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## Global mapping of cholera *Vibrio* and outbreaks in the Pre-Millennium Development Goals (MDG)/Sustainable Development Goals (SDG) and MDGs/SDGs era of 1990–2019



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#### ABSTRACT

Vibrio species and cholera outbreak yet remain a frequent health emergency despite progress made in integrated implementation of the MDGs/SDGs/WASH worldwide. Hence, this study aimed at appraising the impacts of MDGs/SDGs/WASH campaigns on the mitigation of cholera outbreak and associated consequences. The study mapped scientific production related to Vibrio outbreak from 1990 to 2019, identified trend, institutional/international concerted efforts toward outbreak research/response and gaps for future preparedness. Relevant documents were identified from the Web of Science database using an optimised title-field specific search Boolean that accommodated all pre-set inclusion criteria for the study. A total of 901 documents were identified including 869 available abstracts were retrieved for content-review of human incidence cases, mortality, culprit Vibrio species, strains, and biotypes. Explanatory analysis showed that the trend of outbreak documents approximately increased in 6th order quadratic relationship ( $R^2 = 0.7948$ ) from 1990 to 2019 with an annual growth rate of 3.21% and a mean value of 30.0 ± 18.0 per year. Other details revealed an increased and undulating case report/mortality rate of cholera outbreaks especially in the MDGs/SDGs era. Decadal comparison of Vibrio outbreak during the period showed significant variation in documents distribution (Kruskal-Wallis p = 0.00077). based on countries' efforts, the USA, ranked first in terms of article numbers (191), publication frequency (24.6(%) and total citations (5962). Four prevailing conceptual frameworks were identified in the outbreak documents with global community interest revealed as the largest topical coverage. All conceptual frameworks consisted in Vibrio characterisation, methodology-related, intervention-related, geographic-related concepts and some replete with health and climate-change depicting concepts. Also, the study observed high mortality in Vibrio outbreaks during 1990-1999 (29080 deaths), and 2010-2019 (386606 deaths) compared to 2000–2009 (7705 deaths) (Kruskal-Wallis, p < 0.05). High number of outbreaks due to V. cholerae and V. parahaemolyticus and a limited outbreaks attributed to emerging strains. In conclusion, vibrio outbreak has not lived up to various investment put into its control from various programme evolutions. The broad spectrum Vibrio vaccines that could cater for outbreak caused by common and emerging strains is inevitable and a significant thrust for future research.

#### 1. Introduction

Vibrio species, cholera and other waterborne diseases outbreaks are usually consequences of inaccessibility to improved drinking water supplies and sanitations from time immemorial. Meanwhile, among the primary priorities of the United Nations e.g., the Millennium Development Goals (MDGs) and the Sustainable Development Goals (SDGs) for some decades include access to enough safe drinking water

and sanitation, which has gained widespread attentions from one-health perspectives. While the United Nations' efforts on global safe drinking water targets can be traced early to 1959 [1,2], since then, five phases of programmes could be recognised namely, 1959–1980, 1981–1990, 1991–2000, 2001–2015 (MDGs) and 2016–2030 SDGs periods [3]. The 1959–1980 had its target to achieve 'reasonable access and safe water supply [1], while the 1981–1990 period aimed at 'providing all people with water of safe quality, adequate quantity and basic

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sanitary facilities by 1990' [4,5]; the 1991–2000 hinged on 'safe drinking water coverage at a convenient distance from the user's dwelling' [6,7]; the 2001–2015 (MDG) focused at 'reducing to half, the percentage of individuals who lack safe water' by 2015 and 'safe water for everyone' by 2025' [8]; and the SDGs centred at 'achieving universal and equitable access to safe and affordable drinking water for all' by 2030 [9]. Both the MDGs and SDGs goals especially SDGs 3 "ensure healthy lives and promote well-being for all at all ages", and 6 "Clean water and sanitation". It is therefore hypothesised that they could meritoriously support possible reduction in disease outbreaks if a level of progress in their implementation is achieved.

Fortunately, all the aforementioned phases, have witnessed some progresses towards safe water supply and sanitation against their respective baselines. For instance, the World Health Organization/United Nation International Children's Emergency Fund (WHO/UNICEF) Joint Monitoring Programme for Water Supply and Sanitation (JMP) in 2012 declared that 'halving the proportion of those have-nots connected with safe drinking water' was achieved in 2010 [10]. Also, that the rural population without access to drinking water reduced by  $6.33 \times 10^8$ [11] in the same periods. In similar manner, the period 1990-2015 witnessed 9.79  $\times$  10<sup>8</sup> and 1.48  $\times$  10<sup>9</sup> increases in rural and urban populations with access to improved water sources, respectively, excluding developed nations; and  $6.03 \times 10^8$  deceased in the population that relied on unimproved water (WHO/UNICEF JMP (https:// washdata.org/)). Similarly, the JMP in 2017, revealed on global population scale that 92% used 'improved water sources' in 2015 during the MDG and 71% of which used 'safely managed drinking water services', situated on the premises or available at will and without priority chemical and faecal contaminants [12]. The most notable progress related to safe water supply was recorded in India involving 3.84  $\times$  10<sup>8</sup> increase and 1.68  $\times$  10<sup>8</sup> decrease in rural population with and without access to improved water respectively, notwithstanding a total increase of  $2.16 \times 10^8$  in India's rural populations during the period [3].

Despite these progresses, it is unknown whether the achievements recorded in the MDGs/SDGs are related to improved water and sanitation access, which is translated to reduced outbreaks of cholera/Vibrio globally or not. It is against this backdrop that this study assessed contributions of the MDGs/SDGs activities on water and sanitation targets to reducing cholera outbreaks. There exist no formal analysis or study related to contributory impacts of MDG/SDG campaigns towards the mitigation of global Vibrio/cholera outbreaks. This study investigated whether MDGs/SDGs progress translated to reduced cholera outbreaks or not. The approach involved mapping of scientific production related to Vibrio outbreak from 1990 to 2019 as an indirect source-track of cholera outbreaks during the period. This investigation also identified outbreak trend, institutional/international concerted efforts toward outbreak research/response, topical concerns and gaps for future outbreak preparedness.

#### 2. Methods

#### 2.1. Retrieval of outbreak documents

Published peer-reviewed article, proceedings paper, editorial material letter, meeting abstract, news item, and note on *Vibrio* outbreaks globally were searched on the Web of Science (WoS) core collection database on 23/05/2019; 12.08 GMT+2). The study adopted title-specific search with the Boolean "(Vibrio\* AND epidemic\*) OR (Vibrio\* AND outbreak\$) OR (choler\* AND outbreak\$) OR (choler\* AND epidemic\*))" to retrieved all available *Vibrio* outbreak information from 1990 to 2019 (23/05/2019). This was done to enhance specificity, maximum recovery and as well minimized loss compared to a topical search [13]. The adoption of WoS database is pre-informed by the availability of news items. News item is normally unavailable in other databases; meanwhile news constituted the first outlet for outbreak information to enhance prevention or halt further spread. The wildcard

\* and \$ ensured inclusion of words such as "Vibrio spp", "Vibriosis", "Vibrio cholerae", "Vibrio parahaemolyticus", "Vibrio vulnificus", "Vibrio anguillarum", "Vibrio alginolyticus", "epidemic(s)" and "outbreak (s)" as the case may be. The search result was further refined by excluding document types such as correction addition, review, book review, biographical item, book chapter, correction, avian cholera, book and reprint, as they do not constitute primary sources of outbreak information and/or are synthesis of primary articles. All documents that meet the inclusion criteria were downloaded in the BibTeX file format. In addition, the documents' titles and abstracts were retrieved in PDF file format for extraction of bacterial strain, number of human, and death cases involved. SDGs (2016 jan).

#### 2.2. Data analytics

#### 2.2.1. Data pre-processing and descriptive analysis

The retrieved data were pre-processed for quality control. Data fields related to authors' names, affiliation, country, document source, keywords and other bibliometric variables were extracted for normalization. All relevant fields including authors' names and keywords were extracted by two investigators (IBE and ETC) and checked for spelling errors. Further analysis was based on agreement between data normalized by the two investigators. Keywords with similar meanings or multiple occurrences in a document were grouped together and regarded as one word respectively (e.g., "Cholera", 'Cholera epidemic", and "Cholera Outbreak", or "India" and "Calcutta").

The standardised data was analysed for descriptive indices and rates for topmost 10 productive authors, top productive countries, total citations per country and 10 topmost relevant sources.

#### 2.2.2. Outbreak trend analysis

Time series of annual scientific production related to *Vibrio* outbreak was generated in term of documents. The time series data was further grouped into 3 decadal periods (1990–1999, 2000–2009, and 2010–2019) for comparison of distribution of outbreak related documents in pre-MDGs/SDGs and MDGs/SDGs period. The study achieved the decadal comparison via non-parametric ANOVA test (Kruskal-Wallis H test) visualized as composite violin-boxplots. The study further modelled/predict future trend of authors' productivity or publication frequency in terms of Lotka's inverse square law [15].

### 2.2.3. Determination of the prevalence/incidence of cases, mortality, culprit Vibrio species, strains and biotypes

The study also performed content-review of 869 available abstracts for records of incidence of human cases, mortality, culprit *Vibrio* species, strains and biotypes. Decadal analysis as mentioned in the previous section was carried out in addition and visualized using pie graphs.

#### 2.2.4. Topical concerns in Vibrio outbreaks

The study also assessed topical concerns associated with *Vibrio* outbreaks via Co-Word analysis [16,17]. Co-Word analysis was performed by K-means clustering via metric multidimensional scaling (MDS) of 517 individuals described by 183 variables/keywords. Where necessary, inflectional words were regulated to their root form using Porter's stemming algorithm [18]. The study visualized trending topics in outbreak using dendrogram based on average Euclidean distance technique.

2.2.5. Assessment of concerted action on outbreak response and mitigation
The study considered concerted action or collaboration on Vibrio
outbreak response/mitigation in terms of joint effort from authors';
institutional and country/international point of views. Different matrix
(Documents × Authors, Documents × Countries, and
Documents × Institutions) was built from the retrieved bibliographic
data for corresponding joint effort or collaboration network. A

collaboration (joint effort) network has its nodes representing authors/institutions/countries and the corresponding links relationships/joint actions. Country collaboration network, authors' collaboration network, universities collaboration networks, keyword co-occurrence network, and co-occurrences network were built based on 92 countries, 3538 authors, 961 institutions, 1095 keywords, and 9935 items involved in the documents, respectively. All networks were normalized via the Jaccard's similarity index and graphed using Fruchterman force-directed algorithms.

#### 2.2.6. Software

All analysis was performed using an excel 2016 and Rstudio versions 3.4.4 & 3.6.0 [14,19] with ggpubr version 0.2 package [20] https://CRAN.R-project.org/package=ggpubr) and the bibliometrix R-package [16,20].

#### 3. Results and discussions

#### 3.1. Characteristics of Vibrio outbreak documents

A total of 901 Vibrio outbreak documents were identified during the study period (Table 1). The documents were primarily from 307 journal sources and altogether contained 1063 author's keywords and 1117 keywords plus. Average citations per the retrieved documents was 17.58. The articles were authored by 3544 authors with a total of 5255 author appearances. Summarily, 106 authors published single authored articles, 3438 authors published multi-authored articles (5.83 co-authors/documents), and 4.6 collaboration index. It is unfortunate that 4.7% (n = 42) of the documents were only news item, an indication that first-hand information on outbreaks are not so much treasured or available. It is also an indication that news on outbreaks are really documented or archived. While the reminders of the documents distributed as article (n = 656, 72.8%), proceedings article (n = 18,2.0%), editorial material (n = 48, 5.3%), letter (n = 53, 5.9%), meeting abstract (n = 66, 7.3%) and note (n = 18, 2.0%). Although, proceedings articles, meeting abstracts, editorial materials, letter and note could serve as primary source of outbreak information, in most cases, they are not peer-reviewed. Thus make them less reckon with among scientific communities. On the other-hand, meeting abstracts, editorial materials, letter and note had served as early notification channels in case of dengue virus [21], Ebola virus [22,23], John Cunningham virus [24], Mayaro virus [25], Middle East respiratory syndrome coronavirus [26], yellow fever virus [27], West Nile virus [28], and Zika virus [29]. Meanwhile articles normally contain detail information, they required longer time to be published and thus, articles

**Table 1**Characteristics of *Vibrio* outbreak documents.

Variable	Count/rate	Variable	Article (%)
Documents	901	Document Types	
Sources (Journals)	307	Article	656(72.8)
Keywords Plus (ID)	1085	Proceedings Article	18(2.0)
Author's Keywords (DE)	989	<b>Editorial Material</b>	48(5.3)
Period	1990-2019	Letter	53(5.9)
Average citations/documents	17.58	Meeting Abstract	66(7.3)
Authors	3538	News Item	42(4.7)
Author Appearances	5255	Note	18(2.0)
Authors of single-authored documents	118	Language	
Authors of multi-authored documents	3420	English	854(93.9)
Single-authored documents	146	French	542(2.8)
Documents per Author	0.255	German	4(0.4)
Authors per Document	3.93	Korean and Dutch	1 (0.1) each
Co-Authors per Documents	5.83	Portuguese and Russian	7(0.8) each
Collaboration Index	4.53	Spanish	10(1.1)

**Table 2**Topmost 10 productive authors from 1990 to 2019.

Rank	Authors	Articles (% of 901)	h_index	TC	ATC	Country
1	Nair GB	32(3.6)	20	1762	55.1	India
2	Ramamurthy T	24(2.7)	11	949	39.5	India
3	Tauxe RV	22(2.4)	16	835	38.0	USA
4	Luquero FJ	21(2.3)	10	325	15.5	France
5	Azman AS	18(2.0)	6	135	7.5	USA
5	Sack RB	18(2.0)	14	1087	60.4	USA
6	Bhattacharya SK	17(1.9)	11	863	50.8	India
6	Faruque SM	17(1.9)	14	1321	77.7	Bangladesh
6	Mintz ED	17(1.9)	13	678	39.9	USA
7	Sack DA	16(1.8)	11	608	38.0	Bangladesh

ATC: average total citatiom; TC: total citatiom.

are not good sources of outbreak immediacy or instantaneous actions and lack short time intervening agency. As for languages of *Vibrio* outbreaks dissemination, 93.9% were communicated/published in English, followed by 2.8% in French, and 1.1% in Spanish. Other languages include German (0.4%), Korean and Dutch (0.1% each), and Portuguese/Russian (0.8% each). Dissemination of outbreak information in native languages in endemic regions could provide a local content in attempt to communicate emergency of outbreak and halt further spread via campaign and preventive measure education.

Table 2 lists 10 top productive authors related to Vibrio outbreaks. These authors included Nair GB (32, 3.6), Ramamurthy T (24, 2.7), Tauxe RV (22, 2.4), Luquero FJ (21, 2.3), Azman AS (18, 2.0), Sack RB (18, 2.0), Bhattacharya SK (17, 1.9), Faruque SM (17, 1.9), Mintz ED (17, 1.9), and Sack DA (16, 1.8) and they were majorly affiliated with institutions from India (n = 3), USA (n = 4), France (n = 1) and Bangladesh (n = 2). The thrust and interest of these 10 top productive authors can be as an attempt geared toward providing solutions to the menace of the cholera Vibrio in their countries (e.g., India and Bangladesh) and/or collaborative effort to combat spread of outbreak in other countries (e.g., USA and France). Major reports from India and Bangladesh were reports of outbreak surveillance studies. French authors also reported food associated cholera cases after outbreaks. The authors' h-index ranged from 6 (Azman AS) to 20 (Nair GB), total citation from 135 (Azman AS) to 1762 (Nair GB), and average total citations from 7.5 (Azman AS) to 77.7 (Faruque SM). The domination of Nair GB both in terms of h-index and total citations is instructive of the author's productivity and jointly pointing to endemicity of Vibrio outbreaks in the author's country India. Faruque SM from Bangladesh had the highest average total citations (77.7) among the authors. This revealed that Faruque's work received more recognition in term of the number of citations.

The 10 topmost productive countries related to Vibrio outbreak research is listed in Table 3. The USA ranked first with a total number of 191 articles followed by India (n = 111), France (46), Bangladesh (n = 25), UK (n = 22), and Japan (n = 21). Others were China (n = 19), Brazil (n = 18), Canada (n = 17) and Switzerland (n = 16). The USA and India possessed higher frequency of production of 24.7% and 14.3% respectively; while others have <5.9%. Based on multicountry publication ratio, Switzerland ranked 1st with 100% multiple country publication ratio, followed by Bangladesh (80%), France (69.6), Japan (66.7%) and the least were India (16.2) and China (15.8%). The 100% publications from Switzerland as multiple country publication probably suggests that Vibrio outbreak might not be endemic in Switzerland and showed that the country has strong collaboration network or play supportive roles to other countries that experienced Vibrio epidemics. The China and India ranked low based on multi-country publication ratio among the countries due to their large population, and large number of institutions that probably encouraged intra-national collaborations compared to international ones. While the USA and India retained their 1st and 2nd position based on country

**Table 3**Topmost 10 productive countries.

s/n	Country	Articles (SC, MC)	Freq(%)	MCP_Ratio (%)	Country	TCs	AACs
1	USA	191 (96, 95)	24.6	49.7	USA	5962	31.21
2	India	111(93,18)	14.3	16.2	India	1606	14.47
3	France	46(14, 32)	5.9	69.6	Bangladesh	1137	45.48
4	Bangladesh	25(5, 20)	3.2	80	France	629	13.67
5	UK	22(12, 10)	2.8	45.5	Denmark	591	42.21
6	Japan	21(7, 14)	2.7	66.7	Netherlands	415	41.5
7	China	19(16, 3)	2.4	15.8	Taiwan	398	39.8
8	Brazil	18(12, 6)	2.3	33.3	Switzerland	395	24.69
9	Canada	17(10, 7)	2.2	41.2	Brazil	377	20.94
10	Switzerland	16(0, 16)	2.1	100	Japan	324	15.43

MC: Multiple Country; SC: Single Country; AACs: Average Article Citations.

total citations with 5962 and 1606 citations respectively, France lost her 3rd position to Bangladesh (1137). Countries such as Denmark, Netherlands and Taiwan made the 5th, 6th and 7th with a total citation of 591, 415 and 398 respectively. Also, Denmark, Netherlands and Taiwan possessed average article citation of 42.21, 41.5 and 39.8 to be ahead of other countries except Bangladesh with 45.48 average article citations. Hence, it is noteworthy that *Vibrio* outbreak publication from the 3 countries receive greater credit and attention in term of the total citations obtained. However, the drop off of UK, Canada and China from the 10 topmost positions based on total citation might be showing lack of recognition and quality coverage of their institutional production in *Vibrio* outbreak research.

Table 4 presents 10 topmost productive Journal sources that published Vibrio outbreak documents during the study period. Among these sources, American Journal of Tropical Medicine and Hygiene ranked 1st by publishing 42% of the outbreak documents, followed by Emerging Infectious Diseases (36%), Journal of Clinical Microbiology (27%), Epidemiology and Infection (26%). These journals have the reputation of publishing articles related to infectious diseases except Plos one that deals in publishing multidisciplinary research. The impact factor of these journals according to InCites Journal Citation Reports (2018) range from 1.251 (Indian Journal of Medical Research) to 7.185 (Emerging Infectious Diseases) with Lancet having exceptionally high impact factor of 59.102. the sources further attest to the importance of Vibrio outbreaks both at infectious diseases perspectives and a need for multidisciplinary responses/actions in combating its menace.

#### 3.2. Vibrio outbreak trend from 1990 to 2019

The trend of *Vibrio* outbreak documents approximately increased in 6th order quadratic relationship ( $R^2=0.7948$ ) from 1990 to 2019 with an annual growth rate of 3.21% and a mean value of 30.0  $\pm$  18.0 per year (Fig. 1a). This annual growth is an indicator of outbreak trend overtime and subsequent *Vibrio* outbreaks in the future. Also, the

**Table 4**Topmost 10 productive journal sources for *Vibrio* outbreak documents from 1990 to 2019.

Rank	Sources	Articles (%)	If (2018 <sup>a</sup> )
1	American Journal of Tropical Medicine and Hygiene	42	2.315
2	Emerging Infectious Diseases	36	7.185
3	Journal of Clinical Microbiology	27	4.959
4	Epidemiology and Infection	26	2.047
5	Indian Journal of Medical Research	25	1.251
5	International Journal of Infectious Diseases	25	3.538
6	Lancet	24	59.102
7	Journal of Infectious Diseases	18	5.045
7	Plos Neglected Tropical Diseases	18	4.487
8	Plos One	17	2.776

<sup>&</sup>lt;sup>a</sup> InCites Journal Citation Reports.

distribution of *Vibrio* outbreak document varied significantly on a decadal scale during the survey period (Kruskal-Wallis, p = 0.0058) (Fig. 1b). While there was no significant difference between article distribution in 1990–1999 and 2000–2009 (p = 0.31), distribution between the period 1990–1999 and 2010–2019/2000–2009 and 2010–2019 was significantly different (0.001  $\leq$  p  $\leq$  0.0028). Summarily, *Vibrio* outbreak article distribution had its 75th percentile (mean, maximum [year]) in 1990–1999, 2000–2009 and 2010–2019 as 22.5 (18.1, 28.0 [1994]), 23.75 (21.90, 34.00 [2009]) and 62.75 (50.1, 71.0 [2011]) respectively.

The observed increase in outbreak documents in the study period might denote more occurrence or incidence of Vibrio outbreaks despite decades of United Nations' programme for safe water supply and sanitation campaign (MDGs and first-five years of SDGs). Control of global cholera outbreak yet remains a menace as concerted efforts and diverse novel strategies are being employed by researchers and public health related non-governmental organizations for the achievement of MDGs/SDGs/WASH. From our bibliometric mapping of cholera outbreaks, it is observed that the level/trend of outbreak reports in the last decade (2010-2019) have increased in diverse endemic area of the world. For a period, greater than three decades, the non-governmental organization and research based strategies have been employed yet the situation remain a dilemma of unending result. Although, various steps employed in some outbreak situations have yielded short-lived results as depicted from the study, the succession on subsequent outbreak report in such area are quite alarming.

The annual growth rate was 3.21%. A decadal comparison of outbreak documents varied in distribution (Kruskal-Wallis, P=0.00077). In the composite violin and box plots, violin area shows the distribution including mild and extreme outliers. Central line in box plot represents median, and its edges the 25% and 75% percentiles. The p-values for comparison of the 3 decadal outbreak documents is showed on the lines above the bins.

Decadal human cases of infection documented in Vibrio outbreaks was 871119, 324323 and 6364070 persons in 1990-1999, 2000-2009, and 2010-2019 respectively (Fig. 2a). High number of cases in 2010-2019 which included the first-5 years of SDGs might connote more detail report of outbreaks compared to other periods as many nondocumentation of the number of people affected were noticed in the article abstracts in other periods. Also, it might connote increase in number of human affected during the late MDGs and the first 5 years of SDGs (2010-2019) periods in comparison to the pre-MDGs and the early MDGs periods (1990-1999, 2000-2009). This in part, can be linked to global warming. Some authors have showed increasing and positive correlation of cholera/Vibrio outbreaks with global warming [30,31]. Similarly, the investigation observed high mortality in Vibrio outbreaks during 1990-1999 (29080 deaths), and 2010-2019 (386606 deaths) compared to 2000-2009 (7705 deaths), (Kruskal-Wallis, p < 0.05) (Fig. 2b). This suggests that progress has been made in combatting mortality due to outbreaks as many intervention options are available than the previous decades. This occurrence may be

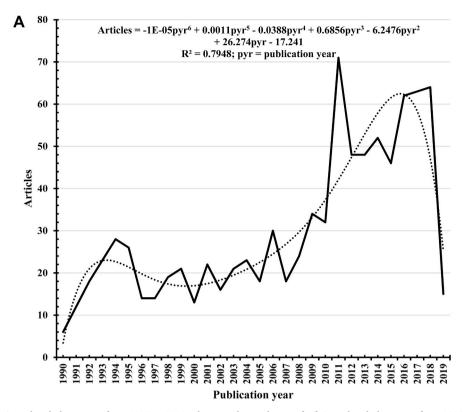


Fig. 1a. Yearly trend of *Vibrio* outbreak documents from 1990 to 2019. The annual growth rate of *Vibrio* outbreak document from 1990 to 2019 was 3.21% with a mean value of 30.0 ± 18.0 per year and a range: 6.0–71.0.

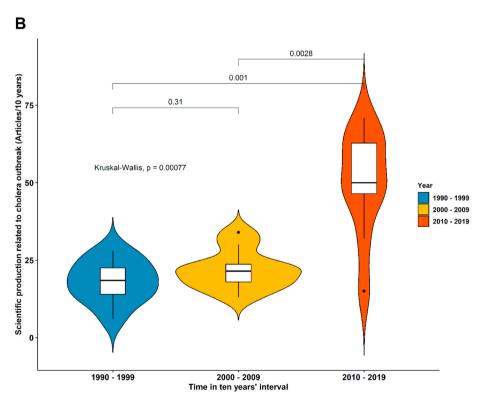


Fig. 1b. Scientific article production related to Vibrio outbreaks from 1990 to 2019.

attributable to non-evaluation, unreported/unpublished, limited investigation, or surveillance of cholera vibrio cases within the decadal boundaries. It could also be primarily linked to difference in the impact of meteorological events or environmental factors such as rainfall,

precipitation, drought, temperature and any other natural disaster in the compared periods. On the contrariwise, abstracts in most cases cannot provide comprehensive outbreak information. The underline factors responsible for high mortality during 1990–1999 and MDGs/

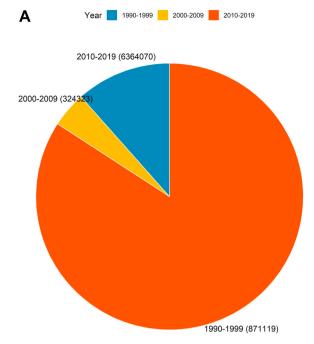


Fig. 2a. Pie graph comparing total decadal cases of human infection during *Vibrio* outbreaks from 1990 to 2019.

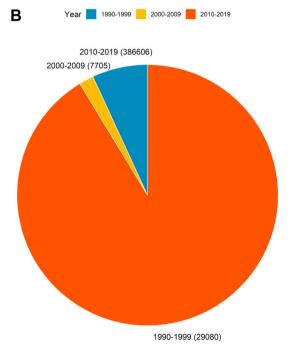


Fig. 2b. Pie graph comparing total decadal human death during *Vibrio* outbreaks from 1990 to 2019.

early SDGs year compared to other period is not clear. However, the mortality rate and case fatality reports from these recorded cases are reduced when a comparative rule is accessed between the first decade reports (1990–1999) and last decade reports based on volume of articles. The outbreak trend may probably continue to increase in SDGs era as indicated by annual growth rates and comparative decadal analysis (Fig. 1a and b).

Table 5a
Prevalence of *Vibrio* species, responsible for outbreaks from 1990 to 2019.

Species	Frequency(%
ND	6 (0.7)
V. alginolyticus	1(0.1)
V. alginolyticus and V. parahaemolyticus	3(0.3)
V. anguillarum	1(0.1)
V. campbellii	1(0.1)
V. cholerae	783(90.0)
V. cholerae and V. parahaemolyticus	1(0.1)
V. fluvialis and other enteric pathogens	3(0.3)
V. harveyi	1(0.1)
V. mimicus	4(0.5)
V. mimicus and V. cholerae	1(0.1)
V. neptunius	1(0.1)
V. parahaemolyticus	45(5.2)
V. Pelagius	1(0.1)
V. rotiferanius	1(0.1)
V. salmonicida	1(0.1)
V. vulnificus	4(0.5)
Vibrio	10(1.2)
Total	869(100)

Table 5b Prevalence of V cholerae and V parahaemolyticus Biotype and Serogroup responsible for outbreaks from 1990 to 2019.

Strain	Frequency(%)
Altered El Tor	1(0.1)
Atypical O1	1(0.1)
Inaba O1	2(0.2)
ND	643(74)
Non-endemic strain	2(0.2)
non-O1/non-O139 and O1 Ogawa	22(2.5)
O:K	1(0.1)
01	17(2)
O1 Ogawa	114(13.1)
01/0139	51(5.8)
O139 and O1 Ogawa	2(0.2)
0141	1(0.1)
O3:K59	1(0.1)
O3:K6	7(0.8)
O37 and O1	1(0.1)
O5:K15, O4:K8, O3:K29, O1:K56	1(0.1)
075	1(0.1)
WO7	1(0.1)
Total	869(100)

## 3.3. Infection cases, mortality, and prevalent Vibrio species, strains and biotypes in outbreak

Table 5 shows the prevalence of Vibrio species, serogroup and biotype responsible for outbreaks from 1990 to 2019. V. cholerae and V. parahaemolyticus were responsible for 783(90.0%) and 45(5.2%) outbreaks in the period respectively. Outbreaks jointly caused by divalent (two) strains include V. alginolyticus and V. parahaemolyticus (3; 0.3%), V. cholerae and V. parahaemolyticus (1; 0.1%), V. fluvialis and other enteric pathogens (3, 0.3%), V. mimicus and V. cholerae (1, 0.1%). Other reported strains in the outbreaks were V. alginolyticus (1, 0.1%), V. anguillarum (1, 0.1%), V. campbellii (1, 0.1%), V. harveyi (1, 0.1%), V. mimicus (4, 0.5%), V. neptunius (1, 0.1%), V. pelagius (1, 0.1%), V. rotiferanius (1, 0.1%), V. salmonicida (1, 0.1%) and V. vulnificus (4, 0.5%). High number of outbreaks due to V. cholerae and V. parahaemolyticus was reported which indicate a major public health concerns associated with the duo while the limited outbreaks caused by other divalent strains is indicative of emerging state and a need for broad spectrum Vibrio vaccines that could cater for outbreak caused by common and emerging strains. It is unknown whether, Vibrio serogroups are

Table 6
Most Relevant Keywords accessed during study.

s/n	Author Keywords	Articles	Keywords-Plus	Articles
1	CHOLERA	166	VIBRIO CHOLERAE	103
2	VIBRIO CHOLERAE	68	STRAINS	76
3	OUTBREAK	34	BANGLADESH	75
4	EPIDEMIC	22	TRANSMISSION	71
5	EPIDEMIOLOGY	22	EMERGENCE	47
6	EPIDEMICS	18	AFRICA	44
7	PASTEURELLA	16	DYNAMICS	43
	MULTOCIDA			
8	VIBRIO	16	01	43
	PARAHAEMOLYTICUS			
9	DISEASE OUTBREAKS	13	EPIDEMIC	42
10	AVIAN CHOLERA	11	INDIA	37
11	INDIA	11	OUTBREAK	37
12	VIRULENCE	11	HAITI	36
13	CHOLERA OUTBREAK	10	IDENTIFICATION	33
14	HAITI	10	TOXIN	31
15	GLOBAL STABILITY	8	PCR	26
16	VIBRIO CHOLERAE O1	8	BIOTYPE	24
17	DIARRHOEA	7	POLYMERASE CHAIN	24
			REACTION	
18	DIARRHOEA	7	WATER	24
19	FOWL CHOLERA	7	GENE	23
20	SANITATION	7	DISEASE	22
21	V CHOLERAE	7	EL TOR	21
22	CHOLERA EPIDEMIC	6	INFECTIOUS DISEASE	21
23	GASTROENTERITIS	6	EPIDEMIOLOGY	20
24	HYGIENE	6	UNITED STATES	19
25	MORTALITY	6	CALCUTTA	18

Conceptual themes associated with *Vibrio cholerae* outbreak studies. Beta = 2.45, C = 0.52, R2 = 0.96.

p.value = 0.10 (Kolmogorov-Smirnoff goodness-of-fit of 0.96 (P = 0.10, two-sample *t*-test).).

implicated in cross-infections as well as confer cross immunity against multiple biotypes and serogroups, an area that may be a significant thrust for future research. About 643(74%) of the articles failed to provide information on *Vibrio* serotypes or biotypes responsible for outbreaks, some yet provided were associated with avian cholera. However, the common serotypes/biotypes encountered in most outbreaks spanned from non-O1/non-O139 and O1 Ogawa (22, 2.5%), O1 (17, 2%), O1 Ogawa (114, 13.1%), O1/O139 (51, 5.8%) to O3:K6 (7, 0.8%) among others. A multivalent vaccine composed of non-O1/non-O139, O1 Ogawa and O1/O139 might be ideal and necessary for outbreak prophylactic measures in a cholera endemic region (see Table 6).

#### 3.4. Conceptual framework and trending topics related to Vibrio outbreaks

MCA performed on 300 individuals described by 50 variables identified four distinct conceptual frameworks (CF) (Fig. 3). The first framework (purple) includes terms related to characterisation of *Vibrio* such as genetic diversity, pathogenicity island, pandemic strains, ctx-phi, evolution, sequences, serotype inaba/Ogawa or O1 strain. The methodology-related concepts in the purple CF were molecular analysis and field gel electrophoresis. Geographical pointers found in the purple CF were western-hemisphere. The second framework (green CF) include interventions, strategies, and human mobility during outbreak; systems, diffusion, stability, dynamics, seasonality and hyperinfectivity nature of *Vibrio* outbreak. Other concepts involve basic reproduction number and mathematical models. The geographic pointer in green CF was Zimbabwe.

The CF (blue) consisted in terms associated with *Vibrio vulnificus*, hemolysin, gastroenteritis, infections, trh trait, clone, O3-k6 strain, *Pasteurella multocida*, avian/fowl cholera, Geographical-related concepts found were coast (gulf-coast, coast of Odisha, India; coastal environments throughout the world), California, USA, and Japan. While, climate depicting concepts were El Nino and temperature, transmission

vehicle associated with the blue CF include water, oysters, turkeys, shellfish and poultry. Methodology related term was PCR.

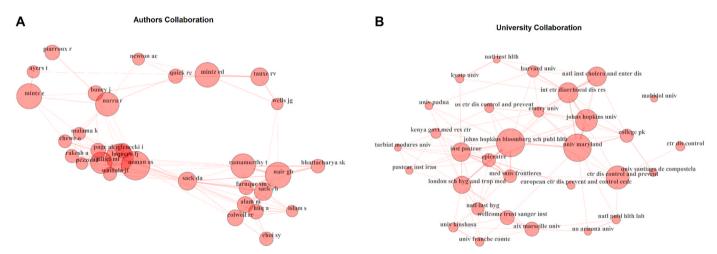
The fourth CF (red) has the largest topical coverage and appeared to present concepts that attracted the global community interests about Vibrio outbreaks. Geographical-based concept in the red CF include Latin America, Bangladesh, Calcutta, developing-countries, India, eastern India, Guinea-Bissau, Haiti, Mozambique, Japan, Kenya, Kolkata, Malawi, Orissa, Peru, rural Bangladesh, South-Africa, Thailand, West-Bengal, Peru, Malawi, Kenya, Thailand, Haiti, Guinea-Bissau, Bengal west, Calcutta, united-states, Kolkata, and Mozambique. Population specific concepts in the CF varied from children, hospitalized-patients, community to slums. Outbreak response concepts also varied from epidemic, epidemic cholera, endemic cholera, surveillance, variable-number, vaccination, vaccines, efficacy, field trial, field-evaluation, strategies, to validation. Methodology-related framework includes identification, polymerase-chain-reaction, DNA, molecular characterization, comparative genomics, molecular epidemiology. sxt, ctx prophage, toxin, regulon, phage, plasmid, thermostable direct hemolysin, colonization factor, virulence, toxigenic Vibrio-cholerae, pathogen, and pathogenesis were pathogenicity identifier concepts found in the red CF. Antibiotic-resistance, resistance, and integrons were concept-marker for the problem of antimicrobial resistance in Vibrio outbreaks. The agency of risk-factors/vehicle for transmission such as immunity, antibodies, drinking-water, environment, water, waters, sanitation, spread, and storage, in outbreak became evident in the CF. the role of rainfall, natural disasters and global climate in Vibrio outbreak had imprint in the CF. Vibrio strain-defining terms in the CF include El-Tor strains, non-O1, O1 strains, O139 bengal, parahaemolyticus, Vibriocholerae, inaba, and Vibrio-cholerae-O1, and O139. Outbreak consequences had it footprints described as burden, diarrhoea, emergence, mortality, impact, infectious-diseases. Health concepts varied from public health, health education, health behaviour, health service, and health policy in Vibrio outbreaks.

#### 3.5. Cooperative action and response in Vibrio outbreak mitigation

Fig. 4a-c shows conjunctive responses and actions in Vibrio outbreaks mitigations. While the network size, density, transitivity, diameter, degree centralization, and average path length of various authors' joint efforts/cooperative response (ACCN) was 3538, 0.003, 0.574, 13, 0.04 and 4.587, respectively (Fig. 4a), that of University/ institutional joint efforts (UCN) was 961, 0.004, 0.348, 12, 0.059 and 4.333 respectively (Fig. 4b). In ACCN, 5 major academic collaboration clusters can be seen. Most clusters and subclusters coordination centred on Sack DA, Nair R, Narra R, Ramamurthy T, Malama K and Azman AZ (Fig. 4a). Central players in UCN include John Hopkins Bloomberg School of Public Health, University of Maryland, Centre for Disease Control and Prevention, National Institute for Cholera and Enteric Diseases, International Institute for Diarrheal Diseases and Research, London School of Hygiene and Tropical Diseases and Pasteur Institutes. It is evident to note that many of the institutions are saddled with responsibility related to infectious diseases mitigation and research. This might influence their central roles in Vibrio outbreak as it is known as one of the deadliest infectious diseases. Collaborative effort in term of country's joint cooperative responses (CCN) has it statistics as 92, 0.092, 0.393, 5, 0.546 and 2.204 for network size, density, transitivity, diameter, degree centralization, and average path length respectively (Fig. 4c). The USA, United Kingdom, France and Switzerland ranked 1st, 2nd, 3rd and 4th in term collaboration initiatives. The centrality of these countries in their various network subclusters may be due to resources advantages in term of funding/aids and vaccines provision to partner countries; personnel and equipment sharing. In most cases, vaccine technology and point-of-surveillance kits/resources are not available in their partner countries (Fig. 4c).



Fig. 3. Trending topics and conceptual frameworks in *Vibrio* outbreaks. The colour of the polygons depicts different conceptual topical framework. The closer the points to one another, the strength of the correlation between items.



**Fig. 4a.** Topmost 30 author joint collaborative response and action network toward *Vibrio* outbreak mitigations. The size of the node indicates the individual university/institution's strength of collaboration or mitigation effort initiatives. Connecting lines shows bilateral collaborative relationships between institutions. Network statistic: Size: 3538; density: 0.003; transitivity: 0.574; diameter: 13; degree centralization: 0.04 and average path length: 0.587.

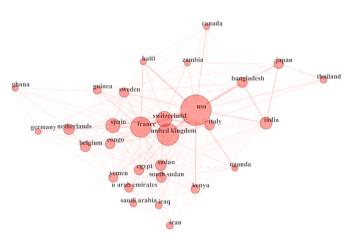
#### 4. Conclusion

Following the observation as mentioned in various section, tables and figures of the study, it can be deduced that the pre-MDG/SDG has recorded an uncertain non-report of cholera outbreaks which are associated with various strains of Vibrio, with indicative prevalence

**Fig. 4b.** Topmost 30 university/institutional joint collaborative response and action network toward *Vibrio* outbreak mitigations. The size of the node indicates the individual university/institution's strength of collaboration or mitigation effort initiatives. Connecting lines shows bilateral collaborative relationships between institutions. Network statistic: Size: 961; density: 0.004; transitivity: 0.34; diameter: 12; degree centralization: 0.059 and average path length: 4.333.

reports traced to the *V. parahaemolyticus* and *V. cholerae*. However, the MDG/SDG which has shown high research based intervention, collaborative approach, control strategies and a public interest studies continues to show increased as well as undulating case report of affected people with yet high death rate and highest percentage mortality





**Fig. 4c.** Topmost 30 country joint collaborative response and action network toward *Vibrio* outbreak mitigations. The size of the node indicates the individual country's strength of collaboration or mitigation effort initiatives. Connecting lines shows bilateral collaborative relationships between countries. Network statistic: Size: 92; density: 0.092; transitivity: 0.393; diameter: 5; degree centralization: 0.546 and average path length: 2.204.

which are associated with *V. parahaemolyticus* and *V. cholerae* as indicated in Fig. 5 and Table 8. Careful and astute approaches are suggestive in studies associated with cholera to enhance future case judgement and encourage appropriateness in research tested control and/or mitigation strategies in the MDG/SDG era. (see Table 7)

#### Declaration of competing interest

No conflicting interest was declared.

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Table 7
Main statistics about the network.

Statistics	CCN	ACCN	UCN	KCocN	CocN
Size	92	3538	961	1095	9935
Density	0.092	0.003	0.004	0.015	0.005

 Table 8

 Annual cases of affected Population and percentage Mortality of cholera.

Year	NO. Of Death	No. of people affect (cases)	%mortality
2019	7745	1162562	0.7
2018	2990	499447	0.6
2017	5654	1227391	0.5
2016	2420	132121	1.8
2015	1304	172454	0.8
2014	2231	190549	1.17
2013	2102	129064	1.63
2012	3034	245393	1.2
2011	7816	589854	1.3
2009	4946	221226	2.24
2008	5143	190130	2.7
2004	2345	101383	2.3
2003	1894	111575	1.74
2002	4564	142311	3.95
2001	2728	184311	1.48
2000	4908	137071	3.6
1999	DF	> 265000	DF
1998	DF	>290000	DF
1997	DF	>170000	DF
1996	DF	>160000	DF
1995	DF	>210000	DF
1994	DF	>370000	DF
1993	5572	>360000	0.9
1992	DF	>470000	DF
1991	23395	>585000	28.5
1990	DF	>65000	DF

DF: documented not found (http://www.who.int/disease-outbreaknews/index. html) [32].

Death cases.

Total cases.

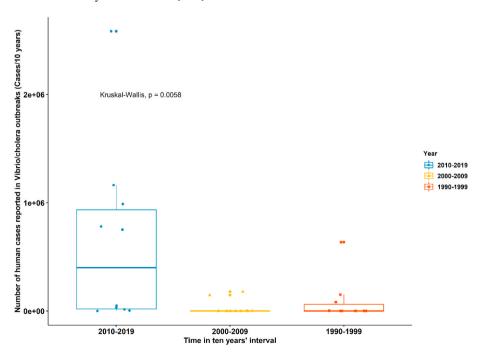


Fig. 5. Kruskal-Wallis representation of decadal cholera cases reports within the study period where; Blue (2010–2019), Yellow (2000–2009), Red (1990–1999) shows 1e+06, less than 1e+01 and 0e+00 respectively.

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