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Review article

Modern knowledge-scape possess petite influence on the factual persistence of resistance determinants (ARGs/MGEs): A map and assessment of discharged wastewater and water bodies

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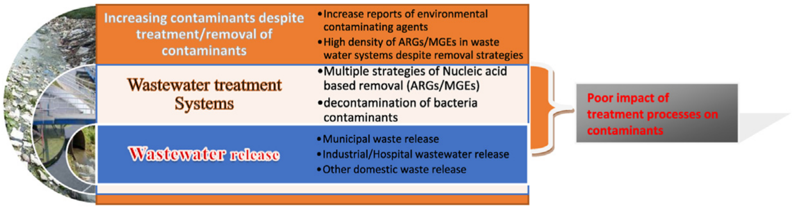
GRAPHICAL ABSTRACT



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ABSTRACT

Antibiotic resistance genes (ARGs) and Mobile genetic elements (MGEs) are major global emerging pollutants of the environment and water nexus which various investigators of related studies have reported. Observing ARGs and MGEs in water bodies, wastewater treatment systems, and estuaries is indicative of relevant risk, resistant bacteria/ARGs spread or potential health concern and may result environmental pathogen bloom if appropriate research-based strategies are not implemented to remove these lethal genetic materials. Despite reports and knowledge-based strategies for removal, the challenge yet persists. This study aims to appraise the impact/contribution of related studies and emphasize the necessity for applying combined research-based/practitioners approach in addressing the expanding challenge of ARGs/MGEs in wastewater/waterbodies. The study describes a bibliometric assessment of antibiotic resistance determinants annual scientific publications on the Web of Science, an annual growth rate of related articles, top articles per citations with search topics and content-review analysis to evaluate the methods of removal of ARGs/MGEs. A total of 1301 articles of wastewater treatment systems were retrieved with date range of 1997–2019. A description of the study Annual Growth Rate of 37.82% at R^2 of 0.7863 was observed with an increasing article publication and a decreasing total citation rate indicating persistent reports of dispersion on ARGs/MGEs studies in the water bodies and environment. Although there abound extensive studies and reports of ARGs and MGEs in water nexus and wastewater release with research based removal strategies, the impact of such reports have not been fully actualized amongst wastewater system practitioners. A lucid drive towards implementing ARGs/MGEs removal strategies from the environment by applying affirmed research-based methods are suggestive.

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1. Introduction

Over the years, there have been updated reports of antibiotic resistance genes (ARGs), antibiotic resistant bacteria (ARB) and mobile genetic elements (MGEs) in wastewater release (effluents), water environments and wastewater treatment systems. Some of these studies revealed that ARGs in the water bodies are associated with the wide use of antibiotics for human/animal health and food preservative, which are released into the environment unchanged (Kumar et al., 2020a,b; Igere et al., 2020b; Kemper, 2008; Rodriguez et al., 2006; Kim et al., 2005; Iversen et al., 2004). On the other hand, MGEs are myriad of mobile genetic materials that fuels adaptive/persistence of living organisms and are implicated in sharing/transfer of genetic elements (inter and intra). It's members may include plasmids, genomic islands (GIs), phages or bacteriophages, insertion sequences (ISs), integrative and conjugative elements (ICEs), transposons (Tns), miniature inverted repeat transposable elements (MITEs) and integrase or integrons (Igere et al., 2021, 2022a, 2022b, 2022c; Onohuean et al., 2022c; Gogarten et al., 2009). Although their origin seems nonspecific/undetermined, it is traceable to partial broken pieces of genetic materials from antibiotic treated cells which found their way (release) into water run-off or water nexus (Igere et al., 2022a, 2021; Onohuean et al., 2022a; Gogarten et al., 2009; Zhang et al., 2009). Other ARGs and MGEs have also been reported in groundwater and domestic water sources of unidentified origin (Kumar et al., 2019; Wargin et al., 2007; Batt et al., 2006). Increase in industrialization, technological advancement, urban/population growth and development are the primary drivers of such sizeable transformations of water bodies which results descent of water quality and/or poor environmental wellness. Activities in advancing societies and built-environments {including the release of high composition of industrial chemicals (Nitrates, phosphates, chloride, ammonium, with other anions/cations and other transition elements)}, hospital waste release, domestic and household waste release as well as municipal release have also contributed to the poor state of water (Kumar et al., 2020a,b; Igere et al., 2020a). The presences of these agents (ARGs/MGEs) in water bodies and its potential impact on the environment have aroused concern as its global impact continues to ascend geometrically.

Diverse knowledge-based scape and research affirmed strategies have been reported by investigators and researchers with other strategies yet in the pipeline in the hope of giving a lasting solution to the problem of ARGs/MGEs in water bodies (Kumar et al., 2020a,b; Subirats et al., 2019; Jumat et al., 2018; Hu et al., 2018; Wen et al., 2018; Lu et al., 2018; Zhu et al., 2018; Kong et al., 2014). Some of those reported knowledge-scape were application of Ultraviolet (UV) and Ozone; application of aerated lagoon (AL) and biological nutrient removal (BNR) system; use of fabricated photo-catalytic reactive membrane (polyvinylidene fluoride ultrafiltration membrane) with titanium oxide nanoparticles; application of *Galdieria sulphuraria* which encourages the removal of ARG/MGE in algal-based wastewater treatment plant; use of powdered activated carbon; ultraviolet, chlorination, and ozone; granular activated carbon filtration (GACF); Fenton reaction in addition to UV irradiation; photocatalytic oxidation; Anaerobic membrane bioreactors (AnMBRs); Laboratory-scale electrochemical (EC); Ozonation, chlorination, chromatography-filtration with diethylaminoethyl-cellulose-monolithic column (C-FDECMC); Fe(II)-activated persulfate oxidation; modified HPC; combined coagulation-dissolved air flotation (DAF); Ultrasonic coupled bioleaching,UV-C/H_2O_2 and Sunlight/H_2O_2; Mobbing Bed Biofilm Reactor (MBBR); wastewater microbiomes fueling cells (WMFCs); newer innovative infrastructural systems (NIIS) etc, as all techniques revealed significant removal rate of ARGs/MGEs in wastewater treatment plants (Ghernaout and Elboughdiri, 2020; Ghernaout and Ibn-Elkhattab, 2020; Krzeminski and Popowska, 2020; Lou et al., 2020; Li et al., 2020; Wei et al., 2020; Calderón-Franco et al., 2020; Qiu et al., 2020; Asadi-Ghalhari et al., 2020; Choi et al., 2020; Huang et al., 2020; Igere et al., 2020; Orimolade et al., 2020; Rizzo et al., 2019; Beheshti et al., 2019; Liu et al., 2019; Ravasi et al., 2019; Sun et al., 2019; Ren et al., 2018; Cheng et al., 2020; Ravasi et al., 2019; Jäger et al., 2018; Mane et al., 2018; McConnell et al., 2018; Zheng et al., 2017; van der Kooij et al., 2015; Chen and Zhang, 2013a; Laht et al., 2014 Clauwaert et al., 2007).

Despite the research based published reports, the environment yet continues to show emerging contaminants of public health concern in published studies, some of which are associated with ARGs and/or MGEs both in wastewater release and water nexus. The possible reason for such continuous reports still remain unclear, although current publications reveals ARGs/MGEs in the water environments. It is to this end, this study determines a cosmopolitan map and research assessment of ARGs/MGEs in water nexus and wastewater release to appraise the application of knowledge-scale removal strategies of ARGs/MGEs. It also emphasized the necessity to expend ARGs/MGEs removal research reports and/or communicate related reports to an applicable public use.

2. Materials and method

The various retrieved documents were articles, book chapters, data paper, proceedings, meeting abstracts, corrections, editorial materials, reviews, proceeding papers, and reviewed book chapters, which were searched by topic from Web of Science (WoS) core collection database. The reported and published studies on ARGs and MGEs in water bodies and wastewater treatment systems were assessed and filtered from 1997 to 2019 from Web of Science (WoS), following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: (PRISMA) (Onohuean et al., 2022c; Moher et al., 2009). This study adopted a topic-specific code or algorithm with the Boolean "(Antibiotic Resistance Genes* AND wastewater$) OR (Bacteria Antibiotic Resitsance* AND wastewater$) OR (Mobile genetic elements* AND wastewater$) OR (Mobile genetic elements* AND Effluents$))" to retrieve all available reports on ARGs/MGEs and wastewater after due consultation by 'IBE and OH'. Accessed documents are Indexed in the following: SCI-EXPANDED, SSCI, A&HCI, CPCI–S, CPCI-SSH, BKCI–S, BKCI-SSH, ESCI, CCR-EXPANDED, IC and retrieved at 10:20 pm on 7-18-2020 as previously applied by other related investigators, Aleixandre and his colleagues (Onohuean et al., 2022b; Aleixandre et al., 2015). The adoption of WoS core database is informed by its universality and applicability for this study. Identified documents which conform to the inclusion criteria were downloaded in the PlainTeX file format while documents published in other forms and non-conforming documents were excluded.

2.1. Inclusion criteria

Articles/publications included in this study were reports which focus on ARGs/MGEs in water environment and wastewater systems. In addition, such reports must provide information on ARGs, MGEs, wastewater systems, study countries, methods of resistance determinants removal and assessment from the environments and their potential implications as documented by diverse investigators. Other non-conforming documents to the stated conditions above were excluded.

2.2. Data analysis

Before the analysis of collated data, the non-complying data and incomplete data from related studies (wastewater treatment and removal of ARGs/MGEs), applied research-based patented documents for ARGs/MGEs removal were excluded since some of such data were incomplete.

2.3. Considered analysis of data

Descriptive chrematistics was used in analyzing the retrieved information while the results were presented in tables and percentages. The frameworks and collaborative networks were presented in viewer charts from RStudio v.3.5.1 software and analyzed using the bibliometric R-package plugin. We adopted the codes and commands for bibliometric analysis from https://www.bibliometrix.org to evaluate bibliometric indices with specific attributes including; annual scientific production, annual growth rate, most productive authors, top articles per citations, corresponding authors countries, total citations per country, most relevant sources, collaboration networks, most cited articles, keyword co-occurrence, authors coupling among others as applied previously by Aleixandre and group (Aleixandre et al., 2015).

2.4. Data analytics

Primarily published documents on ARGs and MGEs from water nexus included in the study were retrieved, normalized in batches onto the PlainTeX file (which contains 500 documents each) and combined to make a single uploadable file. Pre-analytical activity include spelling verification, removal of duplicates, percentage of reported studies, normalized data to describe the trend of articles during the period, minimizing/removing error and synonym. Data from the R-analysis were exported to excel and tables were organized to authors' desire. The evolution of research advancement on the subject was plotted in an excel sheet while the bibliometric collaboration networks were computed and visualized exploiting the bipartite networks tools (https://cran.r-project.org/web/packages/bibliometrix/vignettes/bibliometrix-vignette.html).

2.5. Determination of ARGs/MGEs and research-based removal methods in water nexus

The study also performed content-review of 93 available abstracts on water sources, method of ARGs/MGEs assessment, types of ARGs and MGEs observed, country of study and methods of removal of ARGs/MGEs applied or tested which were presented using tables.

2.6. Results/discussions

Figure 1 above shows the PRISMA schematic flow Chart of both included and excluded documents employed. The descriptive chrematistics of published articles and extracted documents are presented in Figure 1 and Table 1. The retrieved documents by investigators ("IBE-OH") were 1301, with 268 sourced books and journals, 2423 authors keywords (DE) and keyword plus (ID) each. An average citation per document was 32.33 amongst 4335 authors, 7552 authors' preferences, 15 single authored documents, 4320 multiple authored documents, while collaborative index of authors and articles was 3.36. Average retrieved document per author was 0.3, the average author per document was found as 3.33, while the average number of co-authored documents was 3.36. Amongst the 1301 documents retrieved, one thousand one hundred

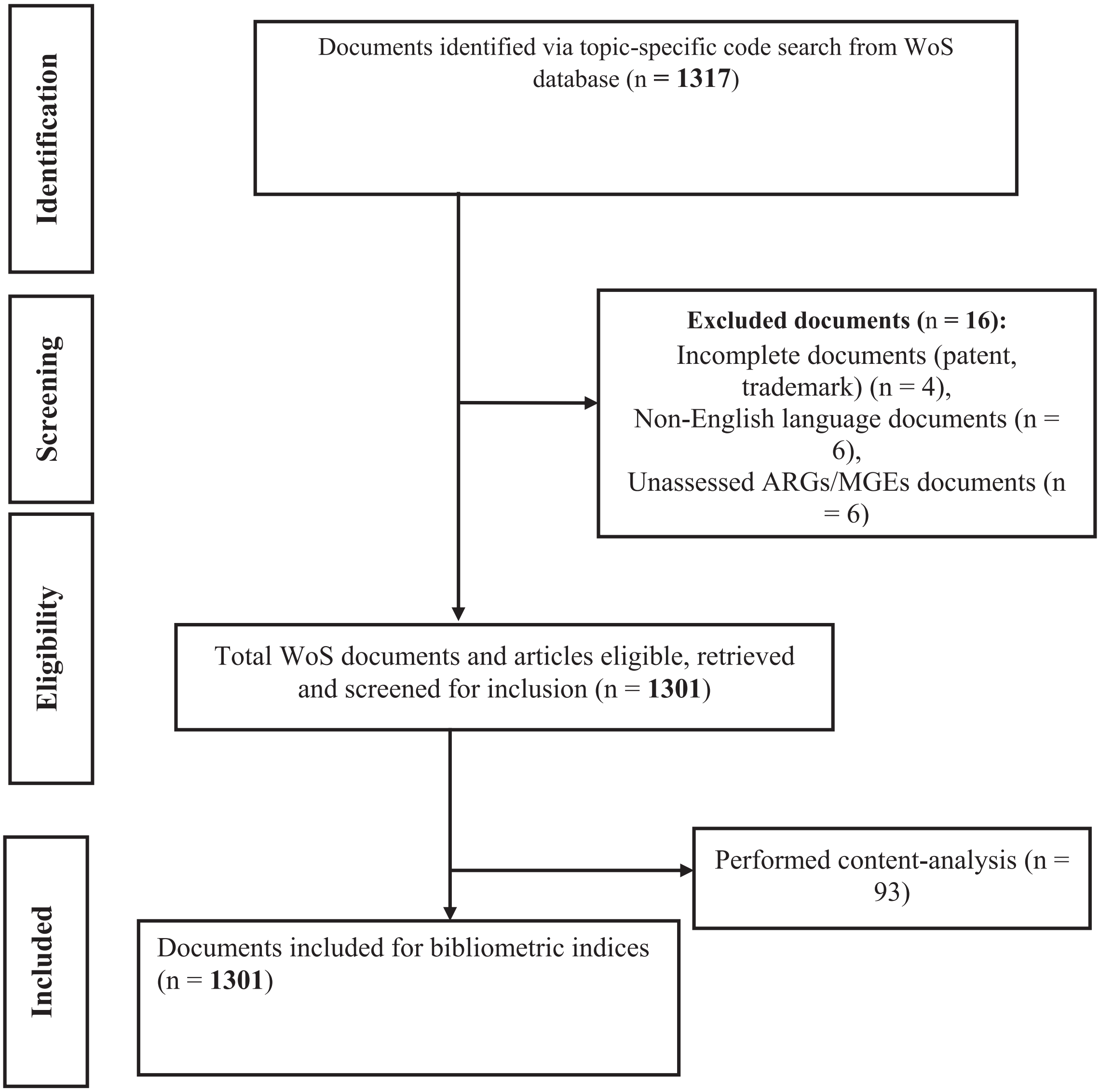

Figure 1. Schematic flow chart of steps in identifying and screening ARGs/MGEs documents within the wastewater systems and water bodies.

Table 1. Descriptive chrematistics of extracted documents.

Description	Results
Documents	1301
Sources (Journals, Books, etc.)	268
Keywords Plus (ID)	2423
Author's Keywords (DE)	2423
Period	1997–2019
Average citations per documents	32.33
Authors	4335
Author Appearances	7552
Authors of single-authored documents	15
Authors of multi-authored documents	4320
Single-authored documents	15
Documents per Author	0.3
Authors per Document	3.33
Co-Authors per Documents	5.8
Collaboration Index	3.36
Document types	
Article	1130
Article, Book Chapter	7
Article, Data Paper	3
Article, Proceedings Paper	19
Correction	3
Editorial Material	3
Meeting Abstract	10
Proceedings Paper	12
Review	112
Review, Book Chapter	2

and thirty of them were articles, 7 of them were book chapter, 3 were published data papers, 19 were conference proceedings, 3 were editorial published documents while 112 of them were reviewed manuscripts (Table 1). The various retrieved documents were indexed in high-profile public scientific domain as listed in section 2 above. Although studies on ARGs/MGEs and the water nexus have been documented in relevant public domains (with 86.9% of them as articles and more-than 8.6% of these articles been reviewed by experts), we could not retrieve any information on documented patent, trademark or trade secret or industrially adopted methods from these reports. In addition, there is yet a growing report of the occurrence and prevalence of ARGs/MGEs in wastewater treatment systems or water nexus. This is reflected in Figure 2 below as there is an inverse proportionality in the annual growth rate reports and the annual mean total citation. Whereas there was an observed undulating and decreasing mean total citation per article, there were increasing numbers of published articles reporting the incidence and prevalence of the ARGs/MGEs in both wastewater treatment systems and water environments.

The decreasing average total citation and the total citation which is relatively increasing are possible pointer to the repeated reporting of studies on ARGs/MGEs with no follow-up report of application and implementation of research recommendation after a laboratory-scale assessment. Also, as could be observed in Figure 2, the research and advancements so far (from 1997 to date, on published/reported articles or studies on ARGs/MGEs in wastewater systems per year), had an annual growth rate of 37,82% at R^2 of 0.7863. Both the articles growth rate and the numbers of articles published between 2009 and 2019 have showed a consistent increase with the notable increase between 2017 and 2019. The reports may continue to increase as seen in the trend over the past years if no appropriate action on intervention is implemented quickly. Considering another view point, the high proportion of published articles observed in the study may also be a pointer to the adequacy of the scientific communities and interest in the study. As shown in the analyzed reports in Figure 2, there was an observed zero documents/articles published between 1998 and 2001, implying that there was a low research interest rate on the subject. The sudden rise in reports and publication from 2008 (12) to 2019 (322) is attributable to increased research interest, environmental activities including; increased industrialization and increased waste release, increased domestic waste due to population increase, inappropriate and/or poor therapeutic application and possible indiscriminate release of unwholesome waste/contaminants. Suffix to say that one major contributor to ARGs/MGEs spread in the environment is the release of unwholesome waste impacting environmental wellness (Igere et al., 2020a) and the need to remove such agents is imminent. However, the observation in this study has showed that reports have not lived up to expectation as regards multinational participation/collaboration with specific stakeholders on implementation of findings on large scale to control the prevalence of this particular concern. Perhaps, there is a problem with the media of communicating research findings and/or advancement with the public, stakeholders and the governments or there is a gap that needs to be bridged between researchers' reports, publication and relevant stakeholders' participation. Although the language of communication was not assessed, the various articles included in the study were published in English, a general and acceptable medium for communicating such research-tested approach for needed advancement. The diversity of the scientific discipline may also be slow effectors' on the participation/collaboration of governmental organization and other multinationals. The heterogeneity of diverse environmental systems, geographical as well as the socio-economic status may also contribute to the aforementioned concerns. In addition, one may propose that the communication via published documents is ineffective to reveal specific knowledge-scape and research based or tested approach of contaminants/pollutants removal to the public and respective stakeholders (Igere and Ekundayo, 2020).

2.7. Top 10 authors productivity within the designed period (1990–2019)

Most of the authors involved in ARGs/MGEs and water nexus studies were ranked based on their total published articles, total citations and h_index as shown in Table 2. The top 10 authors reporting studies on ARGs/MGEs are: Zhang Y (n = 48, 3.69%), Manaia CM (n = 38, 2.92%), Pruden A (n = 29, 2.23%), Chen H (n = 28, 2.15%), Zhang T (n = 27, 2.08%), Li X (n = 25, 1.92%), Liu Y (n = 23, 1.77%), Schwartz T (n = 23, 1.77%), Wang Y (n = 23, 1.77%), Yang M (n = 23, 1.77%), all originating decreasingly in ranking order from China, and other regions. The authors h_index range from 21 to 9 with total citation (TC) ranging from 321 to 1321. The author with the least TC and h_index ranked the sixth position amongst the numbers of articles published within the study period (Table 2). A notable deduction from the table on the top 10 authors is that, there is an observed continuous reporting of ARGs and MGEs in water bodies revealing the scientific research interest of these researchers. Whereas the continuous reporting indicates objectiveness, pro-activeness and productivity of researchers whose interest and related studies birthed the various report.

2.8. Top 10 countries with frequency of relevant articles citations

The various countries publication frequency has been used as a basis for defining productivity in diverse research area. Table 3 reveals the top 10 countries productivity on studies of ARGs/MGEs and water environments within the study period (1997–2019). China ranked the highest with 389 (29.90%) total number of articles which was followed by the United States of America (USA) with 197 (15.14%) total number of articles while Germany ranked the third position with 54 (4.15%) total numbers of articles. These three countries also retained their rank order/position as regards the total citation (TC: 10089, 8359, 3915), multiple citation publication (MCP: 79, 40, 18), and single citation publication (SCP: 310, 157, 36). A high average article citation (AAC) was observed in Cyprus, Germany and Italy in a decreasing order (AAC: 151.11, 72.5, 67.17). These observations affirms that although various countries

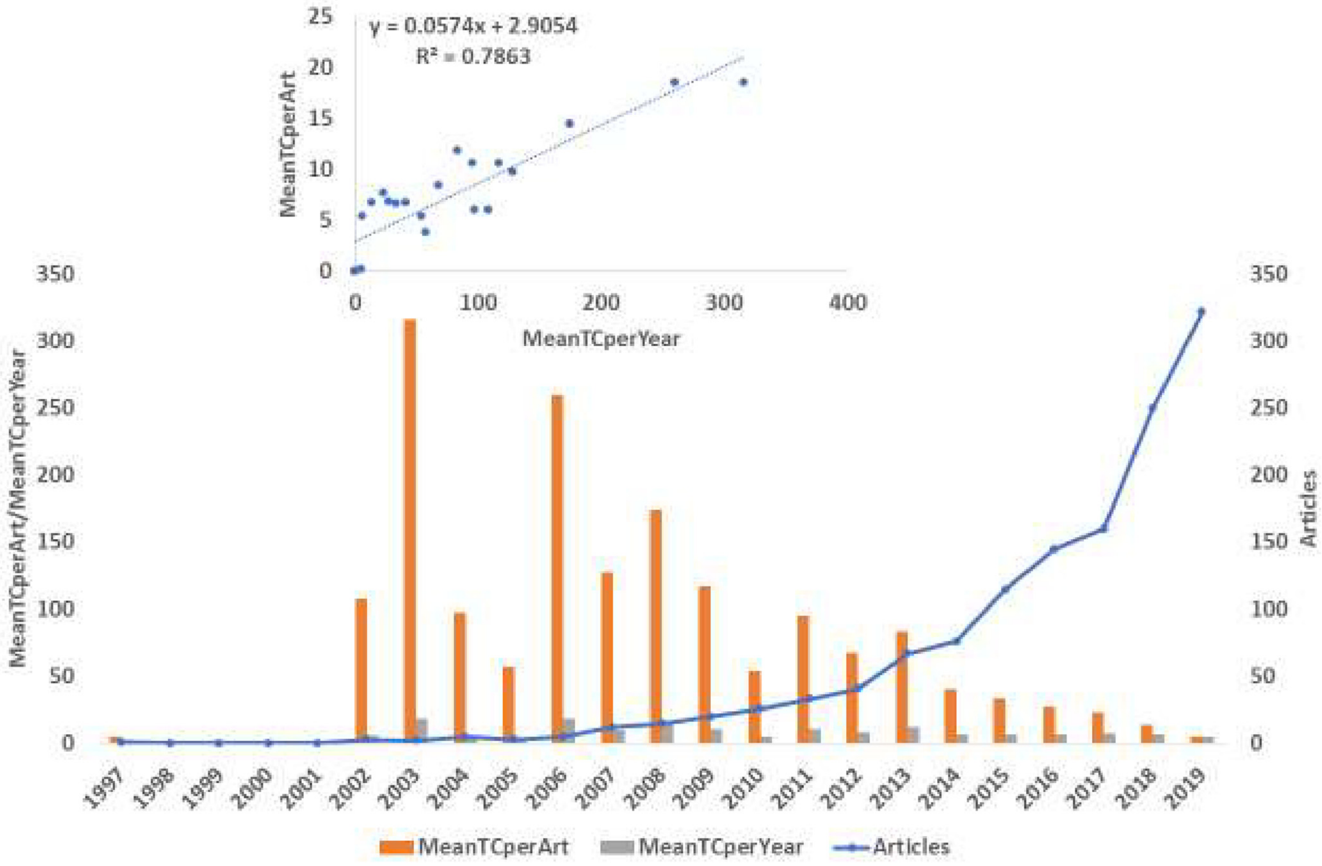

Figure 2. Evolution of research and advancement of articles on ARGs/MGEs per year. TC = Total citation; Annual Growth Rate: 37.82%.

Table 2. Top 10 productive authors from 1997 to 2019.

Rank	Authors	nA (% of 1,301)	h_index	TC	ATC
1	Zhang Yu	48 (3.69)	20	1321	27.52
2	Manaia Celia Maria	38 (2.92)	21	2464	64.84
3	Pruden Amy	29 (2.23)	16	2295	79.14
4	Chen Hong	28 (2.15)	17	1174	41.93
5	Zhang Tong	27 (2.08)	15	1279	47.37
6	Li Xiqing	25 (1.92)	9	321	12.84
7	Liu Yu-hong	23 (1.77)	10	376	16.35
7	Schwartz Thomas	23 (1.77)	16	2876	125.04
7	Wang Yuqiu	23 (1.77)	11	901	39.17
7	Yang Min	23 (1.77)	12	811	35.26

nA = Number of Articles, TC = Total citation, ATC = Average total citation.

collaborated in the studies related to environmental water and the release of ARGs/MGEs into the water environment, the studies have not lived up to the needed relevance for which reports are intended.

Table 4 shows the various authors and keywords plus used by authors while carrying out research within diverse environments. The most reoccurring keyword was antibiotic resistance genes (225). Although some studies prefer to use the term resistance genes, others preferred the use of integron genes. Some other studies prefer to use the specific name of the bacterium harboring the resistance genes and/or the name of the organism such as *Escherichia coli* and the family of the organisms such as enterobacteriaceae. Some investigators use the name of sampled water type as activated sludge, wastewater treatment plant, effluents/influent, hospital, communities etc.

The authors keywords and keywords plus network used by the various authors from various countries were mapped to show their

Table 3. Top 10 countries with frequency of relevant articles citations.

Rank	Country	nA (% of 1,301)	Freq (%)	SCP	MCP	MCP_Ratio (%)	Country	TC	AAC
1	China	389 (29.90)	0.29	310	79	0.2	China	10089	25.94
2	Usa	197 (15.14)	0.15	157	40	0.2	USA	8359	42.43
3	Germany	54 (4.15)	0.04	36	18	0.33	Germany	3915	72.5
4	Poland	51 (3.92)	0.04	46	5	0.09	Spain	2689	59.76
5	Spain	45 (3.46)	0.04	29	16	0.36	Italy	2015	67.17
6	Portugal	43 (3.31)	0.03	30	13	0.3	Portugal	1861	43.28
7	Canada	40 (3.07)	0.03	20	20	0.5	Sweden	1462	58.48
8	Italy	30 (2.31)	0.02	16	14	0.47	Cyprus	1360	151.11
9	Brazil	29 (2.23)	0.02	24	5	0.17	Poland	1052	20.63
10	South Africa	28 (2.15)	0.02	23	5	0.18	France	892	33.04

nA = Number of Articles, SCP = Single citation publication, MCP = Multiple citation publication, TC = Total Citations, AAC = Average Article Citations.

Table 4. Top 20 most relevant authors and plus keywords.

Author Keywords		Keywords plus	
Words	Occurrences	Words	Occurrences
antibiotic resistance genes (args)	225	Bacteria	340
antibiotic resistance	199	*Escherichia coli*	290
Wastewater	158	antibiotic resistance	223
Antibiotics	137	Genes	213
wastewater treatment	72	antibiotic resistance genes	206
antibiotic resistant bacteria	49	treatment plants	193
wastewater treatment plant	46	antimicrobial resistance	190
Escherichia coli	41	waste water	173
antimicrobial resistance	36	Removal	157
horizontal gene transfer	35	activated sludge	155
antimicrobial resistance gene	34	resistance genes	126
Tetracycline	33	Prevalence	123
Metagenomics	31	waste water treatment	123
microbial community	30	Environment	122
Antibiotic/antimicrobial	27	Fate	122
activated sludge	26	tetracycline resistance	119
Environment	25	Diversity	104
hospital wastewater	25	Tetracycline	96
bacterial community	24	Enterobacteriaceae	94
		Pharmaceuticals	91

association using connecting lines. Whereas those cross-links with similar colours reveal an association or relationship, the most prominent node shows the strength and linkage of the association. Figure 3 shows a word cross-linked with lines and two distinct colours blue and red. It can be observed that the blue colours linked to a large word antibiotic resistance genes while the red colours linked to another large red word tagged as antibiotic resistance indicating an association despite the diversity in the usage of the keywords or keyword plus. In addition, all similar words clustered together revealing their association, while the non-similar words were dispersed apart as shown in Figure 3.

2.9. *Trending topics and conceptual frameworks of ARGs/MGEs documents*

The multiple conceptual analysis (MCA) performed on 200 individuals described by 50 variables identified four distinct conceptual frameworks (CF) (Figure 4). The purple shows the swine wastewater release with no specified analytical method, removal method or geographical concern. The second CF is green which shows the released wastewater, aquatic environment, activated sludge, sewage treatment plant, pearl river, constructed wetlands, surface water, tetracycline, emerging contaminants, veterinary antibiotics, transformation products, personal care products and the removal process by advance oxidation process, nitrogen removal process, activated carbon,. The specified analytical methods were risk assessment, mathematical modeling, mass spectrometry, liquid chromatography, tandem mass spectrometry, solid phase extraction, performance liquid chromatography and adsorption. This CF has Southern China as its geographical pointer. The third CF (blue) consists of the Gram negative bacterial family, strains and

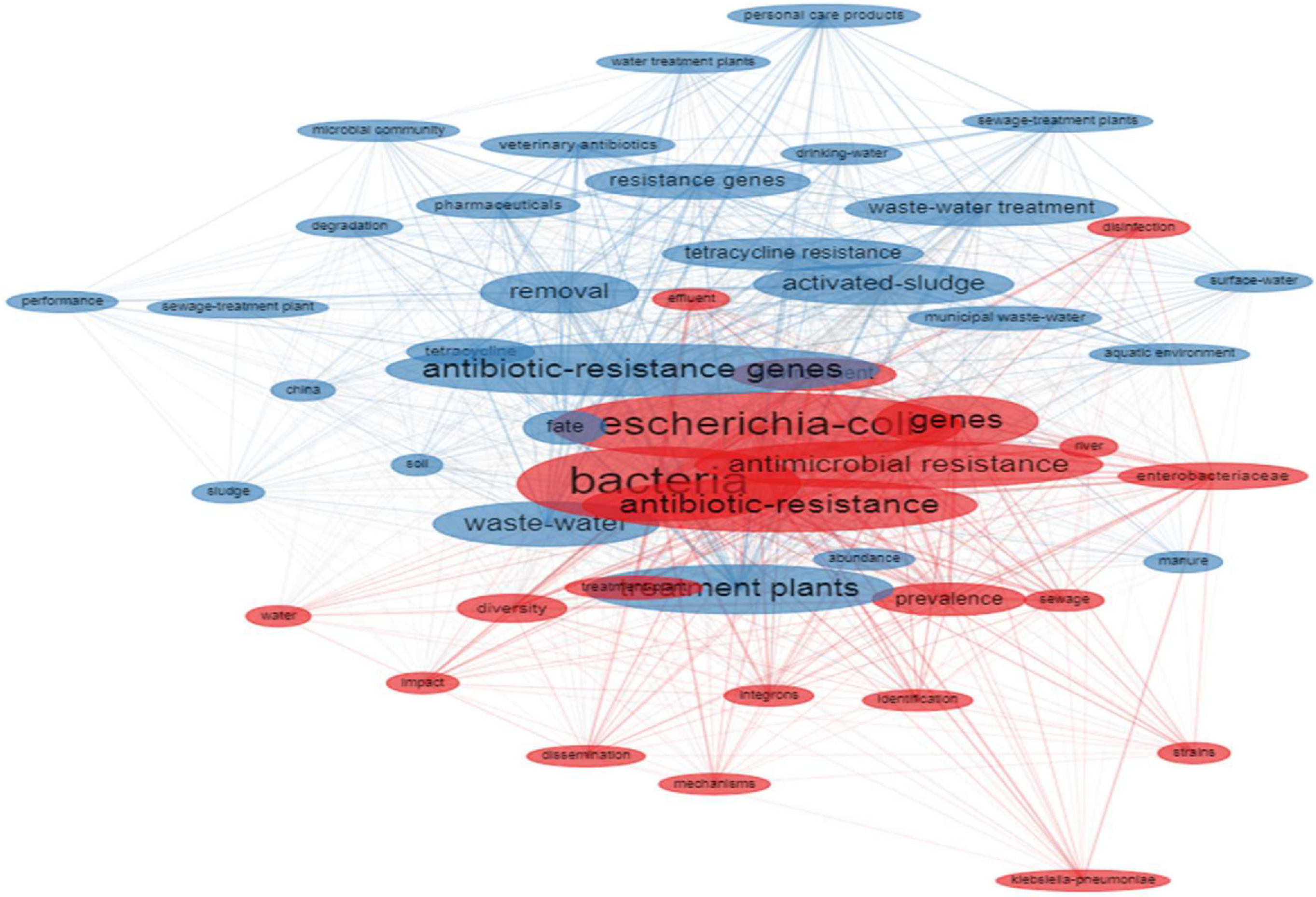

Figure 3. Keyword plus co-occurrence network.

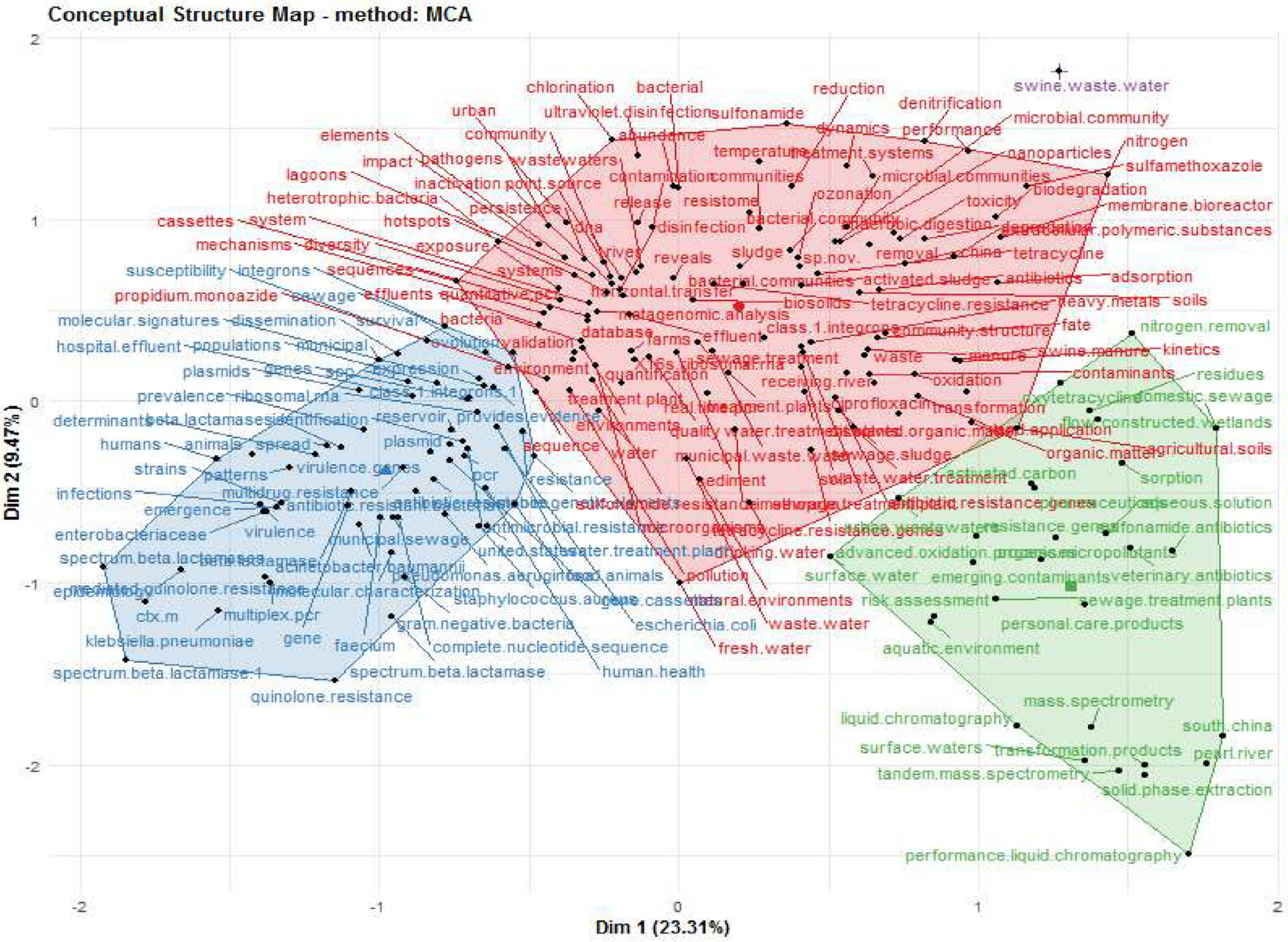

Figure 4. Trending topics and conceptual networks in ARGs/MGEs. The colour of the polygons depicts different conceptual topical network. The closer the points to one another, the higher the strength of link/network between items.

members such as enterobacteriaceae, *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia* and other Gram positive strains (*Enterococcus faecium, Staphylococcus aureus*). It also reveals the sources, human health, animal source, infections, reservoir, provided evidences, hospital effluents, virulence, molecular signatures, dissemination, resistant genes (betalactamase, quinolone resistance, *CTX-M* betalactamase encoding plasmids), spread patterns, the analysis conducted were complete nucleotide sequence, multiplex polymerase chain reaction (PCR) and simplex PCR. The fourth CF (red) consisted of hotspots of sources, exposure, wastewater systems, lagoons, activated sludge, urban communities, sediments, fresh water, wastewater, sludge, treatment plants, municipal waste, database, effluents, farms, contaminants, toxicity, agricultural soil, organic matter and contamination community. It also mentioned bacteria community, heterotrophic bacterial, microbial community and described the mobile elements, resistomes, sulfonamides, class 1 integron, tetracycline resistant genes, horizontal transfer and sequencing. The various analyses conducted include effluents quantitative PCR, metagenomic analysis, validation, dynamics performance and other PCR techniques. The approach employed for the removing the ARGs and/or MGEs were ultraviolet disinfection, denitrification, ozonation, chlorination, nanoparticles, anaerobic digestion, adsorption, oxidation, temperature treatment systems and ARGs quantitation. The health association ranges from human, animal and other biotic health determinants in the environment. Of important note is the closeness of the polygons to each other which indicates a high correlation strength between the various items. Although there is a high report of networked studies, it continues to reflect a repetition of previous works without any recognized advancement or absence of such noxious agents.

MCA performed on 200 individuals described by 50 variables identified four distinct conceptual frameworks (CF) (Figure 4).

Figure 5 presents a 30 topmost authors collaboration network (ACN) between 1997–2019. The colours greyish-arsh, blue, green and purple shows the few links and authors collaboration which occurs locally within countries. On a global consideration, it can be deduced that the authors collaborative relationship is poor among diverse countries. Such weak collaborative network is probably associated with non-availability of funds or poor connectivity in related researchable area of interest. From the above, a simple deduction could be a relative interest shared amongst related researchers in diverse countries/continents. The network of various studies conceptual frameworks and collaborative networks amongst authors in diverse institutions within different countries such as China, USA, United Kingdom, Germany, Netherlands, Singapore, Cyprus, Japan, South Africa etc is poor depicts the predominance of studies on ARGs/MGEs in China where there are higher authors, collaborating institution and countries studies. In addition, these region-wise reports remain repeated and non-impactful on wastewater, water bodies and the environment necessitating prompt action.

Figure 6 shows the 30 top institutional collaborative networks within the stated period of study. Among the 30 selected countries, it was observed that the Chinese University Academy of Science had collaboration with six other institutions making it the topmost institution involved in regular collaboration with other universities. This is followed

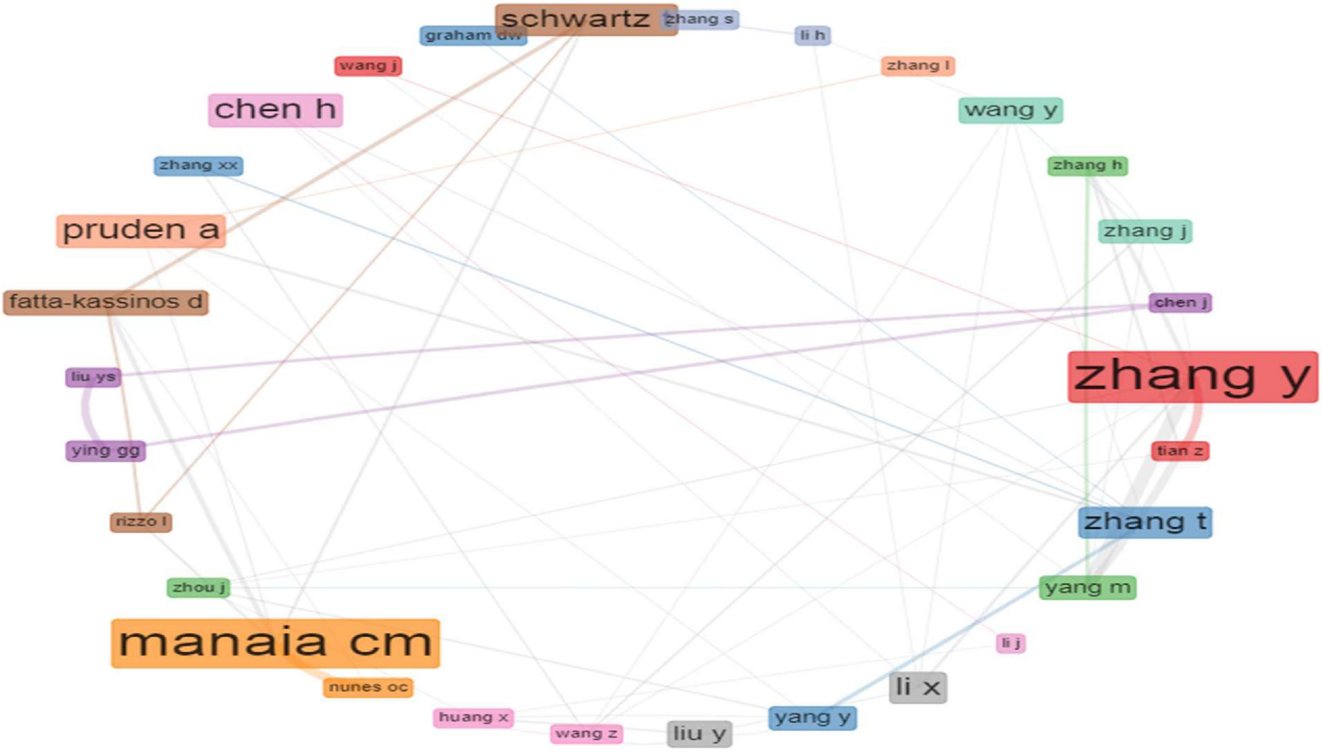

Figure 5. 30 topmost author collaboration networks.

by the Portuguese institution which had four Universities collaboration. Other institutions such as the University of Cyprus, Virginia tech, and German institutions had two collaborations each with other institutions. These circle sizes each corresponds to their publication sharing capacity and the universality of the linking/collaborating institution. Despite the noted collaborative strength, some notable concerns may have informed the poor participation of their research reports. These may include the need for a refocused attention on the application of water reuse policy, implementation of recent water treatment systems knowledge-based and research affirmed strategies, an appropriate and more suggestive strategy

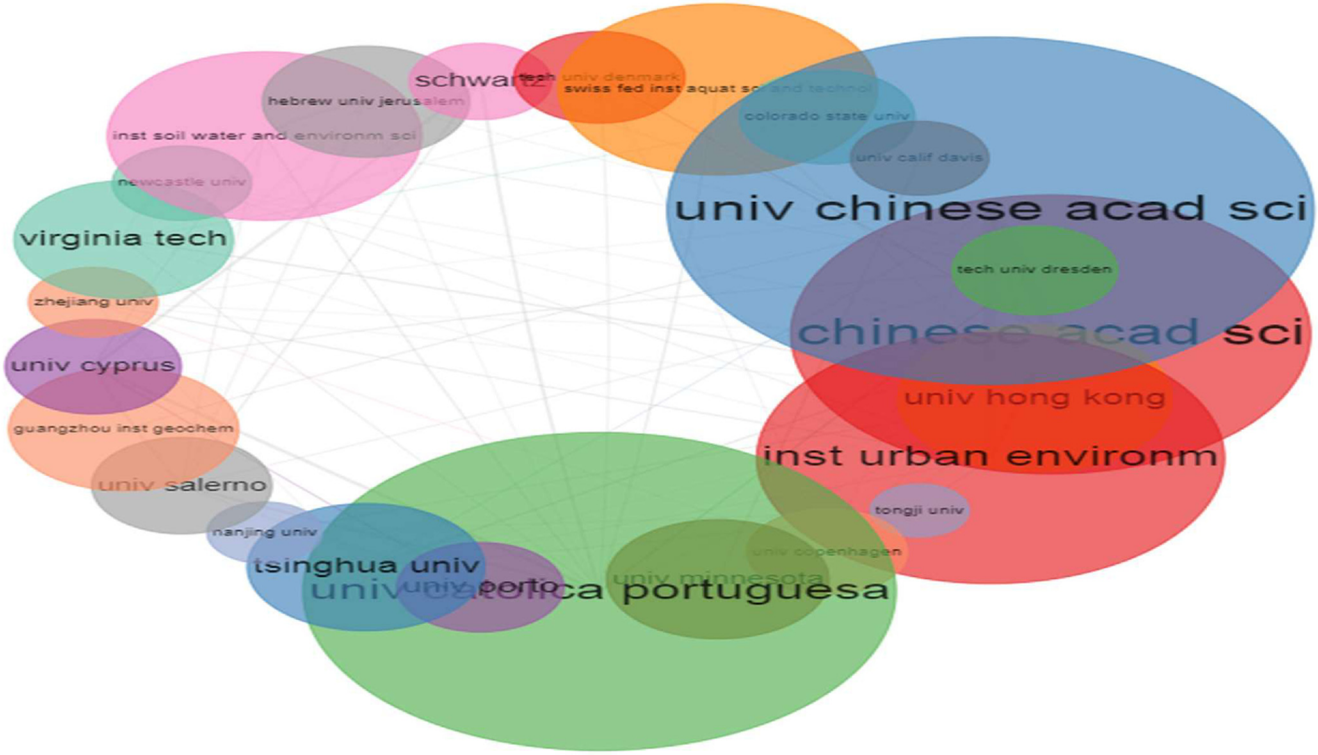

Figure 6. 30 topmost institutions collaboration networks.

Figure 7. 30 topmost countries collaboration networks.

for the communication of research output or findings based on removal of ARGs/MGEs in wastewater release and estuaries, regulatory organization interest and redefinition of a framework based on the reports from diverse environment.

One major highlight from this study is a poor focus and/or attention on knowledge-scape and research-based steps to eliminating and/or reducing the risk of the released ARGs/MGEs in the environmental nexus and wastewater treatment plants. Figure 7 shows the 30 top countries collaboration networks with continuous reporting of noxious agent release. Although there are notable collaboration between some countries such as China, USA, United Kingdom, Germany, Canada, Spain, Czech Republic, Netherlands, Singapore, Cyprus, France, Japan, South Africa etc, the call to expend such collaboration to an applicative end with specific report of reduced ARGs/MGEs in the water nexus remains an area of prompt action.

2.10. ARGs/MGEs and research-based removal methods in water nexus

Table 5 reveals the research-based and tested laboratory-scale methods for removing various ARGs/MGEs from water system. Eighteen of the authors describe the various enlisted methods including; high-quality treated wastewater reuse (HQTWR), Anaerobiotic treatment, Biologically aerated filter (BAF), Iron-based advanced oxidation processes, Combined processes of Powdered Activated Carbon (PAC)/Biological PAC (BPAC)-ultrafiltration (UF), Sequencing Membrane Bioreactor (SMBR) at pilot-scale, Pilot-scale CSTR thermal anaerobic digesters, Intimately coupled Photocatalysis and biodegradation (ICPB), TiO_2 and WO_3 nanoparticles, TiO_2 photocatalysis, Lignin-derived hierarchical porous carbon, Combined Membrane Bioreactor (CMBRs) with biological processes or physical technology, Bioelectrochemical system (BES), cathodic electro-Fenton (EF) process, $Cu_2O/ZnO/Ag_3PO_4$ Photocatalysis, Advanced Oxidation Process (AOP) or photo Fenton process using UV-C/H_2O_2/IDS-Cu, Membrane bioreactor (MBR), Enhanced Biological Phosphorus Removal (EBPRS) System, lab-scale anoxic/oxic-membrane bioreactor, Persistence of Acesulfame (ACE), Sand Settling Reservoirs (SSRs) and Drinking Water Treatment Plants (DWTPs), laboratory-scale anoxic/aerobic membrane bioreactor (ADO-MBR) etc. These laboratory-scale tested methods have shown appreciable removal reports for both ARGs/MGEs and other chemical contaminants in wastewater release, yet there remain increasing reports of ARGs/MGEs contaminants in environmental water nexus and water bodies. The studies of diverse investigators as outlined above have reported a significant removal tendency of ARGs/MGEs (*NDM-1, ere1, AmpC, OXA, sul 1, sul 2, tet M, Ns78p, tetA* and *tetC, tetM,* and *tetS, bla*($_{CTX\text{-}M}$)*, bla*($_{SHV}$)*, bla*($_{TEM}$)*, qnrA, qnrB, qnrS, sulI, sulII, tetM, tetW, tetO, transposon, plasmid, integron*) up to a third order magnitude or degree on reduction of such contaminating agents from municipal wastewater treatment systems (Di Cesare et al., 2020; Taddesse et al., 2020; Beheshti et al., 2019; Cheng et al., 2020; Liu et al., 2019; Petrovich et al., 2018 Ravasi et al., 2019; Sun et al., 2019; Ren et al., 2018; Jäger et al., 2018; McConnell et al., 2018; Zheng et al., 2017; Chen and Zhang, 2013b; Zhang et al., 2008, 2009). Although these studies have shown appreciable removal of ARGs/MGEs contaminants, the frequency of reports yet remains. This possibly indicates that the reports on relevant research-based strategic methods for the removing these genetic materials are either not adequately applied for public use or there is a gap at the communication phase of such

Table 5. Identified ARGs/MGEs and research-based removal methods in water nexus.

Authors	WTTPs	ARGs	MGEs type	Method of assessment	Method of ARGs/MGEs removal	location/site	country
He et al., 2019	Activated sludge	*tet-C, tet-X, bla*$_{TEM}$*, mefA, sul1, sul11* and *cat*	*IntI 1*	Nucleic acid			China
Pazda et al., 2019	raw sewage, treated wastewater or activated sludge	beta-lactam, macrolides, quinolone, sulfonamides, trimethoprim and tetracyclines	plasmids, transposons, bacteriophages, integron	Review			Global
Han et al., 2019	Submicron aerosols (SAs)	Nsp	Nsp	Aerosol simulation			Japan
Carney et al., 2019	Coastal water	quinolones, trimethoprim, sulfonamides, tetracycline, vancomycin and carbapenems	Nsp	Nucleic acid		nsp	nsp
Subirats et al., 2019	mesocosms	beta-lactams and carbapenems (*bla*$_{TEM}$*, bla*$_{CTX\text{-}M}$*, bla*$_{OXA}$, and *bla*$_{KPC}$), fluoroquinolones (*gnrS*), tetracyclines (*tetA*), sulfonamides (*sul2*), macrolides (*ermB*), arsenic and cadmium (*arsB* and *czcA*	*IntI 1*	Nucleic acid	high-quality treated wastewater reuse (HQTWR)		France
Mrozik et al., 2019	micropollutant	Tetracycline	Nsp	Nucleic acid		Bangkok	Thailand
Rodriguez-Molina et al., 2019	Municipal	Nsp	Nsp	Review			Global
Du et al., 2019	anoxic-aerobic wastewater	*tetC* and *sul1*	*IntI 1*	Nucleic acid		nsp	nsp
Liu et al., 2019	Effluents	sulfamethoxazole, sulfamethazine, ofloxacin, and clarithromycin	*IntI 1*	Nucleic acid	Anaerobiotic treatment		South China
Sanderson et al., 2019	Municipal	Vancomycin resistant enterococci (VRE), streptomycin resitant, nitrofurantoin resistant	Nsp	Nucleic acid	Biologically aerated filter (BAF)	Nil	nsp
Shrestha et al., 2019	Municipal	Nsp	Nsp	Nucleic acid		Southern Arizona	USA
Alaton et al., 2019	Municipal	Nsp	Nsp	Nucleic acid	Iron-based advanced oxidation processes	Istanbul	Turkey
Sun et al., 2019	Municipal	Nsp	*IntI 1*	Nucleic acid	Combined processes of Powdered Activated Carbon (PAC)/ Biological PAC (BPAC)-ultrafiltration (UF)		nsp
Oladipo et al., 2019	Effluents	*mecA, nuc* and *luk-pvl*	Nsp	Nucleic acid		Ile-Ife	Nigeria
Traversi et al., 2019	Activated sludge	Nsp	Nsp	Nucleic acid		nsp	nsp
Bougnom et al., 2019	Municipal	Nsp	Nsp	Nucleic acid		African Cities	nsp
Sui et al., 2019	Agro-Effluents	*Sul 1*	*IntI 1*	Nucleic acid	Sequencing Membrane Bioreactor (SMBR) at pilot-scale	nsp	China
Yin et al., 2019	Activated sludge	Nsp	Nsp	Nucleic acid		nsp	Hong Kong

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Table 5 (*continued*)

Authors	WTTPs	ARGs	MGEs type	Method of assessment	Method of ARGs/MGEs removal	location/site	country
Mills and Lee, 2019	Municipal	Carbapenem-resistant Enterobacteriaceae (CRE), New Delhi Metallo-beta-lactamase (*NDM*), Oxacillinase-48-type carbapenemases (*OXA-48*), and Verona Integron-Mediated Metallo-beta-lactamase (*VIM*)	Nsp	Nucleic acid		Montpellier and Cairo	France and Egypt
Reichert et al., 2019	Municipal	Nsp	Nsp	Nucleic acid		Latin America	Brazil and Mexico
Sun et al., 2019	Activated sludge	Nsp	Nsp	Nucleic acid	Pilot-scale CSTR thermal anaerobic digesters		nsp
Yuan et al., 2019	Agro-Effluents	*sulI, tetA, mphB, qnrD*, and *mcr-1*	*IntI 1*	Nucleic acid		nsp	nsp
Wang et al., 2019	Effluents	Nsp	Nsp	Photocatalysis and Nucleic acid	Intimately coupled photocatalysis and biodegradation (ICPB)	nsp	nsp
Kneis et al., 2019	Municipal	*Mcr 1,3,4,5,7*	Nsp	Nucleic acid		nsp	Germany
Wang et al., 2019	Municipal	*Sul 1*, bla_{TEM}	Nsp	Nucleic acid		nsp	nsp
Adekanmbi et al., 2019	Municipal	sulfamethoxazole-trimethoprim, linezolid, clindamycin, tetracycline, erythromycin, vancomycin, ciprofloxacin and chloramphenicol	Nsp	Nucleic acid		nsp	Nigeria
Yazdi et al., 2019	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Tikariha and Purohit, 2019	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Beheshti et al., 2019	Effluents	Nsp	Nsp	Nucleic acid	TiO2 and WO3 nanoparticles		nsp
Zhang et al., 2019	Municipal	TET, SMZ, AMP, CHL, GEN, STP, *tetA* and *sul3*	*IntI 1*	Nucleic acid		nsp	nsp
Cabrera-Reina et al., 2019	Effluents	Nsp	Nsp	Nucleic acid	TiO2 photocatalysis		nsp
Dai et al., 2018	Municipal	Nsp	Nsp	Nucleic acid	Lignin-derived hierarchical porous carbon		nsp
Kerrigan et al., 2018	Municipal	sulfonamides, tetracyclines, fluoroquinolones, and macrolides	Nsp	Nucleic acid		Minnesota lake-sediment cores	Canada
Wang et al., 2018	Municipal	*qnrD, sul3, tetX, Tn916/Tn1545 and sul2*, and *ISCR1* and *sul3*	*intI1, intI2 intI3*	Nucleic acid		nsp	China
Cheng et al., 2018	Agro-Effluents	Nsp	Nsp	Nucleic acid	Combined Membrane Bioreactor (MBRs) with biological processes or physical technology	nsp	nsp
Guo et al., 2018	Municipal	*cmlA, floR* and *tetC*	*IntI 1*	Nucleic acid	Bioelectrochemical system (BES)	nsp	nsp
Pepper et al., 2018	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp

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Table 5 (*continued*)

Authors	WTTPs	ARGs	MGEs type	Method of assessment	Method of ARGs/MGEs removal	location/site	country
Liu et al., 2018	Municipal	sulfonamide, trimethoprim, quinolone, and tetracycline	Nsp	Nucleic acid		Dongting Lake	China
Li et al., 2018	Agro-Effluents	Nsp	Nsp	Nucleic acid		North China (Beijing, Hebei, and Tianjin)	China
Petit, 2018	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Bekele et al., 2018	Municipal	Nsp	Nsp	Nucleic acid		Perth, Western Australia, Monterey, California and Changwon	South Korea
Jumat et al., 2018	Municipal	Nsp	Nsp	Nucleic acid	Membrane bioreactor (MBR	nsp	Saudi Arabia
Oliveira et al., 2018	Municipal	*AmpC*	Nsp	Nucleic acid		Southeast Brazil	Brazil
Kyriacou, et al., 2018	Activated sludge	Nsp	Nsp	Nucleic acid		Athens	Greece
Gardner et al., 2018	Activated sludge	Nsp	Nsp	Nucleic acid		nsp	USA
Hu et al., 2018	Municipal	Nsp	Nsp	Nucleic acid	Enhanced Biological Phosphorus Removal (EBPRS) System		nsp
Hultman et al., 2018	Municipal	*tetM, int1, qacE Delta 1* and *bla*$_{OXA\text{-}58}$	Nsp	Nucleic acid		nsp	nsp
Wen et al., 2018	anoxic-aerobic wastewater	Nsp	Nsp	Nucleic acid	lab-scale anoxic/oxic-membrane bioreactor		nsp
Wang et al., 2018	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Kahl et al., 2018	Municipal	Nsp	Nsp	Nucleic acid	Persistence of Acesulfame (ACE)	nsp	nsp
Chu et al., 2018	Municipal	Nsp	Nsp	Nucleic acid		Lake Michigan	USA
Park et al., 2018	Municipal	*aadA2, aadAl2, aadA22,* and *dfrA15*	*IntI 1, IntI 3*	Nucleic acid		nsp	nsp
Jiao et al., 2018	Municipal	*aadA5-02, aac-6-II, cmlA1-01, cmlA1-02, bla*$_{OXA10\text{-}02}$*, aadA-02, tetX, aadA1, ereA, qacE Delta 1-01, bla*$_{TEM,}$ *tet-32, tetA-02, aacC2, vanC-03, aac-6-I1, tetE, ermB, mefA, tnpA -07*, and *sul2*	Nsp	Nucleic acid		nsp	nsp
Eckert et al., 2018	Municipal	Nsp	*IntI 1*	Nucleic acid		nsp	nsp
Kim et al., 2018	Agro-Effluents	Nsp	Nsp	Nucleic acid		nsp	nsp
Lou et al., 2018	Agro-Effluents	Tetracycline	Nsp	Nucleic acid		nsp	nsp
Daoud et al., 2018	Municipal	*ESBL, NDM-1, AmpC, OXA*	Nsp	Nucleic acid		nsp	Lebanon
Metch et al., 2018	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Yang et al., 2018	Municipal	Nsp	Nsp	Nucleic acid		Dongjiang River basin	South Korea
Lu et al., 2018	Municipal	Nsp	Nsp	Nucleic acid	Sand Settling Reservoirs (SSRs) and Drinking Water Treatment Plants (DWTPs)		Yellow river
Zhu et al., 2018	Municipal	*sull, sulll, tetC, tetX and ereA*	*IntI 1*	Nucleic acid	laboratory-scale anoxic/aerobic membrane bioreactor (ADO-MBR)	nsp	nsp
Hong et al., 2018	Municipal	Nsp	*IntI 1*	Nucleic acid		nsp	nsp
Colomer-Lluch et al., 2014	Municipal	*bla*$_{TEM}$, *bla*$_{CTX\text{-}M1}$, *bla*$_{CTX\text{-}M9}$, *qnrA, mecA* and *qnrS*	Nsp	Nucleic acid		nsp	Tunisia and Spain

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Table 5 (*continued*)

Authors	WTTPs	ARGs	MGEs type	Method of assessment	Method of ARGs/MGEs removal	location/site	country
Matos et al., 2014	Municipal	Tetracycline	Nsp	Nucleic acid		nsp	nsp
Mulamattathil et al., 2014	Municipal	KF-AP-C-E-OT-K-TM-A	Nsp	Nucleic acid		Mafikeng area, in the North-West Province	South Africa
Everage et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		Thibodaux, Louisiana	USA
Junejo et al., 2014	Municipal	cefdinir, cefditoren, cefiximee, ceftriaxone sodium and doxycycline	Nsp	Nucleic acid		nsp	nsp
Rahube et al., 2014	Municipal	macrolide, tetracycline, beta-lactam, trimethoprim, chloramphenicol, sulphonamide	plasmids, transposons, bacteriophages, integron	Nucleic acid		nsp	nsp
Krzyzanowski et al., 2014	Activated sludge	Nsp	Nsp	Nucleic acid		nsp	nsp
Tao et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Liu et al., 2014	Activated sludge	Macrolide-Lincosamide-Streptogramin	Nsp	Nucleic acid		nsp	nsp
Singh et al., 201	Municipal	Nsp	Nsp	Nucleic acid		Lucknow and Ghaziabad	nsp
Chen et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		Beijing and Tianjin	China
Chandran et al., 2014	Municipal	*ESBL, NDM-1, AmpC, OXA*	Nsp	Nucleic acid		nsp	nsp
Yang et al., 2014	Activated sludge	Nsp	Nsp	Nucleic acid		nsp	nsp
Berglund et al., 2014	Activated sludge	Nsp	Nsp	Nucleic acid		Lake	Sweden
Marti et al., 2014	Municipal	*qnrA, qnrB, qnrS and aac(6′)-Ib-cr*	plasmids, transposons, bacteriophages, integron	Nucleic acid		River	nsp
Piotrowska et al., 2014	Municipal	fluoroquinolones and cefotaxime	plasmids, transposons, bacteriophages, integron	Nucleic acid		nsp	nsp
Broszat et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		Mezquital Valley	Mexico
Li et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Rebello and Regua-Mangia	Municipal	Nsp	Nsp	Nucleic acid		Rio de Janeiro	Brazil
Liu et al., 2014	Municipal	*sulI, sulII, tetM, tetW* and *tetO*	Nsp	Nucleic acid		nsp	nsp
Moura et al., 2014	Municipal	Nsp	plasmids, transposons, bacteriophages, integron	Nucleic acid		Berlenga Island	Portugal
Ben et al., 2014	Activated sludge	Nsp	Nsp	Nucleic acid		nsp	nsp
Kong et al., 2014	Municipal	Nsp	Nsp	Nucleic acid	biocathode bioelectrochemical system (BES		nsp
Sidrach-Cardona et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp
Yuan et al., 2014	Municipal	*vanA, ampC, sull* and *ereA*	Nsp	Nucleic acid		nsp	China
Laht et al. (2014)	Effluents	*ESBL, NDM-1, AmpC, OXA, sul 1, sul 2, tet M*	Nsp	Nucleic acid		Helsinki, Tallinn, and Tartu	China
Hsu et al., 2014	Municipal	Sulphonamide	Nsp	Nucleic acid		nsp	nsp
Blaak et al., 2015	Effluents	*Ns78p*	Nsp	Nucleic acid		Ghent	Belgium
Huang et al., 2014	Municipal	*tetA* and *tetC, tetM,* and *tetS,*	Nsp	Nucleic acid	aerobic and anoxic conditions		nsp
Marti et al., 2014	Municipal	*bla(CTX-M), bla(*$_{SHV}$*), bla(*$_{TEM}$*), qnrA, qnrB* and *qnrS*	Nsp	Nucleic acid		nsp	nsp
McNamara et al., 2014	Municipal	Nsp	Nsp	Nucleic acid		nsp	nsp

nsp: not specified; WTTPs: water treatment type plants.

reports. In addition, there was also a high citation of reported studies which may be attributed to documenting without appropriate application amongst practitioners. Furthermore, the heterogeneity of ecosystem, global socio-economic status and geographical diversity of countries may also serve as contributing factors.

2.11. The studies limitations

The studies limitation encompasses excluded articles which were written in local, indigenous and/or non-English language, absence of articles published in other forms such as patent, articles not conforming to the topic-specific code/algorithm of this study, governmental intervention, single universal database employed (WoS) for retrieval of included articles, unrelated and unassociated articles which may impact or change the weight of publications and other notable post publication synthesis factors which might affect the study. Studies that included the general public in decision-making and evaluating the general public interaction with research findings were excluded and not accessed during the study.

3. Conclusion

Assessing quality water sources and implementation of water reuse policy remains sacrosanct as it affects the quality of human life and livelihood. It also defines environmental wellness or state of wellbeing of the environment. Observing Antibiotic resistant genes (ARGs) and mobile genetic elements (MGEs) in water bodies, wastewater treatment systems release, and estuaries is a relevant risk or health concern and may result in environmental pathogen bloom if appropriate research-based strategies are not implemented to remove these lethal genetic materials. This study has shown that although there are extensive studies of antibiotic resistant genes (ARGs) and mobile genetic elements (MGEs) in wastewater release in addition to reports on removal, the impact of such report has not been fully actualized amongst wastewater practitioners. These may be associated with the heterogeneity of the ecosystem, global social-economic heterogeneity and geographical heterogeneity of countries. Actions to trim down the predominance of ARGs/MGEs reports to mitigate these potential noxious resistant markers and contaminants remains under-actualized, hence assessing ARGs/MGEs in wastewater using comprehensive/standard knowledge-scape and research-based monitoring of waterways/water bodies, including periphyton, aerosol, dusts, and surfaces water remains germane. Emphasis on public awareness campaign as well as novel media of reporting and communicating research-based and tested studies to the public or relevant stakeholders may contribute to lowering the low collaboration and collaborative index. Other contributors may include: the need to reawaken the water engineering organizations/engineers to include scientific findings in their structural design for control of such ARGs/MGEs; The multinational and governmental organizations are encouraged to use the publication media as means for communicating findings to the public and encourage researchers on application of workable methods to prevent or reduces the prevalence of these agents in our environment; A combined application of diverse practitioners/researchers and experts approach is required for addressing the current challenge.

Declarations

Author contribution statement

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

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