Systematic Review on the Antibacterial Resistance of Vibrio Cholerae

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INTRODUCTION

Vibrio cholerae causes acute rice watery stool disease that affect human beings 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 challenges 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.
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 1: Systematic Literature Search](image)

**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

![Figure 2: Distribution of articles published on resistance strains of *Vibrio cholerae* between January 2000 to October 2015](image)
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, Nalidixic Acid and Streptomycin (Dixit et al., 2014) *V. cholerae* pathogens genes research has demonstrated high prevalence in spreading of toxS, toxA 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*

<table>
<thead>
<tr>
<th>SN</th>
<th>Year</th>
<th>Country</th>
<th>Strain</th>
<th>Antibiotic resistant</th>
<th>Mechanism</th>
<th>Laboratory methods</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2018</td>
<td>Lima (Peru)</td>
<td><em>Vibrio alginolyticus</em></td>
<td>penicillin group</td>
<td>mutT gene</td>
<td>PCR</td>
<td>(Sulca et al., 2018)</td>
</tr>
<tr>
<td>2</td>
<td>2014-2015</td>
<td>Ghana</td>
<td>classical <em>V. cholera</em> 01 biotype El Tor, serotype Ogawa</td>
<td>Trimethoprim/sulfamethoxazole, ampicillin and ceftriaxone</td>
<td>SXT, CtxAB and Tep gene</td>
<td>ND</td>
<td>(Teglo and Sewurah, 2018)</td>
</tr>
<tr>
<td>3</td>
<td>2017</td>
<td>China</td>
<td>O1 and O139</td>
<td>Macrolides:Azithromycin</td>
<td>IncA/C plasmid, mphR-mrx-mph(K) and mel-mph2</td>
<td>minimum inhibitory concentration (MIC)</td>
<td>(Yu et al., 2012)</td>
</tr>
<tr>
<td>4</td>
<td>2012-2015</td>
<td>Mozambique</td>
<td>El Tor <em>Vibrio cholerae</em> 01</td>
<td>Sulphamethoxazole-trimethoprim, Trimethoprim</td>
<td>CTX genotype</td>
<td>Culture, standard biochemical tests, serotypes by antisera agglutination and PCR.</td>
<td>(Dengo-Baloi et al., 2017)</td>
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<tbody>
<tr>
<td>5</td>
<td>2017</td>
<td>India</td>
<td><em>Vibrio cholerae</em></td>
<td>Amoxicillin, ampicillin, chloramphenicol, doxycycline, erythromycin, and tetracycline.</td>
<td>MurB protein</td>
<td>molecular docking</td>
<td>(Ragunath n et al., 2018)</td>
</tr>
<tr>
<td>6</td>
<td>2016</td>
<td>Mexico</td>
<td><em>V. alginolyticus</em></td>
<td>beta-lactams Antimicrobial, cephalotin, amikacin, cefotaxime, and pefloxacin,</td>
<td>proA, wza, vopD, vopB, hcp, vasH and vgrG genes</td>
<td>PCR amplification</td>
<td>(Hernandez-Robles et al., 2016)</td>
</tr>
<tr>
<td>7</td>
<td>2017</td>
<td>Thailand</td>
<td><em>V. cholerae</em> O1 and non-O1/non-O139</td>
<td>ND</td>
<td>horizontal gene transfer (HGT) of the SXT element</td>
<td>ND</td>
<td>(Mal a et al., 2016)</td>
</tr>
<tr>
<td>8</td>
<td>2012-2013</td>
<td>Iran</td>
<td><em>V. cholerae</em></td>
<td>streptomycin, trimethoprim, cotrimoxazole, tetracycline and minocycline</td>
<td>Class 1 integron, SXT element CarR confers polymyxin Bregulating expression of the almEFG genes, glycine and diglycine modification of lipid A.</td>
<td>(Rezaie et al., 2017)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2015</td>
<td>German</td>
<td><em>Vibrio vulnificus</em> and <em>Vibrio cholerae</em> non-O1/non-O139</td>
<td>aminopenicillins and aminoglycosides</td>
<td>Carabepenemases</td>
<td>Biochemical testing</td>
<td>(Bier et al., 2015)</td>
</tr>
<tr>
<td>10</td>
<td>2008</td>
<td>South Africa</td>
<td><em>Vibrio cholerae</em> O1 serotype Ogawa</td>
<td>Quinolone</td>
<td>mutations in the quinolone resistance-determining regions of GyrA (Ser83-Ile), ParC (Ser85-Leu), and produced TEM-63 β-lactamase.</td>
<td>PCR</td>
<td>(Ismail et al., 2011)</td>
</tr>
<tr>
<td>11</td>
<td>1970-1998</td>
<td>Russia</td>
<td><em>Vibrio cholerae</em> El Tor</td>
<td>Tetracycline and Chloramphenicol</td>
<td>ND</td>
<td>ND</td>
<td>(Savel'ev et al., 2010)</td>
</tr>
<tr>
<td>12</td>
<td>1998</td>
<td>Ethiopia</td>
<td><em>V. cholerae</em> O1</td>
<td>Ampicillin, chloramphenicol, streptomycin, sulfamethoxazole and trimethoprim</td>
<td>IncC plasmid</td>
<td>Random Amplified Polymorphic DNA and Disk diffusion (KBDDT)</td>
<td>(Scrascia et al., 2009)</td>
</tr>
</tbody>
</table>
**Table 1: Continued**

<table>
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</thead>
<tbody>
<tr>
<td>13</td>
<td>2005</td>
<td>Cameroun</td>
<td>V. cholerae O1</td>
<td>Cotrimoxazole, Ampicillin</td>
<td>genes ctxA and ctxB</td>
<td>KBDDT, pulsed field gel electrophoresis patterns.</td>
<td>(Ngandjio et al., 2009)</td>
</tr>
<tr>
<td>14</td>
<td>2010</td>
<td>Nigeria</td>
<td>V. cholerae O1 El Tor biotype</td>
<td>Ciprofloxacin and chloramphenicol</td>
<td>SXT element, gyrA (Ser83Ile), parC (Ser85Leu) allelesCTX phage, TCP rstR(ElTor), ctxB-7 and tcpA(CIRS) alleles</td>
<td>standard culture methods by disk diffusion method and E-test, multilocus sequence analysis and pulsed-field gel electrophoresis.</td>
<td>(Marin et al., 2013)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The review found that all the 77 articles reported resistance to one or more Antibacterials in *Vibrio cholerae* O1 El Tor Ogawa between January 2000 to October 2018 and most of the Antibacterials 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 the 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 findins 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.

**REFERENCES**


