Plasmid Mediated Quinolone Resistance in Enterobacteriaceae: A Review

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Abstract: Antimicrobial resistance (AMR) is a global problem which is hindering treatment of bacterial infections. Evaluation of the prevalence of PMQR genes is important in terms of selection of antibiotics for treatment options. The aim of this work is to review prior data on PMQR with a view of evaluating the prevalence of PMQR genes in Enterobacteriaceae and to identify the knowledge gap if any. This systematic review was conducted in line with the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) guideline. Pubmed and Ajol online databases were primarily searched for relevant articles. The eligible articles were evaluated using a set of eligibility criteria. Ninety five (95) full text article were selected for screening using the eligibility criteria. Twenty four (24) articles with majority emanating from Iran and China and only one article reporting study carried out in Nigeria where selected for qualitative synthesis for this review. The PMQR genes include qnr, aac (6') Ib-cr and qepA gene. 46% of the articles focused on only one type of PMQR gene but not any of the two or three together while 54% screened for more than one type of the PMQR genes. Most frequently isolated PMQR gene is Qnr gene (96%) followed by Aac (6')Ib-cr gene (46%) and QepA gene (13%). High occurrence of QepA gene (18.7%) was reported in the only study in Nigeria.The review showed a high prevalence of PMQR genes especially in Nigeria. With the limited studies evaluating the burden of PMQR there is also the need for the establishment of antibiotics surveillance policies especially in Nigeria.

Key words: Plasmid-Mediated Quinolone Resistance, Enterobacteriaceae, *aac(6')-Ib-cr", "qnr", "qepA"* "Antibiotic resistance

INTRODUCTION

Antimicrobial resistance (AMR) is a global problem which is hindering treatment of bacterial infections, making many aspects of modern medicine less effective (CDC, 2013; Buckner *et al*., 2018). AMR has become one of the major threats facing society because of the increase in the number of antimicrobial-resistant (AMR) bacteria (O'Neill, 2016). Among all of the bacterial resistance problems, gram-negative pathogens are particularly worrisome, because they are becoming resistant to nearly all drugs that would be considered for treatment (CDC, 2013). The most serious gram-negative infections are healthcare-associated, and the most common pathogens are Enterobacteriaceae, *Pseudomonas aeruginosa, and Acinetobacter* spp (CDC, 2013; Ruiz *et al*., 2017).

There are various strategies for the control of AMR, these are: preventing infections and preventing the spread of resistance, tracking resistant bacteria, improving the use of today's antibiotics by stewardship, promoting the development of new antibiotics and developing new diagnostic tests for resistant bacteria, anti-plasmid and plasmid curing, use of non-antibiotics strategies like bacteriophages, probiotics and anti-virulence agents (CDC, 2013; Tillotson, 2015; Ruiz *et al*., 2017; Buckner *et al*., 2018).

One of the major class of antimicrobial agents that have been used is the Quinolones. Fluoroquinolones are broad-spectrum antibiotics that are often given orally, making them convenient to use in both inpatients and outpatients and are currently among the most heavily prescribed antimicrobials in the world (Grillon *et al.,* 2016). Quinolones inhibit bacterial DNA synthesis by interfering with the action of DNA gyrase and topoisomerase IV (Drlica and Zhao, 1997; Chen *et al*., 1999; Drlica *et al.,* 2008).

However, mechanisms of resistance to quinolones that have been described include target modification (topoisomerase and DNA gyrase mutations), efflux pumps, Qnr (plasmid-mediated gene encoding quinolone resistance), porins, and quinolone-modifying enzymes with reported PMQR genes including Qnr, Aac(6')-ib-cr, and the QepA genes (Martinez-Matinez *et al.,* 1998; Robicsek *et al.,* 2006; Perichon *et al.,* 2007; Rice, 2012; Ogbolu et al., 2016).

Global human use of antibiotics increased by 36% between 2000 and 2010 (Van Boeckel *et al*. 2014) and there are many non-human uses of antimicrobials including in food animals for growth promotion, veterinary treatment and aquaculture (Cabello 2006; Meek *et al.,* 2015; Van Boeckel *et al*. 2015). The abuse and uncontrolled use of antibiotics has resulted in the emergence and spread of resistant bacteria including Enterobacteriaceae (Ruiz *et al*., 2017; WHO, 2018).

Studies have reported cross-resistance among the fluoroquinolones (Tankovic *et al*., 1999; Soussy *et al*., 2003; CDC, 2013; Grillon *et al*., 2016). Plasmid-mediated quinolone resistance (PMQR) genes conferring low levels of quinolone resistance may provide a favourable background where the selection of additional chromosomally-encoded quinolone resistance mechanisms can take place (Poirel *et al*., 2008).

A systematic review will help in understanding the scale of emerging resistance, new resistance determinants, and their mode of transfer to inform policy direction on the use of antimicrobial agents. It will also help to assess the level of occurrence of PMQR genes and further help to compare reported evidences of PMQR genes among Enterobacteriaceae.

The aim of this work is to review prior data on PMQR with a view of evaluating the prevalence of PMQR genes in Enterobacteriaceae and to identify the knowledge gap if any.

MATERIAL AND METHODS

This was a systematic review of plasmid-mediated quinolone resistance among Enterobacteriaceae. This systematic review was conducted in line with the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) guideline (Moher *et al.,* 2009).

Search Strategies

PubMed and African Journals Online (AJOL) databases were primarily searched for relevant articles. Google scholar was also searched for additional studies. Search terms used for this systematic review are shown in figure 1. Figure 2 illustrates the flow diagram of study selection. The literature search included all accessible articles on Plasmid-mediated quinolone resistance published on the databases used for the study from year 2005 to 2019. Duplicate references and publications reporting the same data were excluded. The full texts of potentially relevant studies that were accessible were obtained and the reports were scrutinized independently. The enlisted articles were also screened for further eligibility.

Study Selection and Criteria

The criteria for the inclusion and exclusion of the studies were established by the investigators before the literature was reviewed;

Inclusion Criteria

Included in this review were specifically studies reporting Plasmid-Mediated Quinolone Resistance encoded by *qnr gene, qepA gene* and/or *aac (6')-Ib-cr gene* from Enterobacteriaceae isolates. The review focused on studies reporting PMQR occurring among Enterobacteriaceae isolates from Clinical samples and studies that were conducted in human population. The review also included studies that reported the pattern of resistance to quinolones by the Enterobacteriaceae isolates assessed by antibiotic resistance testing. Studies that stated clearly the means of identification of the isolates were also included.

Exclusion Criteria

Studies that did not state clearly means of identification of isolates were excluded. In addition, studies that did not evaluate PMQR in humans were also excluded. Other exclusion criteria are duplicate and overlapping studies, review articles, meta-analysis or systematic reviews and articles that are only available in abstract form.

Search terms used in the systematic review

"Plasmid-Mediated Quinolone Resistance", "Quinolone Resistance ", "Enterobacteriaceae", "Quinolones", "Mechanism of Quinolone Resistance", "*aac(6')-Ib-cr", "qnr", "qepA"* "Antibiotic resistance"

Data Extraction

A database was created in which the study location, study period, prevalence of PMQR, isolated Enterobacteriaceae as reported by the reviewed studies were recorded where applicable (Table 1).

Assessment of Study Quality

The quality of the included studies was independently assessed using the Joanna Briggs Institute Checklist for Studies Reporting Prevalence Data (Munn, 2015). The prevalence checklist consists of nine (9) inquiries in which the reviewers answered questions on the selected articles on an individual basis according to the evidence. The Yes answer to each question got a point; evidently, the scores ranged from zero to nine. Afterwards, studies that attained greater than 5 points were included in this study.

Questions

1. *Was the sample frame appropriate to address the target population?*
2. *Were study participants sampled in an appropriate way?*
3. *Was the sample size adequate?*
4. *Were the study subjects and the setting described in detail?*
5. *Was the data analysis conducted with sufficient coverage of the identified sample?*
6. *Were valid methods used for the identification of the condition?*
7. *Was the condition measured in a standard, reliable way for all participants?*
8. *Was there appropriate statistical analysis?*
9. *Was the response rate adequate, and if not, was the low response rate managed appropriately?*

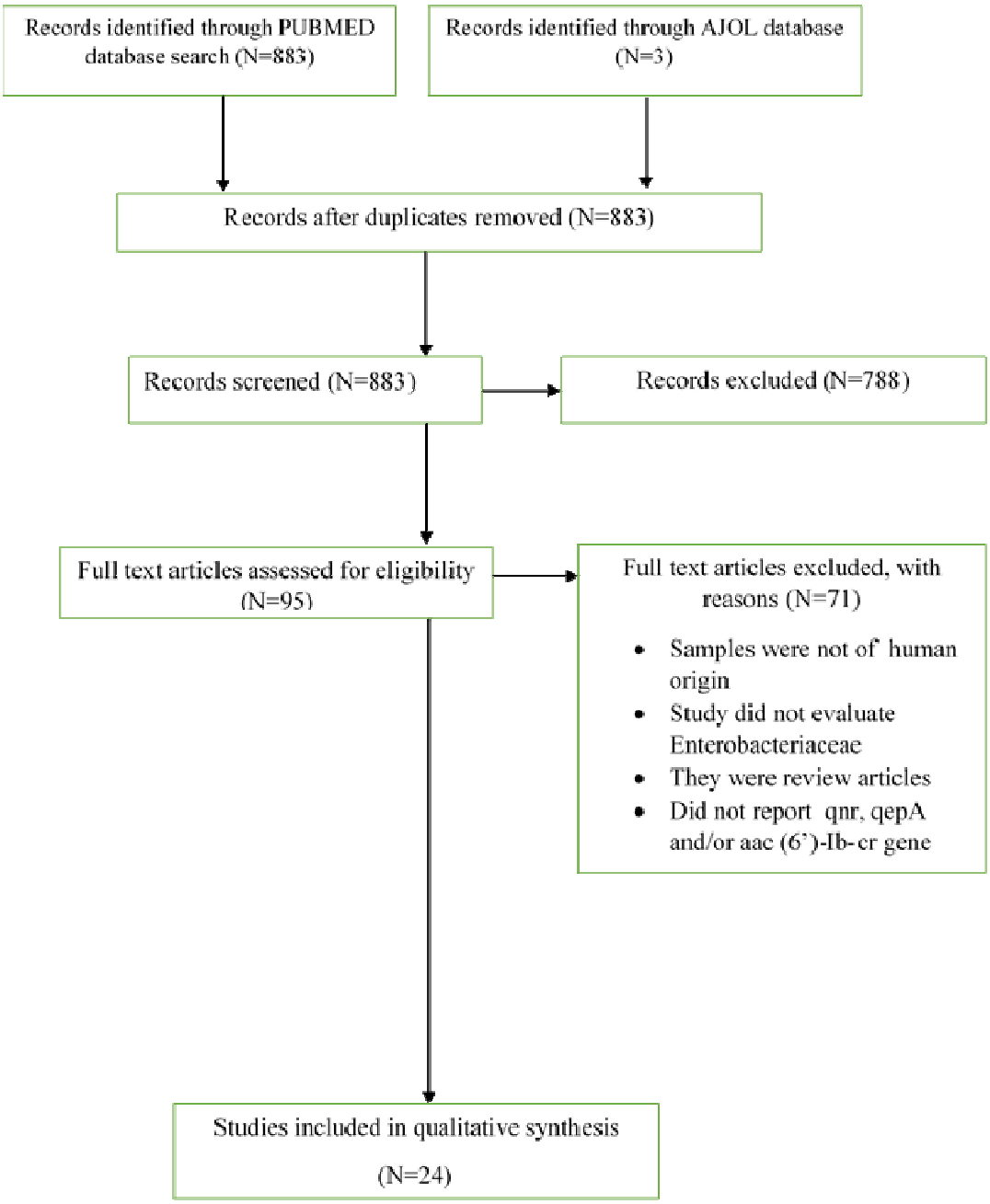

Figure 2: Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) Summary of Data Selection

RESULTS

Literature Search and Characteristics of the Studies Included in the Systematic Review

A total of 886 records were identified from the search of the electronic databases (PUBMED and AJOL). After the removal of duplicate studies, 883 full-text articles were screened among which 97 studies were potentially eligible. However, only 24 articles where finally selected for qualitative synthesis for this review according to the aforementioned inclusion criteria. The majority of the reviewed articles were from Iran and China. Only one article reporting study carried out in Nigeria was accessible (Table 1).

Table 1: Summary of the reviewed eligible articles on PMQR among Enterobacteriaceae Isolate

S/N	Location of Study	Period of Study	Prevalence (%)			Associated Organisms			References
			Qnr	*QepA*	*Aac(6')-Ib-cr*	*Qnr*	*QepA*	*Aac(6')-Ib-cr*	
1	Turkey	1 Year	6.4			*E. coli* *K. pneumoniae*			Oktem *et al.* (2008)
2	China	7 years	3.9		49.2	*E. coli*		*E. coli*	Zhou *et al.* (2011)
3	Greece	1 months	10			*E. coli*			Vasilaki *et al.* (2008)
4	China	5 months	1.3			*E. cloacea* *E. coli* *Citrobacter spp*			Xu *et al.* (2007)
5	Europe	1 year	0.3			*E. coli*			Mammeri *et al.* (2005)
6	Morocco	6 Months	36			*E. coli* *K. pneumoniae* *E. cloacea*			Bouchakour *et al.* (2010)
7	United States	3 years	11.1			*K. pneumoniae*			Wang *et al.* (2004)
8	Japan	4 years		0.3			*E. coli*		Yamane *et al.* (2008)
9	China	1 year	16.3			*E. cloacea*			Wu *et al.* (2007)
10	China	2 years	5			*E. coli* *K. pneumoniae*			Wang *et al.* (2008)
11	Vietnam	1 year	67	0.5	14	*E. coli* *K. pneumoniae* Others	*E. coli*	*E. coli* *K. pneumoniae* Others	Vien *et al.* (2009)
12	Iran	1 Year	60.2			*E. cloacea*			Peymani *et al.* (2016)
13	Spain	1 year 10 months	21		2.6	*Enterobacter* spp		Enterobacter spp	Cano *et al.* (2009)
14	Iran	1 year	39.5			*K. pneumoniae*			Peymani *et al.* (2015)

Table 1 Continue

S/N	LOC	Period of Study	Prevalence (%)			Associated Organisms			References
			Qnr	*QepA*	*Aac(6')-Ib-cr*	*Qnr*	*QepA*	*Aac(6')-Ib-cr*	
15	China	5 Months	7.4		8.1	KP *E. coli* *P. mirabilis*		KP *E. coli* *P. mirabilis*	Jiang *et al.* (2014)
16	Kuwait	2 years	15.6		14.5	KP		KP	Vali *et al.* (2015)
17	India	7 years	2.8		7.5	*Shigella*		Shigella	Bhattacharya *et al.* (2011)
18	Korea		14.7		3.9	*E. coli* KP		*E. coli* KP	Yang *et al.* (2014)
19	Iran	1 year	6.5		53	KP		KP	Eftekhar and Seyedpour (2015)
20	Iran	1 year	17		13	KP		KP	Eftekhar and Seyedpour (2014)
21	Iran	1 year	51.7		70	KP			Shams *et al.* (2015)
22	Iran	1 Year 5 months	2.9			*E. coli*			Rezazadah *et al.* (2016)
23	Sing	3 months	46.2			KP *E. coli*			Deepak *et al.* (2009)
24	Nigeria	Not Specified	28.2	18.7	25.4	KP *E. coli* *C. frueundii* *P. agglomerans*	KP *E. coli* *C. frueundii* *P. agglomerans*	KP *E. coli* *C. frueundii* *P. agglomerans*	Ogbolu *et al.* (2016)

Key: LOC = Location of study; Sing = Singapore, KP = *K. pneumoniae*

Five (21%) of the reviewed articles focused on prevalence of PMQR in different Enterobacteriaceae isolated from target study population (Xu *et al*., 2007; Vien *et al*., 2009; Bouchakour *et al*., 2010; Jiang *et al*., 2014; Ogbolu *et al*., 2016). Meanwhile, 79% focused on prevalence of PMQR in specific organisms isolated from study populations (Wang *et al*., 2004; Mammeri *et al*., 2005; Wu *et al*., 2007; Vasilaki *et al*., 2008; Oktem *et al*., 2008; Yamane *et al*., 2008; Wang *et al*., 2008; Cano *et al*., 2009; Deepak *et al*., 2009; Zhou *et al*., 2011; Bhattacharya *et al*., 2011; Yang *et al*., 2014; Eftekhar and Seyedpour, 2014; Peymani *et al*., 2015; Vali *et al*., 2015; Eftekhar and Seyedpour, 2015; Shams *et al*., 2015; Peymani *et al*., 2016; Rezazadah *et al*., 2016; Ogbolu *et al*., 2016).

Among the studies that considered Enterobacteriaceae in general, the different Enterobacteriaceae isolated include *Escherichia coli, Klebsiella pneumoniae, Pantoea agglomerans, Citrobacter freundii, Proteus mirabilis* and *Enterobacter cloacea*. *Escherichia coli* was isolated in all five (5) studies,

Phenotypic method was mostly utilized for the identification of the microorganisms in the laboratory according to Clinical Laboratory Standards Institute guideline.

Klebsiella pneumoniae was isolated in four (4) of the articles while *Enterobacter cloacea* was isolated in two (2) of the articles. Most frequently isolated Enterobacteriaceae are *Klebsiella pneumoniae* (58%) followed by *Escherichia coli* (50%), *Enterobacter cloacea* (16%), *Citrobacter freundii,* (8%), *Proteus mirabilis* (4%), *Shigella* spp (4%) and *Pantoea agglomerans* (4%). This agrees with the organisms that were most frequently isolated from the studies which considered Enterobacteriaceae in general.

Antibiotics susceptibility testing was conducted using quinolones and other antibiotics. The quinolones that were used in the reviewed studies include Ciprofloxacin, Nalidixic acid, Norfloxacin, Ofloxacin, Levefloxacin and Gatifloxacin. Ciprofloxacin was used in 22 (92%) of the reviewed study, Nalidixic acid was used in 16 (67%) of the reviewed studies while Norfloxacin, Levefloxacin, Ofloxacin and Gatifloxacin were used in 6 (25%), 9 (38%), 5 (21%) and 19 (8%) of the reviewed studies respectively.

The antibiotic susceptibility patterns of all isolates were determined by disc diffusion method in Mueller–Hinton agar. The disc diffusion technique was employed in 58% of the reviewed study for the assessment of antibiotics susceptibility study. Resistant isolates were selected for minimum inhibitory concentrations (MICs) using fluoroquinolone drugs, MIC testing was performed using the agar dilution or E-test strip methods according to stated guidelines. Sixteen (67%) of the studies included in this review determined the MIC of the isolates to the quinolones, 50% assessed the MIC of the isolates using the E-test strips technique while 69% assessed the MIC of the isolates to the quinolones using the agar dilution techniques. One (4%) of the studies determined the MIC of the isolates using the broth microdilution technique.

Polymerase chain reaction (PCR) was used to amplify plasmid-mediated quinolone resistance (PMQR) genes and to screen isolates for the gene of interest using primers. The PMQR genes screened for among the reviewed articles include *qnr, aac (6') Ib-cr and qepA* gene. Eleven (46%) of the articles focused on only one type of PMQR gene i.e either *qnr* or *aac (6') Ib-cr* or *qepA* gene but not any of the two or three together (Wang *et al*., 2004; Mammeri *et al*., 2005; Wu *et al*., 2007; Xu *et al*., 2007; Oktem *et al*., 2008; Vasilaki *et al*., 2008; Wang *et al*., 2008; Bouchakour *et al*., 2010; Peymani *et al*., 2015; Peymani *et al*., 2016; Rezazadah *et al*., 2016), while 54% screened for more than on type of the PMQR genes (Yamane *et al*., 2008; Vien *et al*., 2009; Deepak *et al*., 2009; Cano *et al*., 2009; Zhou *et al*., 2011; Jiang *et al*., 2014; Yang *et al*., 2014; Eftekhar and Seyedpour, 2014; Vali *et al*., 2015; Eftekhar and Seyedpour, 2015; Shams *et al*., 2015; Ogbolu *et al*., 2016). However Six (6) of the reviewed articles considered PMQR genes in relation to the existence of other genes. The genes include *gyrA* and *parC* (Vien *et al*., 2009; Bhattacharya *et al*., 2011)*, intII* and *ISCR1* (Cano *et al*., 2009)*,* Cephalosporinases (beta - lactamases) - $bla_{SHV,}$ and bla_{TEM} (Vali *et al*., 2015) *oqxAB* (Yang *et al*., 2014) and beta - lactamase bla_{CTX-M} (Shams *et al*., 2015).

PMQR genes have been reported to occur among ESBL producing isolates. Nine (38%) of the reviewed articles focused on the occurrence of PMQR genes among ESBL producing isolates (Mammeri *et al*., 2005; Xu *et al*., 2007; Wu *et al*., 2007; Wang *et al*., 2008; Oktem *et al*., 2008; Bouchakour *et al*., 2010; Vali *et al*., 2015; Eftekhar and Seyedpour, 2015; Shams *et al*., 2015). ESBL production among isolates was screened phenotypically using appropriate beta-lactams. Wang *et al*., 2008; Vien *et al*., 2009; Deepak *et al*., 2009; Cano *et al*., 2009; Bouchakour *et al*., 2010; Zhou *et al*., 2011; Bhattacharya *et al*., 2011; Yang *et al*., 2014; Eftekhar and

The most frequently isolated PMQR gene is *Qnr* gene 96% (Wang *et al*., 2004; Mammeri *et al*., 2005; Xu *et al*., 2007; Wu *et al*., 2007; Oktem *et al*., 2008; Vasilaki *et al*., 2008; Seyedpour, 2014; Jiang *et al*., 2014; Peymani *et al*., 2015; Vali *et al*., 2015; Eftekhar and Seyedpour, 2015; Shams *et al*., 2015; Rezazadah *et al*., 2016; Peymani *et al*., 2016; Ogbolu *et al*., 2016) followed by the *Aac (6')Ib-cr* gene 46% (Vien *et al*., 2009; Cano *et al*., 2009; Zhou *et al*., 2011; Bhattacharya *et al*., 2011; Jiang *et al*., 2014; Yang *et al*., 2014; Eftekhar and Seyedpour, 2014; Eftekhar and Seyedpour, 2015; Shams *et al*., 2015; Ogbolu *et al*., 2016) and then the *QepA* gene 13% (Yamane *et al*., 2008; Vien *et al*., 2009; Ogbolu *et al*., 2016).

The ability for these PMQR determinants to be transferred from one isolate to another was determined by conjugation experiment. From the review, 54% of the reviewed studies carried out the conjugation experiment (Wang *et al*., 2004; Mammeri *et al*., 2005; Xu *et al*., 2007; Wu *et al*., 2007; Oktem *et al*., 2008; Vasilaki *et al*., 2008; Yamane *et al*., 2008; Cano *et al*., 2009; Zhou *et al*., 2011; Yang *et al*., 2014; Jiang *et al*., 2014; Ogbolu *et al*., 2016) and *Escherichia coli* was used as the recipient for all. The occurrence of Plasmid-mediated quinolone resistance (PMQR) in the reviewed studies was reported to be high in 67% of the reviewed studies and Low in 33% of the reviewed studies.

DISCUSSION

This review focused on assessing the occurrence and prevalence of Plasmid-Mediated Quinolone resistance among Enterobacteriaceae isolates. From the report of this review, some articles examined the occurrence of PMQR in specific Enterobacteriacea while some others examined the occurrence of PMQR generally in Enterobacteriacea isolated from study population.

PMQR Genes isolated in Enterobacteriaceae

Qnr homologs can be found on the chromosome of many *γ-Proteobacteria, Firmicutes*, and *Actinomycetales*, including species of *Bacillus, Enterococcus, Listeria*, and Mycobacteria, as well as anaerobes such as *Clostridium difficile* and *C. perfringens* (Jacoby and Hooper, 2013; Rodriguez-Martinez *et al.,* 2008). The small, non-conjugative plasmids that carry *qnrD* can be found in other Enterobacteriaceae but are especially likely to be found in Proteeae, such as *Proteus mirabilis, P. vulgaris,* and *Providencia rettgeri* (Zhang *et al.,* 2013). This agrees with the choice of microbial population of the reviewed study, majority of which included specific Enterobacteriaceae isolates while others included all Enterobacteriaceae that were isolated from the study population.

Study Duration in Relation to Prevalence

The different study durations employed by the studies included in this review ranged from 1 month to 7 Years. Prevalence of PMQR was not impacted by the duration of the study. A study by Yamane *et al*. (2008) conducted in Japan reported a prevalence of 0.3% during a period of 4 years while another study by Vasilaki *et al*. (2008) conducted in Greece reported a prevalence of 10% during a period of 1 month. Hence increase in prevalence of PMQR in Enterobacteriaceae may not be accurately defined based on length of the study.

Spread of PMQR Genes

PMQR genes have been found in a variety of Enterobacteriaceae, especially *Escherichia coli* and species of *Enterobacter, Klebsiella*, and *Salmonella* (Table 1). From the review, *Qnr* genes were isolated in all the articles reviewed at different prevalence rates and in different geographical locations (Table 1). This can possibly be due to the fact that the first isolated PMQR gene was *Qnr* gene with *QnrA* being the first horizontally transmissible element (Sumrall *et al.,* 2014),

conferring resistance to quinolones, and its spread to different regions over time. Studies have reported a *Qnr* gene as the most frequent PMQR gene (Robicsek *et al.,* 2006; Strahilevitz *et al*., 2007). All the reviewed studies isolated either *QnrA, QnrB, QnrC, QnrS* and/or a combination of them. However only one of the review studied isolation of the *QnrD* (Ogbolu *et al*., 2016).

The *QnrD* allele, which has previously been found in Salmonella isolates from China (Cavaco *et al.,* 2009), was identified in two Proteus isolates and one Pseudomonas isolate in a study by Ogbolu *et al*. (2011) in Nigeria. The *QnrVc* gene was not isolated in any of the reviewed studies among Enterobacteriaceae, but other studies have reported their occurrence in the Vibrionaceae family (Fonseca *et al.,* 2008; Kim *et al*., 2010; Kumar and Thomas, 2011; Fonseca *et al.,* 2013). There has not been any report of isolation of the *QnrVc* gene in Nigeria.

As reported in this review, *QepA* gene was isolated in only three studies (Yamane *et al*., 2008; Vien *et al*., 2009; Ogbolu *et al*., 2016). The prevalence rate of *QepA* in the above mentioned studies were 0.3% in Japan, 0.5% in Vietnam and 18.7% in Nigeria respectively. The occurrence of *QepA* was high in Nigeria from the reviewed study which is a cause for concern. Studies have reported low occurrence of *QepA* gene in different countries ranging from 0.3% – 4.6% (Yamene *et al*., 2008; Kim *et al*., 2009; Deng *et al*., 2013) and these reported prevalence is not as high as the 18.7% prevalence reported by Ogbulu *et al*. (2016) in Nigeria. A study by Kim *et al.* (2013) reported no isolation of *QepA* from the study isolates.

Survey of PMQR in Nigeria

Studies to assess the prevalence of PMQR in Nigeria are limited especially the occurrence of PMQR in isolates from human origin. Most studies in Nigeria focused on assessing the prevalence of PMQR in animals and environmental sources (Fortini *et al.,* 2011; Ajayi *et al*., 2012; Nsikan *et al.,* 2019). The prevalence of PMQR in Nigeria as reported by Ogbolu *et al*. (2016) among the reviewed studies was high (Table 1). The reported organisms associated with the PMQR were *K. pneumoniae, E. coli, Citrobacter frueundii,* and *Pantoea agglomerans*. In the study *Qnr, Aac (6')-Ib-cr* and *QepA* genes where also isolated from human sources and resistance to quinolone was seen with Ciprofloxacin and Levefloxacin. Ciprofloxacin is known to be very effective and commonly used drug in the treatment of Enterobacteriaceae infections, an increasing trend of resistance to the drug has been noted. Consequently this resistance leads to failure in treatment, increased morbidity, mortality and cost of health care (CDC, 2013). The reported high resistance could be attributed to quinolones being the drugs of choice for treatment of most Enterobacteriaceae related infections.

CONCLUSION AND RECOMMENDATION

The review showed that there are limited studies evaluating the burden of PMQR in Nigeria. It also suggests the need for the establishment of antibiotics surveillance policies in Nigeria. PMQR although confers low level of resistance will provide favourable backgrounds for increased chromosomally mediated quinolone resistance. The single study reviewed in Nigeria reported high prevalence for PMQR genes and also the three (3) genes Qnr, Aac(6')-Ib-cr and QepA were reported in the study population, thereby suggesting a possible prevalence of these genes in other regions of Nigeria. It is necessary for the control strategies especially antimicrobial stewardship to be adopted in Nigeria with the introduction of policies and sensitizations to help drive them.

Data on antibiotic use in human healthcare are not systematically collected hence routine systems of reporting and benchmarking antibiotic use wherever it occurs need to be piloted and scaled nationwide.

Survey of plasmid mediated quinolone resistance will help to determine the magnitude of the problems caused by PMQR in terms of infection control and guide the strategies for control to be enacted to avoid escalation of resistance and dissemination problem especially in Nigeria.

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