poor sanitation, major population movements, and food insecurity have further exacerbated the situation [12].

The first case of the 2017–2020 cholera outbreak in Somalia was confirmed in December 2017 in the Beletweyne district of the Hiraan region following heavy rains [8,35]. The outbreak then spread to 27 districts in four regions located in the river basins in Jubba and Shabelle. Cumulatively, from December 2017 to November 2020, Somalia reported a total of 16,003 suspected cases and 83 deaths (CFR 0.52%). The 2017 outbreak was the largest in Somalia, with a peak of 5000 cases reported in week 22 (May 29 to June 4); the reported cases then declined gradually, with only sporadic cases reported in December 2017. Cholera cases, however, continued to be reported in the period 2018–2020 at lower levels. In 2018, the cumulative total of suspected cholera cases was 6448, with 45 associated deaths and a high CFR of 0.70%, while in 2019, the cumulative sum of suspected cholera cases was 3100, with 4 associated

deaths and a low CFR of 0.13%.

In April 2020, the floods caused by heavy Gu rains displaced 400,000 people in 23 districts exacerbating the outbreak [36]. In June 2020, towns along river Shabelle experienced Hagaa rains that led to the contamination of water sources and thus increased cholera spread. In 2020, Somalia recorded 6582 suspected cholera cases, including 33 associated deaths (CFR 0.5%), mainly from the Banadir region. Baidoa-Bay region reported 935 cholera cases, including three deaths (CFR 0.3%) in the same year. The cumulative number of suspected cases reported from December 2017 to December 2020 was 16,756, including 83 deaths (CFR 0.49%). In response, WHO supported the Ministry of Health in Somalia to enhance the implementation of preventive interventions, including OCV, distribution of risk communication materials, and strengthening WaSH activities in hotspots [35].

OCV was first implemented in Somalia from March to October 2017 as part of a comprehensive cholera response strategy that targeted 1.1 million people $\geq$1 year in 11 high-risk districts, with two doses of the OCV. Overall, 2-dose administrative OCV coverage achieved in all targeted districts was 95.5%, proving that OCV campaigns can be implemented successfully even in challenging humanitarian settings. A subsequent pre-emptive OCV campaign was conducted in 2018 and 2019 in high-risk areas of Somalia, with a total of 345,157 and 616,726 OCV doses, respectively [8]. In collaboration with the Ministry of Health, WHO manages disease surveillance and continuously monitors the outbreak trends through EWARN to promptly investigate and respond to alerts [17].

Parallel to the Yemen and Somalia situation, Sudan in 2019 reported 344 cases, including 11 deaths (CFR 3.18%) from 15 localities in the four states of Blue Nile (BN), Sennar, Khartoum, and Al Jazirah [15,37]. Blue Nile (204) and Sennar (130) accounted for more than 95% of all the cases, including 11 deaths [38]. Prior to this, Sudan also experienced an outbreak of suspected cholera, officially described as Acute Watery Diarrhoea, in August 2016 that began in the Blue Nile State and spread rapidly to Gedarif, White Nile, Khartoum, Sennar, River Nile, North Kordofan, and Gezira states with estimated 15,000–23,000 people infected, with 280–820 deaths. Although WHO and her partners acted promptly to control the outbreak, the affected areas remain on WHO's watchlist with active surveillance and laboratory investigations, case management, OCV campaign planning, hotspot mapping, WaSH, and risk communications [15] ongoing. During the last outbreak, WHO supported the MoH in implementing WaSH activities and two rounds of OCV campaigns in October and November 2019 to vaccinate the target population in the most affected states (Blue Nile State (coverage 85%), Sennar (Coverage 98%). WHO also provided regular support to health authorities for laboratory confirmation of suspected cases and sustained implementation of WaSH activities for long-term prevention and control.

4. Challenges facing cholera prevention and control in the EMR

The EMR is home to more than 679 million people, representing a diverse group of 22 countries, including Arab states in North Africa, Gulf nations, and West Asia [39, 58]. Persistent political instability, conflict, insecurity and large population movements within the region add pressure to the existing weak social services (i.e., water and sanitation), increasing the risk of cholera outbreaks [3,31, 40]. Cholera and other waterborne disease outbreaks remain the most commonly reported epidemics in some EMR countries with complex emergencies [30,39]. Mass gatherings and overcrowded environments with limited WaSH programmes, such as camps for refugees and internally displaced people, and social behaviour practised during religious ceremonies also increase the risk of transmission and spread of cholera [20,26].

The EMR also harbours the highest IDPs and refugee populations globally [40,41]. Across the region, more than 108 million people currently need humanitarian assistance, and it is the source of 64% of the world's refugees [40,41]. Many of these refugees and IDPs live in congested camps with inadequate essential social services, including education, health, water, and sanitation [31]. Refugees, IDPs, and other populations affected by the humanitarian crisis are especially vulnerable to emerging infectious diseases, particularly cholera [35]. Some of the endemic cholera countries in the region, such as Afghanistan, Iraq, Somalia, and Yemen, are disproportionally affected by massive population movement from protracted political instability or acute conflicts that damaged WaSH and health infrastructure as well as compromised immunization efforts [6,12]. Restoration of these infrastructures requires long-term political commitment and a significant investment, but many countries in the region lack the resources necessary to finance the rehabilitation [3,6]. The protracted complex emergencies affecting the region, most of which have no short-term or medium-term solutions, have reduced accessibility to affected communities, negatively impacted the fragile health system, and weakened the preparedness and response capacities [6,18].

Cholera outbreaks have been reported to increase during the dry season in some countries and the rainy season in others [2,20]. Climatic changes and environmental degradation are now considered key drivers to the increased risk of emerging and re-emerging infectious diseases, particularly cholera [2,20]. Climate change impacts human displacement, including droughts and flooding, which favour cholera outbreaks by reducing access to clean water [42,43]. Besides limited access to clean water, drought such as that experienced in Yemen promotes the marginalization of refugees and nomadic populations as well as the expansion of informal urban settlements, all of which promote cholera spread [44].

The impact of climate change on the occurrence and frequency of epidemics, including cholera, is now progressively being realized and discussed. In the prelude to the 2022 United Nations Climate Change Conference (COP27), it was noted that floods and rising sea levels have affected environmental hygiene leading to waterborne and diarrhoeal diseases, with extreme weather conditions negatively impacting water supply [45]. Thus unless remedial measures are put in place, we expect to see increased cholera outbreaks in the region and globally attributed to climate change.

Another important challenge is the lack of adherence to the IHR (2005) obligation of declaring and reporting cholera outbreaks. Some countries in the region have tended to avoid declaring cholera outbreaks preferring instead to report AWD, and this undermines the spirit of IHR (2005) of declaring and reporting disease outbreaks [24]. Governments' denial of cholera outbreaks often results in non-disclosure of laboratory test results and the deliberate underreporting of cases, with inadequate control measures being instituted.

Consequently, the frequency and severity of cholera outbreaks in the region have risen significantly in recent years, affecting millions of vulnerable populations.

Over the period 2015–2020, EMR recorded an average of three cholera outbreaks every year, excluding the year 2017, when the Yemen situation pushed the number to nine. The risk and threat of a cholera outbreak spreading to non-endemic countries in the region are high due to population movements and the consequences of the humanitarian crises [30]. Member states' preparedness and response capacities are inadequate, while the failure of existing public health interventions is evident. Although many factors influence the resurgence of cholera outbreaks in the region, many countries are not prioritizing utilizing all available and practical tools to prevent or control potential cholera outbreaks.

In the recent past, cholera has been making a comeback globally, laying bare the health systems' capacities to withstand the pressure of sustained cholera outbreaks. In 2022, more than 29 cholera outbreaks were reported globally, 8 of them from EMR countries. A perfect-storm aggregation of risk factors, including effects of climate change, armed conflicts, forced migration, natural disasters as well as the adverse economic and social effects of the COVID-19 pandemic, saw countries that had not been affected by cholera for years, including Haiti, Lebanon, and Syria, battle with renewed cholera outbreaks [42].

Due to a surge in the number of countries reporting cholera outbreaks globally, the demand for cholera prevention and control commodities, including the OCV, has skyrocketed, with stockouts becoming a reality [42]. The pressure on OCV supplies saw the International Coordinating Group (ICG), which governs the use of the Gavi-funded OCV stockpile, make the difficult decision in 2022 to temporarily hold back the second dose of OCV in outbreak settings, a factor that may cause delays in controlling the outbreaks in the region, in the absence of proper WaSH facilities [42]; WHO, 2022; [46].

4.1. Current prevention and control measures

In collaboration with the member states, the WHO has prioritized the implementation of comprehensive and integrated cholera

Table 1
Summary of WHO Support to EMR Member States affected by Cholera.

Disease	Country	Type of Support
Cholera	Yemen	• Surveillance through an electronic system –EWARN • Provision of test kits • Mapping of hotspots • WaSH activities • Oral cholera vaccine administration to high-risk populations • Provision of drugs and case management training • Deployment of experts • Case management training and laboratory investigation • Early warning system surveillance (eDEWS) • community awareness campaigns; waste management and chlorination of water; and use of oral cholera vaccine.
	Somalia	• In collaboration with the Ministry of Health, WHO manages disease surveillance and continuously monitors the outbreak trends through EWARN to promptly investigate and respond to alerts • OCV administration to high-risk populations • Distribution of risk communication materials, • Strengthening WaSH activities in hotspots •
	Sudan	• Active surveillance and laboratory investigations • Case management, • OCV campaign planning, • Hotspot mapping, • WHO supported the MoH in implementing WaSH activities and risk communication • Support to health authorities for laboratory confirmation of suspected cases and sustained implementation of WaSH activities for long-term prevention and control.
	Iraq	• Coordinated Risk assessment exercises • Sharing of EWARN surveillance data; • Activation of rapid response teams to investigate suspected cases and rumours; • Enhancing laboratory capacity to confirm cases early and ascertain antibiotic susceptibility at both national and governorate levels; • Preventive mass campaign with oral cholera OCV) conducted in 62 high-risk camps in Iraq to prevent the spread to Syria • Dissemination of case management protocols and refresher training, • Put Cholera prevention and preparedness measures on the agenda of the Health and Water, Sanitation and Hygiene (WaSH) clusters to ensure coordination between different partners.
	Afghanistan	• Surveillance through EWARN
	Pakistan	•surveillance through EWARN
	Syria	•Improved reporting of imported cases from neighbouring countries of Iraq

prevention and control plans within the health and WaSH sectors [31,35]. See Table 1. In addition, it has embarked on many initiatives to scale up the regional and national preparedness and response capacities. Despite these interventions, some member states' morbidity and mortality rates associated with cholera infections are unacceptably high [31,35]. Ordinarily, the cholera response measures are reactive, focusing on emergency health sector response instead of investing in long-term infrastructure and plans to strengthen prevention and control efforts.

Although the effectiveness of different cholera interventions varies from country to country, WaSH interventions are preferred to reduce the burden of cholera in high-risk areas in the long run [2,26]. In developed and some developing countries, cholera was effectively eliminated through investing in proper environmental health solutions, including water supply with appropriate treatment and distribution, adequate disposal of human waste, and sanitation infrastructure [47]. Therefore, improving environmental health conditions, especially water and sanitation, is the most significant intervention to prevent cholera or other waterborne disease outbreaks [47,48]. However, this requires sustained commitment and investment to improve the infrastructure and services [31,35,49].

Real-time surveillance through strengthening reporting, ensuring timeliness, data quality through deploying electronic systems, strengthening laboratory capacity, and case management of cholera cases are other essential interventions that can save lives and reduce the mortality rates often associated with cholera outbreaks when individuals have access to good quality treatment as and when the symptoms appear [33]. Effective case management can be achieved by establishing well-equipped and staffed treatment centres within the existing health facilities and community centres. Improving the knowledge and skills among health workers is critical in clinical signs and symptoms, patient assessment of dehydration, appropriate treatment protocols, and how to protect themselves and prevent the spread of infection at the treatment facilities [2].

In recent years, OCV has become another essential and cost-effective tool to prevent and control cholera in emergency and non-emergency settings [2,19,26,50,51]. Three killed, whole-cell (WC) OCVs are currently pre-qualified by the WHO for procurement by United Nations agencies and are available for global use: Shanchol, Euvichol, and Dukoral [3,11,51]. According to the manufacturers, Shanchol™ and Euvichol® should be administered orally in 2 liquid doses 14 days apart in individuals aged $\geq$1 year. These vaccines stimulate the production of both antibacterial and anti-toxin antibodies, including IgA antibodies produced locally in the intestines [51] and have been found to offer both direct and herd immunity based on the available evidence from studies done in other settings [52,53] In both pre-licensure studies and post-marketing surveillance, WC-rBS has been shown to have a good safety profile, including when used in pregnancy and in HIV-infected or other immunocompromised individuals. Single dose effectiveness in individuals $\geq$1 year old was 40% effective against all cholera episodes and 63% against severely dehydrating cholera episodes. A single dose of OCV provides protection of up to 6 months, and two doses are recommended for the most extended protection of up three years. According to previous studies, OCV is less effective in children $<$5 years of age [11,51].

WHO recommends that OCVs be considered in preemptive situations as part of comprehensive cholera control plans and reactive situations depending on the local epidemiology and feasibility of conducting campaigns [32]. Further, OCV should not be used as a stand-alone intervention to replace the other proven public health interventions [3,9–11] but instead as a "supplementary" tool in outbreak control and the long-term prevention of cholera [10,32,38,54].

One of the earliest uses of the OCV in a humanitarian situation was in Darfur, Sudan, in 2004 [55]. It targeted IDPs living in two camps where living conditions, water supplies, and sanitation facilities were appalling. The Darfur campaign was more of a pre-emptive campaign for potential cholera outbreaks, and many lessons were learned in the process [55]. In subsequent years, endemic cholera countries of Iraq, Somalia, and Yemen have implemented large-scale pre-emptive and reactive OCV campaigns targeting IDP/refugee camps and other high-risk areas. The impact of these campaigns was evident as major cholera outbreaks were averted among target populations, and the burden of cholera was reduced significantly. Nonetheless, the success of an OCV campaign in any setting depends on acknowledgement and political commitment from the government, adequate capacities by the health authorities and partners, and timely decision-making for the introduction of the cholera vaccine [19,33]. Therefore, WHO and other international partners should take proactive steps to promote combining OCV campaigns with other proven interventions to prevent or control cholera outbreaks in emergency and non-emergency settings as early as possible.

5. WHO EMR strategic framework

Key to sustaining cholera prevention and control in the region is the WHO-EMRO Framework on eliminating cholera in the EMR being finalized to support effective and efficient cholera prevention and outbreak preparedness and response capacities by member states [25]. The framework created through a broad consultative process aligns with the 'End Cholera – A Global roadmap to 2030' global strategy developed by the Global Task Force on Cholera Control, aimed at reducing cholera deaths by 90% [4].

The new global strategy promotes the integration of multi-sectoral cholera interventions that will harmonize the existing health and WaSH efforts with the use of vaccines in high-risk areas [33]. Moreover, it focuses on early detection, confirmation, and timely response to contain outbreaks; a targeted multi-sectoral approach to prevent cholera recurrence; and an effective coordination mechanism for technical support, advocacy, resource mobilization, and partnership at local and global levels [4]. Cholera-endemic countries and those affected by complex emergencies in the EMR will significantly benefit from the renewed strategy already endorsed by many GTFCC partners.

The WHO-EMRO framework targets the political and technical leadership and all stakeholders to provide guidance to support governments in the EMR to coordinate, plan, implement, and evaluate actions to end Cholera in EMR by 2030. The objectives of the strategic framework are to guide national planning on cholera prevention and control; facilitate coherence, coordination, efficiency, and accountability of multi-stakeholder investments aimed at ending cholera in WHO EMR; and provide a robust framework for inter-country collaboration and shared learning on actions to end cholera in WHO EMR [25].

The framework, the first in the region, is a step forward to cholera prevention and control as it serves as a resource from which each EMR member state may summarise priority activities under specific thematic areas given the varied contexts within each country. This is expected to promote standardization of planning and reporting for collaboration and sharing of experiences among member states. The framework recommends several strategic actions to be steered by effective leadership and coordination mechanism, including the definition of national cholera program goals, priority outcomes, targets, and interventions for cholera control or elimination, both in the short and long term. The framework, which was developed collaboratively, will support preventive strategies, including enabling equitable access to safe drinking water and sanitation systems and promoting optimal hygiene practices, and the deployment of OCVs [25].

Effective implementation of the framework will ensure early detection of the outbreak, prompt and effective Response, prevent new outbreaks, and limit the spread of ongoing cholera outbreaks. However, to achieve this action, respective EMR governments should establish active surveillance, laboratory, and reporting systems and support the dissemination of evidence-based guidelines on epidemic alert and Response. Moreover, efforts must be made to create functional systems, including data and information infrastructure, trained human resources, and supplies anchored on effective community communication.

While the framework has not yet been officially rolled out, EMR countries are already implementing the framework strategies and recommendations. See Table 1. WHO and its partners have made remarkable progress in supporting the relevant line ministries of countries in the region. There is ongoing support to countries with active outbreaks to establish a National cholera multi-sectoral task force and ensure its functionality as it plays a crucial role in cholera control. In addition, there are efforts to enhance country capacities to implement an early warning surveillance system, enhanced Risk communication and community engagement (RCCE), appropriate case management practices, infection prevention control (IPC), OCV campaigns' implementation, in addition to continued WaSH interventions among other measures. In addition, the risk assessments of cholera importation and spread are conducted in the countries without cholera outbreaks; accordingly, their capacities are being built for early detection, laboratory confirmation, case management and IPC, RCCE and enhanced WaSH.

The emphasis on a coordinated multi-sectoral approach to preventing and controlling cholera in hotspots, multi-stakeholder engagement, monitoring, evaluation, and continuous learning and adaptation is a positive move. Whereas a broader multi-sectoral stakeholder approach is necessary for ownership and sustained interventions, there is a need for commitment and accountability by the respective political class within EMR [4,56]. Without the investment by donors and the government, the EMR cholera strategy cannot achieve its objectives, especially WaSH and health infrastructure improvement in countries such as Yemen and Somalia. This commitment will ensure that member states implement the framework with fidelity and adequately prepare to prevent, detect, and respond to the threat of cholera disease while guaranteeing protection for their citizens from the disease's health, social, and economic impacts.

WHO continues to advocate for a more significant political commitment among member states in the region to prioritize a sustainable cholera control strategy, which includes using the oral cholera vaccine and allocating adequate resources to finance the implementation of renewed cholera strategies. Response capacities among member states and national organizations to implement the integrated and comprehensive prevention and control of cholera strategies should be scaled up and the required resources mobilized to implement the renewed strategies.

5.1. Progress made thus far

In recent years, the EMR has witnessed an unprecedented level of integration of multi-sectoral cholera interventions to harmonize the existing health and WaSH efforts with the use of vaccines in high-risk areas [33,56]. Although these efforts have resulted in enhanced response capacities by member states and national organizations implementing the integrated and comprehensive prevention and control strategies, there is need to mobilize and scale up the required resources to implement the renewed strategies [56]. Moreover, there has been an appreciation of the complementary and synergistic role played by OCV and WaSH interventions; this is a major shift from the past, where the two had been viewed as competing with one another [3].

Although it has taken considerable effort for the WHO and partners to convince countries to invest in both WaSH and OCV, many EMR countries now regard the combination of WaSH and OCV as an essential and cost-effective tool to prevent and control cholera in both emergency and non-emergency settings [2,26]; Ebob, 2020; [19,51]. This radical shift has seen many cholera-endemic countries of Iraq, Somalia, and Yemen implement large-scale pre-emptive and reactive OCV campaigns targeting IDP/refugee camps and other high-risk areas [32,38,54].

5.2. Future prospects

To sustain the regional efforts made and improve future prospects in cholera prevention and control, the WHO, governments and other partners must consolidate ongoing efforts to eliminate any obstacles while striving to align the regional efforts with the Global roadmap [4], thus:

a) Early detection and quick response to contain outbreaks

The EMR will turn the tide on cholera in an environment where cholera cases are detected and reported promptly and without stigma. This will require long-term investment in real-time surveillance, outbreak detection, laboratory confirmation and Response, timely access to appropriate case management and cholera vaccines, enhancing WaSH, and strengthening RCCE. Moreover, to bolster

future efforts, there is need to enhance functional systems for data and information infrastructure, capacity-build the requisite human resources and ensure community communication systems are improved and sustained [25].

b) A targeted prevention strategy using vaccines in cholera hotspots

A safer EMR free of cholera is one in which a larger regional supply of OCV is sustained to cover those in need, especially in conflict-affected areas of Yemen, Somalia, Syria and Iraq. With limited OCV stocks, more consideration should be used to decide how to more efficiently use the available OCV to ensure reach and equity, such as alternative dosing regimens and targeting specific subpopulations [3]. However, it is important to point out that the success of any proposed OCV campaign must be based on acknowledgement and firm political commitment from regional governments, adequate capacities by the health authorities and partners, as well as timely decision-making [19,33].

6. Support, resources and partnership with GTFCC coordination and support

A future EMR free of cholera requires continued investment by donors and all stakeholders in WaSH and health infrastructure to sustain the progress made this far. Moreover, efforts must be made to support and sustain inter-country collaboration and shared learning across the EMR. [25]. This will require strengthening the already existing multi-sectoral approach systems, multi-stakeholder engagement, monitoring, evaluation, and continuous learning and adaptation. However, to ensure sustainability, there is a need for commitment and accountability by the political class.

7. Conclusion

Despite the challenges in eliminating cholera among the endemic EMR member states, it is crucial to sustain the cholera response needs to minimize the risk of future rebounds and spikes. Effective implementation of the proposed WHO EMR Strategic framework on eliminating cholera through real-time surveillance, outbreak detection and response, timely access to appropriate case management and cholera vaccines, enhancing WaSH, and strengthening risk communication and community engagement will significantly reduce cholera morbidity and mortality among member-states. Major challenges that include prolonged armed conflict with attendant population displacement remain, leading to an increase in vulnerable populations. Recurrent natural disasters comprising floods, drought, cyclones, and others, also contribute to the cholera outbreaks in the region. The impact of climate change in this regard is also real but not yet quantified. Many countries in the region have weak and under-funded health systems, with low institutional capacities, especially in endemic cholera countries. Political interference, lack of transparency by governments, and the lack of respect for IHR 2005 obligations of reporting cholera and sharing data are areas that need urgent attention. National response measures are still not robust, with the insufficient implementation of multi-sectoral Response. OCV is increasingly growing in importance as part of a comprehensive tool kit whose timely uptake would significantly reduce case burden during an outbreak or prevent future outbreaks in hot spot areas. Responding to cholera outbreaks is important, but greater investment in the long term to overall cholera preparedness and Response, including WaSH and health infrastructure, is critical, and donors should allocate more resources to this course.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interest's statement

The authors declare no conflict of interest.

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