

ORIGINAL RESEARCH ARTICLE

Systematic Review on the Antibacterial Resistance of *Vibrio Cholerae*Rabiu Murtala^{1&2*} , Abdulkadir Bashir³ , Isa Abubakar Aliyu⁴ , Kumurya Abdulhadi Sale⁴ ¹Department of Medical Laboratory Services, Ahmad Sani Yariman Bakura Specialist Hospital Gusau, Zamfara State, Nigeria²Department of Public Health Ministry of Health Gusau, Zamfara State, Nigeria³Department of Microbiology Umaru Musa Yaradua University Katsina State, Nigeria⁴Department of Medical Laboratory Science, Faculty of Health Allied Sciences, Bayero University Kano, Kano State, Nigeria

ABSTRACT

Background: *Vibrio cholerae* is the causative agent of cholera illness. Antibacterial resistance of *V. cholerae* is frequently experienced due to the environmental pressure from human and animal overuse and misuse of antibacterials. Among such antibacterials include Tetracycline, Chloramphenicol, Furazolidone, Ampicillin, and Trimethoprim-Cotrimoxazole as used against *V. cholerae* O1, O139 and non O1, O139 strains.

Objectives: This systematic review was aimed at providing an overview of Antibacterial resistant strains of *Vibrio cholerae* in terms of year, location and factors responsible for the resistance.

Material and Method: Systematic Electronic database search of PubMed (NCBI) by means of the key terms MeSH “Antimicrobial resistance of *Vibrio cholerae*” between the period of January 2000 to October 2018 was used.

Results: From the findings it showed that many factors are responsible for Antibacterial resistance of *Vibrio cholerae* which include genetic composition, mutation, enzymes. Also *V. cholerae*, both O1, O139, environmental and non O1/ non O139 such as *V. anguillarum*, *parahaemolyticus* were incriminated in transferring resistance genes from one another. Antimicrobial Susceptibility Testing phenotypic and Polymerase Chain Reaction (PCR) molecular procedure were employed in detecting the resistance and equally the use of Global Antimicrobial Surveillance System (GLASS) and Centre for Disease control (CDC) AR threat report 2019 was used successfully in the management of *Vibrio cholerae* epidemic.

Conclusions: Drug-resistant *Vibrio cholerae* is a problem that needs to be dealt with as soon as possible

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KEYWORDS

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INTRODUCTION

Vibrio cholerae causes acute rice watery stool disease that affect human being which form biofilm on the surface water (Gupta *et al.*, 2018). Antibacterial resistance is the ability of bacteria to defeat the drugs designed to kill them and this is one of the greatest global public health difficulties of our period responsible for deaths, prolong hospitalization, and high expenses health-care for specific pathogen–drug treatment. Antimicrobial susceptibility pattern of humans and environmental isolates of *V. cholerae* is vital in monitoring antibiotic resistance within nations (Gupta *et al.*, 2018). Rise in Antibacterial resistance of *V. cholerae* has been recorded in numerous epidemics globally (Dengo-Baloi *et al.*, 2017). Integrons continue to be responsible in *Vibrio cholerae* Antimicrobial resistance (AMR) with capability to recognize AMR gene cassettes and direct them in their hosts (Sulca *et al.*, 2018). Genomic variation and antibacterial resistant *V. cholerae* have implications in the disease management (Campos *et*

al., 2004). *Vibrio cholerae* turn Antibacterial resistant by moving the agent through efflux pumps, chromosomal accident or developing genetic resistance via the exchange of conjugative plasmids, conjugative transposons, integrons or self-transmissible chromosomally by integrating SXT (Sulphamethoxazole Trimethoprim) elements (Kitaoka *et al.*, 2011).

MATERIALS AND METHODS

A systematized PubMed investigation was done by means of the key terms MeSH “Antimicrobial resistance of *Vibrio cholerae*” between January 2000 and October 2018. Given the extent of the issue, citations were selected for articles published in English. We found 249 papers (Figure 1), but only 77 were chosen and reviewed based on key terms 3 were duplications, 172 were antimicrobial resistance based on other organism and were removed from the review.

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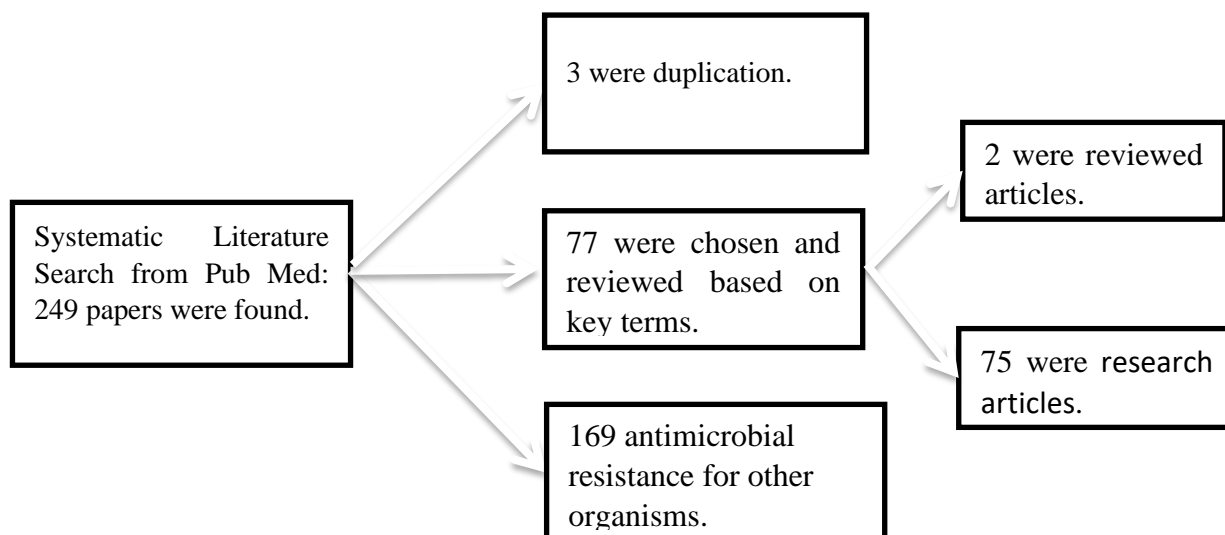


Figure 1: Systematic Literature Search

RESULT

Of the 77 manuscripts reviewed, there are two systematic reviews while the remaining 75 were studies conducted on *Vibrio cholerae* as mentioned in the Figure 2 below.

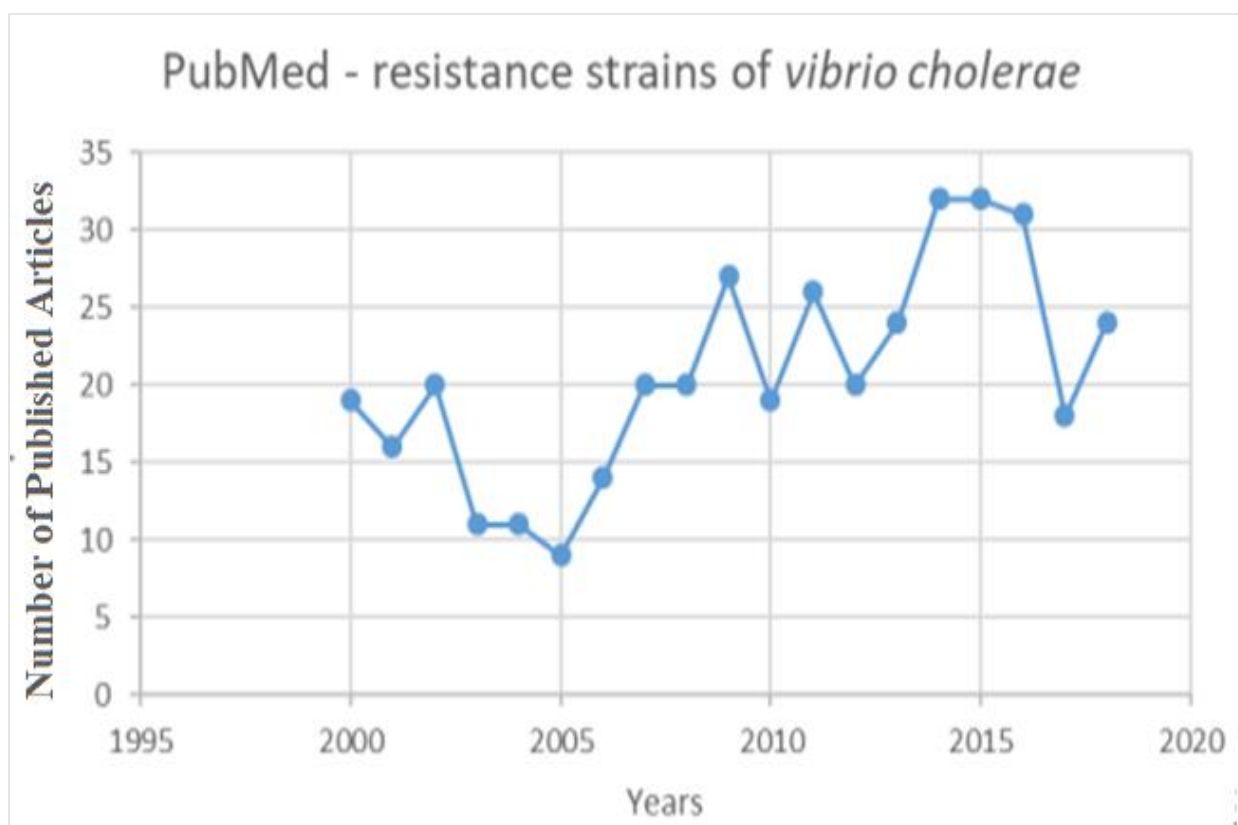


Figure 2: Distribution of articles published on resistance strains of *Vibrio cholerae* between January 2000 to October 2015

Antibacterial Resistance

The antibacterial resistance was discovered from both medical and ecological water origin to harbored the antimicrobial gene resistance of horizontal gene transfer

(HGT) of the Sulfamethoxazole-trimethoprim elements (SXT) element (Mala *et al.*, 2016). The ecological water reported was found to be of significant origin for

antibacterial resistance genes in *V. cholerae* (Mala *et al.*, 2016).

Factors responsible for antibacterial resistance

1. Spontaneous mutations

Resistant to Antibacterial originated from spontaneous genetic accident in the bacterial chromosome, and spontaneous mutation being responsible for cell wall biosynthesis and DNA replication by alafosfalin and quinolones (Kitaoka *et al.*, 2011). Development of D87N in GyrA and D420N or P439S in ParE spontaneously promote resistant to fluoroquinolones in *V. cholerae* O139, and the increase of many changes in the quinolone-resistant determining regions (QRDRs) which is responsible for substantial resistance to fluoroquinolones in *V. cholerae* (Zhou *et al.*, 2013). Genetic variation in gyrA encodes sub-unit of DNA gyrase and followed mutation in parC which encodes DNA topoisomerase sub-unit (Kim *et al.*, 2010).

2. Sulfamethoxazole-trimethoprim elements (SXT)

This are mobile genetic element that encode for antibacterial resistant to *Vibrio cholerae* O1 strains Jain *et al.* (2008) reported Class 1 integrons and SXT elements conferring many Antibacterial resistance in the *V. cholerae*. Also studies show that *V. cholerae* belong to El Tor strain harboring ctxB gene of classical strain were 100% resistant to tetracycline (Kar *et al.*, 2015) equally *V. cholerae* isolated from patients and shallow water, belonging to serogroup O1, Ogawa serotype, biotype El Tor, all strains isolated were resistant to many antimicrobial such as Sulfamethoxazole-trimethoprim, Nalixidic Acid and

Streptomycin (Dixit *et al.*, 2014) *V. cholerae* pathogens genes research has demonstrated high prevalence in spreading of toxS, toxaR and toxT genes among *V. alginolyticus* strains isolated demonstrated multidrug resistant (Mechri *et al.*, 2013) many drug resistant atypical El Tor species, with decreased susceptibility to ciprofloxacin and chloramphenicol, defined by the presence of the SXT element, and gyrA (Marin *et al.*, 2013).

3. Enzymes

Vibrio cholerae produce enzymes responsible for antibacterial resistant such as extended-spectrum-β-lactamase-(ESBL) (Ismail *et al.*, 2011), also Bier *et al.* (2015) reported TEM-63 ESBL gene from the strains were responsible for cholera outbreaks in South Africa, also found the quinolone resistance-determining regions of GyrA (Ser83-Ile), ParC (Ser85-Leu), Some of the *V.cholerae* strains were resistant to aminopenicillins and aminoglycosides and in addition, resistant toward carbapenems, quinolones, and folate pathway inhibitors were periodically studied (Zadnova *et al.*,2013).

4. Efflux Pump

Vibrio cholerae uses multidrug efflux pumps to export a broad range of Antibacterial, soaps and dyes that are chemically and structurally unrelated (Akoachere *et al.*, 2013). NorM, a putative efflux pump of *Vibrio cholerae*, is a member responsible for multidrug resistance and toxic compound extrusion family of transporters, Singh *et al.* (2006) demonstrated that NorM confers resistance to norfloxacin, ciprofloxacin, and ethidium bromide, deactivation of NorM gene rendered *V. cholerae* resistant towards these fluoroquinolones.

Table 1: Summary of some published articles that reported antibacterial resistance of *Vibrio cholerae*

SN	Year	Country	Strain	Antibiotic resistant	Mechanism	Laboratory methods	Reference
1	2018	Lima (Peru)	<i>Vibrio alginolyticus</i>	penicillin group	mutT gene	PCR	(Sulca <i>et al.</i> , 2018)
2	2014 - 2015	Ghana	classical <i>V. cholerae</i> O1 biotype El Tor, serotype Ogawa	Trimethoprim/sulfamethoxazole, ampicillin andceftriaxone	SXT, CtxAB and Tcp gene	ND	(Feglo and Sewurah, 2018)
3	2017	China	O1 and O139	Macrolides:Azithromycin	IncA/C plasmid, mphR-mrx-mph(K) and mel-mph2	minimum inhibitory concentration (MIC)	(Yu <i>et al.</i> , 2012)
4	2012 - 2015	Mozambique	El Tor <i>Vibrio cholerae</i> O1	Sulphamethoxazole-trimethoprim, Trimethoprim Ampicillin, Nalidixic Acid,Chloramphenicol ,Nitrofurantoin ,Cotrimoxazole,Tetracycline,Doxycycline, Azithromycin	CTX genotype	Culture, standard biochemical tests, serotypes by antisera agglutination and PCR.	(Dengo-Baloi <i>et al.</i> , 2017)

Table 1: Continued

SN	Year	Country	Strain	Antibiotic resistant	Mechanism	Laboratory methods	Reference
5	2017	India	<i>Vibrio cholerae</i>	Amoxicillin, ampicillin, chloramphenicol, doxycycline, erythromycin, and tetracycline.	MurB protein	molecular docking	(Ragunathan, et al., 2018)
6	2016	Mexico	<i>V. alginolyticus</i>	beta-lactams Antibacterial, cephalotin, amikacin, cephotaxime, and pefloxacin,	proA, wza, vopD, vopB, hcp, vasH and vgrG genes	PCR amplification	(Hernandez-Robles et al., 2016)
7	2017	Thailand	<i>V. cholerae</i> O1 and non-O1/non-O139	ND	horizontal gene transfer (HGT) of the SXT element	ND	(Mala et al., 2016)
8	2012 - 2013	Iran	<i>V. cholerae</i>	streptomycin, trimethoprim, cotrimoxazole, tetracycline and minocycline	Class 1 integron, SXT element CarR confers polymyxin Bregulating expression of the almEFG genes, glycine and diglycine modification of lipid A.		(Rezaie, et al., 2017)
9	2015	German	<i>Vibrio vulnificus</i> and <i>Vibrio cholerae</i> non-O1/non-O139	aminopenicillins and aminoglycosides	Carbapenemases	Biochemical testing	(Bier et al., 2015)
10	2008	South Africa	<i>Vibrio cholerae</i> O1 serotype Ogawa	Quinolone	mutations in the quinolone resistance-determining regions of GyrA (Ser83-Ile), ParC (Ser85-Leu), and produced TEM-63 β -lactamase.	PCR	(Ismail et al., 2011)
11	1970 - 1998	Russia	<i>Vibrio cholerae</i> El Tor	Tetracycline and Chloramphenicol	ND	ND	(Savel'ev et al., 2010)
12	1998	Ethiopia	<i>V. cholerae</i> O1	Ampicillin, chloramphenicol, streptomycin, sulfamethoxazole and trimethoprim	IncC plasmid	Random Amplified Polymorphic DNA and Disk diffusion (KBDDT)	(Scrascia et al., 2009)

Table 1: Continued

SN	Year	Country	Strain	Antibiotic resistant	Mechanism	Laboratory methods	Reference
13	2005	Cameroun	<i>V. cholerae</i> O1	Cotrimoxazole, Ampicillin	genes <i>ctxA</i> and <i>ctxB</i>	KBDDT, pulsed-field gel electrophoresis patterns.	(Ngandjio et al., 2009)
14	2010	Nigeria	<i>Vibrio cholerae</i> O1 El Tor biotype	ciprofloxacin and chloramphenicol	SXT element, <i>gyrA</i> (Ser83Ile), <i>parC</i> (Ser85Leu) alleles CTX phage, TCP <i>rstR</i> (ElTor), <i>ctxB</i> -7 and <i>tcpA</i> (CIRS) alleles	standard culture methods by disk diffusion method and E-test. multilocus sequence analysis and pulsed-field gel electrophoresis.	(Marin et al., 2013)

KEY ND= Not Determine CTX= cholera Toxin, SXT = Sulphamethoxazole Trimethoprim integaron Element

DISCUSSION

The review found that all the 77 articles reported resistance to one or more Antibacterial in *Vibrio cholerae* O1 El Tor Ogawa between January 2000 to October 2018 and most of the Antibacterial include Tetracycline, Trimethoprim-sulphamethoxazole, Chloramphenicol and Nitrofurantoin. Antimicrobial resistance of *V. cholera* is reported in all regions of the world ([Dengo-Baloi et al., 2017](#)), another important finding was that most of resistance strains are due to genetic composition of SXT element ([Feglo and Sewurah, 2018](#)), In our review we found other factors such as efflux pump, Presence of Enzymes, spontaneous mutation, Also standard culture methods by disk diffusion method and E-test. PCR and pulsed-field gel electrophoresis are the most widely methods used in detection and this is agrees with the findings of [Dengo-Baloi et al. 2017](#), isolation and Antimicrobial susceptibility testing ([Marin et al., 2013](#)) More so virulence genes reported which include Cholera toxin *ctxA* and toxin-coregulated pilus, *tcpA*, contained by the majority of *V. cholerae* O1 strains, confirming the profile found in *V. cholerae* O1 El Tor variants B33 and CIRS 101 ([Marin et al., 2013](#)).

Contribution to knowledge

To our knowledge, this review provides comprehensive information about burdens of antibacterials resistance of *Vibrio cholerae* some of the AR include Tetracycline, Chloramphenicol, Furazolidone, Ampicillin, and Trimethoprim-Cotrimoxazole are not recommended for the management of cholera disease.

CONCLUSION

To our knowledge, this study provides extensive information on burden of Antibacterial resistance of *Vibrio cholerae*, as well as an evaluation of the availability of data. AR is a major cause of mortality across the globe, finally Drug-resistant *Vibrio cholerae* is a problem that needs to be dealt with as soon as possible, and road-map tactics of the Centre for Disease Control (CDC) and Global Antimicrobial Surveillance System (GLASS) should be used to control it.

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