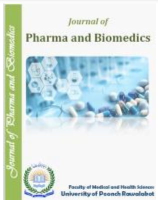

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Prevalence of Colistin Resistance: A Worldwide Meta-Analysis

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ABSTRACT

Background: Colistin is an ancient class of antibiotic which works by rupturing the bacterial cell membrane. Bacteria have developed resistance against colistin antibiotic by various Lipopolysacchride modification mechanisms. Colistin has long been used as treatment option but its resistance is emerging in developing countries. **Methodology:** A systematic meta-analysis was performed to describe the prevalence of colistin resistance in different regions of the World. Web based search was conducted on platforms like Google scholar, PubMed, Scopus, Web of Science. Data was extracted from 2009-2019. **Results:** A total of 286 articles were identified from different electronic databases from which only 143 articles were selected based on our inclusion criteria. The overall pooled proportion of colistin resistance in different regions of the World was 0.21 (CI 95%: 0.20-0.21). The overall significant heterogeneity was (I^2= 99.54%, $p < 0.001$), significant ES=0 (z=62.53, $p < 0.001$). Bacterial isolates like *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Escherichia coli* showed highest rates of colistin resistance. **Conclusion:** The performed meta-analysis showed the rates of colistin resistance worldwide. Asia showed high rates of Colsitin resistance. *Acinetobacter baumannii*, *Klebsiella pneumoniae, Escherichia coli* and *Pseudomonas aeruginosa* were the most prevalent isolates. So, an appropriate and regular surveillance program is required and implementations of effective strategies is also needed that address colistin resistance and helps in controlling the spreading of colistin resistance.

Keywords: Colistin, Prevalence, *Metaprop*, Meta-Analysis, Lipopolysacchride, Heterogeneity, Proportion.

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INTRODUCTION

Antibiotic resistance is the ability of bacteria to protect them from antibiotic attack (1). The last resort of antibiotic to treat infections caused by *Enterobacteriacea* (MDR) due to resistant caused by carbapenemase is colistin (2). Colistin belongs to polymyxin class of drugs and is a cyclic poly-cationic heptapeptide (3). It performs its action by attacking on the lipopolysaccharide membrane of gram-negative bacteria. Positively charged residues of colistin are attracted towards lipid portion of lipopolysaccharide due to presence of negatively charged phosphate group (4, 5). Lipid A binds with the calcium and magnesium divalent cations under normal conditions. This results in the formation and bridging of lipopolysaccharide membrane of gram negative bacteria. Colistin binding affinity with lipid A negative charged group is three times higher than divalent cations of calcium and magnesium therefore colistin compete with these ions and binds to the lipid A. This result in displacement of divalent cations from lipid A. Colistin then reaches in the periplasmic space which termed as self-promoted uptake mechanism (4-6).

Resistance to colistin is rare worldwide. Isolates of colistin resistance are *Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii* and *Pseudomonas aeruginosa* (7).

Colistin resistance is causes by several mechanisms. The main cause of colistin resistance is lipopolysaccharides (LPS) modification. There are diverse routes of LPS modification like modification in the outer membrane i-e porins causes the reduction of LPS negative charge, efflux pump overexpression, capsule polysaccharide overexpression (8), and enzymatic resistance. *Bacillus polymyxa* strains produces colistinase seems to produce resistance to colistin (9). Lipopolysaccharide remodeling in bacterial outer membrane is caused by variations in two regulatory systems, *PhoPQ* and *PmrAB* (10). These genes and operons are responsible for causing mutations in lipopolysaccharides. On the other hand presence of plasmid-mediated genes (*mcr* genes) in different isolates directly produces colistin resistance without any other mechanism of resistance (5).

Isolates of Enterobacteriacea carrying genes of carbapenemase like *NDM (NDM1, NDM5, NDM9), VIM1, OXA48 and KPC2* also contains *mcr* gene (11). Sometimes colistin resistance is caused by the overexpression of *MexAB-OprM* and *KpnEF* efflux pump (12). Spread of colistin resistance in different regions of the world is a result of increase usage of this antibiotic to treat infections caused by bacteria like *Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli* and *Klebsiella pneumoniae.* Polymyxins has greater rate of resistance in South-East Asia including Korea, Singapore and Mediterranean Sea. In these areas colistin resistance is steadily rising. To stop the growth and spread of colistin resistance, there is an urgent need for efficient infection control methods and prevention. Some nations (such as Japan and South Africa) do not acquire colistin, it is available in its parenteral formulation (as Colistin Methanesulphonate) in few regions of the world like Europe and Australia, while in other regions (such as the Brazil, United States, Singapore, and Malaysia), clinicians may choose between colistizn and the parenteral formulation of *Bacillus* polymyxin (13). The purpose of this study is to aware people about distribution and prevalence of colistin resistance worldwide and to check comparative and year wise prevalence in different continents.

METHODOLOGY

Research Design

This meta-analysis research includes different studies reported from different regions of the world. It is a web-based search, which used key words like “colistin resistance worldwide”, “colistin resistance genes”, “colistin resistance bacterial isolates”.

Study Duration

This search was conducted on electronic databases platforms like Pub-Med, Google scholar, web of science and Scopus and included 143 articles from Jan 2009-Dec 2019. Articles having English language were included in this study. We also screened references cited in 143 articles to check other relevant publications.

Selection Criteria

Three steps were used to select the articles. In first step, abstracts and titles of all the articles were checked excluding the irrelevant articles. In second step, selected articles were again checked with full details. In third step, selected articles were evaluated for meta-analysis by using STATA version 14.1 software.

Inclusion Criteria

Articles were chosen using the following criteria: studies that show prevalence of colistin resistance worldwide, bacterial strains from human samples, relevant national or international articles, and studies showing phenotypic detection methods of colistin resistance and studies that uses molecular detection techniques for colistin resistance genes variants (Figure 1).

Exclusion Criteria

Articles were excluded using following criteria: case reports, review articles, letters, posters, duplicate articles were removed, articles with incomplete information regarding phenotypic detection methods were removed, studies on antibiotics resistance other than colistin were removed, studies on different strains other than humans were removed (Figure 1).

Data Extraction

Data extracted from the selected articles included: country name, publication year, study year, author name, sample size, no. of resistance isolates, phenotypic detection methods including Minimum Inhibitory Concentration (MIC), Disk Diffusion Test, Broth Micro dilution, Epsilometric Test (E-test), Agar Dilution, VITEK and molecular detection techniques for colistin resistance gene variants (Table 1). Extraction and analysis of data were performed twice to remove any conflict (14).

Data Analysis

Metaprop command in STATA version 14.1 was used for statistical analysis to pool the published data for colistin resistance world-wide with computational accurate binomial 95% confidence intervals (CI). I^2 statistics was used to calculate statistical heterogeneity. Using p-values, the results of the meta-analysis were transformed into specified statistical tests. Using a random effects model, the pooled prevalence was estimated. In order to statistically assess publication bias, Begg tests and a funnel plot were used.

Table 1: Distribution of articles regarding Colistin Resistance.

Sr. No	Publication Year	Study Year	Authors	Sample Size	Colistin Resistant Isolates	Phenotypic Detection Test						Molecular Detection Test	
						MIC	Disk Diffusion	Broth Micro dilution	E test	Agar Dilution	VITEK	Genes	Most Prevalent genes
					Asia								
1	2009	2006-2007	Suh et al (15)	221	15	Yes	Yes	No	No	No	No	None	None
2	2011	2010	Gill et al (16)	180	69	No	Yes	No	No	No	No	unknown	Unknown
3	2011	2006-2007	Lee et al (17)	215	16	Yes	No	Yes	No	No	Yes	Unknown	Unknown
4	2011	2006-2007	Park et al (7)	33	7	Yes	No	No	No	No	No	*pmr*A, *pmr*B, *pmr*C	*pmr*B, *pmr*C
5	2012	2008-2011	Hamzeh et al (18)	260	241	No	Yes	No	No	No	No	unknown	Unknown
6	2013	2012	Bahador et al (19)	94	5	No	Yes	No	No	No	No	*bla*OXA-51	Unknown
7	2013	unknown	Choi et al (20)	113	51	No	Yes	No	No	No	No	*pmr*AB, *pho*PQ, *par*RS, *lpx*ACD	*Pmr*AB, *Pho*PQ and *Par*RS
8	2013	2009	Huangki et al (21)	253	184	No	No	No	No	Yes	No	none	None
9	2013	2008-2011	Lee et al (22)	213	75	No	No	No	Yes	Yes	Yes	Unknown	Unknown
10	2014	unknown	Naparstek et al (23)	46	3	No	Yes	No	No	No	No	*aac*(3)-II, *bla*KPC	*Bla*KPC
11	2014	unknown	Lee et al (24)	4	2	No	Yes	No	No	No	No	*flg*K, *pdx*B, *era*R, *pvd*Q, *pel*B, *pil*Y1, *cys*Q, *wbp*Z	Unknown
12	2014	Unknown	Kim et al (25)	5	4	No	Yes	Yes	No	No	No	*pmr*A, *pmr*B, *pmr*D, *pho*P, *pho*Q	Unknown
13	2014	2008-2011	GÜVEN et al (26)	252	4	No	Yes	No	No	No	No	Unknown	Unknown
14	2015	2013-2015	Mansoor et al (27)	634	231	No	Yes	No	No	No	No	none	None
15	2015	None	Choi et al (28)	6	3	No	No	Yes	No	No	No	*pmr*B, *pbgp*,	None
16	2015	2014	Nhung et al (29)	24	14	Yes	No	No	Yes	No	Yes	none	None
17	2015	None	Olaitan et al (30)	5	2	No	Yes	No	No	No	No	NDM-1	None
18	2016	2015-2016	Qadeer et al (31)	568	265	No	Yes	No	No	No	No	Unknown	Unknown
19	2016	2014	Bashir et al (32)	885	3	No	Yes	No	No	No	No	Unknown	Unknown

20	2016	unknown	Mu et al (33)	4	1	No	Yes	No	No	No	No	*pmr*B, *lpx*C, *lpx*A, lpxD	Unknown
21	2016	2014	Goli et al (34)	100	68	Yes	Yes	No	No	No	No	*mex*B, *mex*Y	Unknown
22	2016	None	Sonnevend et al (35)	75	8	No	No	Yes	No	No	No	*mcr*-1	*mcr*-1
23	2016	2010-2013	Crawford et al (36)	10	7	No	No	Yes	No	No	Yes	NDM-1	None
24	2016	None	Yilmaz et al (37)	56	29	No	No	Yes	No	No	No	none	None
25	2016	2014	Bashie et al (32)	885	3	Yes	Yes	No	No	No	No	none	None
26	2016	None	Cheng et al (38)	26	17	No	No	No	No	Yes	No	*crr*B	*Pmr*C
27	2016	2014-2015	Ni et al (39)	108	31	Yes	No	No	No	No	No	*mcr*-1, NDM-1	None
28	2016	2016	Zhaong et al (40)	151	17	No	No	No	No	Yes	No	*mcr*-1, *bla*NDM-1	*mcr*-1
29	2016	2008-2009	Sato et al (41)	514	4	No	No	No	No	No	No	*mcr*-1,*mcr*-2	*mcr*-1
30	2016	2015	Ye et al (42)	75	3	Yes	No	No	No	No	No	*mcr*-1	*mcr*-1
31	2016	2010-2013	Crawford et al (43)	10	7	No	No	No	No	No	Yes	NDM-1, OXA-48	*bla*NDM-1, *bla*OXA-48
32	2016	2012-2013	Kumar et al (44)	1590	122	No	Yes	No	No	No	No	*mrg*S	Unknown
33	2017	2015-2016	Qamar et al (45)	251	71	No	Yes	No	No	No	No	e *mgr*B, *pho*P/*pho*Q, *pmr*A, *pmr*B, *pmr*C, and *crr*ABC, *mcr*-1	Unknown
34	2017	2014-2015	Aydin et al (46)	1556	109	No	Yes	No	No	No	No	unknown	Unknown
35	2017	2015	Thong et al (47)	31	30	No	Yes	No	No	No	No	*pmr*A, *pmr*B, *pmr*C, *pmr*D, *pho*P, 83 *pho*Q, *mgr*B, *crr*A and *crr*B	Unknown
36	2017	2014-2016	Cizmeci et al (48)	76	19	No	Yes	No	No	No	No	*bla*NDM-1, *bla*IMP*,* *bla*VIM-like, *bla*GES-like,	Unknown

												*bla*GIM, *bla*SIM, *bla*SPM, *bla*KPC, *bla*OXA-4	
37	2017	unknown	Hua et al (49)	2	1	No	No	No	No	No	No	*lpx*C, *lpx*A, *Ipx*D, *pmr*AB, *vac*J, A1S_1983, *hep*A, A1S_3026, and *rsf*S *pld*A, *ttg*2C, *phe*S,	*Ipx*A, *pmr*B
38	2017	2013-2014	Soudeiha et al (50)	100	19	No	Yes	No	Yes	No	No	*bla*IMP, *bla*VIM, *bla*NDM, *bla*OXA−23−like, *bla*OXA−24−like, *bla*OXA−48, *bla*OXA−51−like, *bla*OXA−58−like, *bla*GES, *bla*KPC	*bla*OXA−23−like, *bla*OXA−24−like
39	2017	2014-2015	Luo et al (51)	1270	40	Yes	No	No	No	No	No	*mcr*, *mgr*B, *pmr*AB, *pho*PQ	*mcr*-1
40	2017	2015-2017	Haeili et al (52)	23	20	No	Yes	No	No	No	No	*mcr*-1, *mcr*-2, *mcr*-3, *mcr*-4, *pmr*A, *pmr*B, *pho*P, *pho*Q, *mgr*B	*mgr*B
41	2017	2016	Hu et al (53)	234	5	No	Yes	No	No	No	No	*mcr*-1,	Unknown

42	2017	None	Tada et al (54)	18	4	No	No	No	No	No	No	*bla*CTX-M-55, *bla*TEM-1, *bla*CTX-M-15, *bla*CTX-M-64, *bla*CTX-M-65, *mcr*-1	*mcr*-1
43	2017	2010-2016	Juhaz et al (55)	504	3	No	No	No	No	No	No	*mcr*-1	None
44	2017	2017	Tada et al (56)	4	1	No	No	No	No	No	No	*mcr*-1, *bla*SHV-14 *bla*TEM-1, *amp*C and *aad*A1	*mcr*-1
45	2017	Unknown	Chew et al (57)	76	48	No	No	Yes	Yes	No	Yes	*mcr*-1	*mcr*-1
46	2017	None	Chung et al (58)	4	2	Yes	No	No	Yes	No	No	*pho*P, *pmr*A, *par*R and *cpr*R	*arn*B
47	2017	None	Wang et al (59)	168	33	Yes	No	No	No	No	Yes	*mgr*B, *pmr*B, and *pho*Q, *mcr*-1	*mcr*-1
48	2017	2012-2013	MiWi et al (60)	77	9	Yes	No	No	No	No	No	*bla*IMP-6, *bla*VIM-2	*bla*IMP-6
49	2018	2016	Singh et al (61)	200	21	No	Yes	No	Yes	No	No	mcr-1, *bla*NDM-1	*mcr*-1
50	2018	2015-2016	Luxmi et al (62)	748	177	No	Yes	No	No	No	No	unknown	Unknown
51	2018	unknown	Forde et al (63)	267	1	No	Yes	No	No	No	No	*mcr*-1, TEM-1B, CTX-M-1, *aac*(3)-Iia, *gyr*A, *drf*A	*mcr*-1
52	2018	2014-2017	Eiamphungporn et al (64)	317	226	No	Yes	No	No	No	No	*mcr*-1	Unknown
53	2018	2013-2016	Farshadzadeh et al (65)	8	4	No	Yes	No	No	No	No	*pmr*B, *lpx*D, *pmr*A, *pmr*C, *lpx*A, *lpx*C	*pmr*B, *ipx*D
54	2018	2015-2016	Lu et al (66)	112	5	No	Yes	No	No	No	Yes	*mcr*-1,	*pmr*B

												*pho*Q, *pmr*B, *bla*SHV-1, *fos*A, *oqx*A, *oqx*B, *bla*SHV−3k86, *bla*SHV−11, *aph*(4)-Ia, *aac*(3)-IVa, *aph*(3')-Ia, *aad*A1, *aad*A2, *bla*CTX−M−14, *cml*A1, *dfr*A1, *dfr*A12, , *qnr*S1, *sul*1, *sul*2, *sul*3, *tet*(A)	
55	2018	2016	Guducuoglu et al (67)	13	9	No	Yes	No	No	No	No	NDM-1, OXA-48	Unknown
56	2018	2016	Haeili et al (68)	5	3	Yes	Yes	No	No	No	No	*bla*OXA-51-like, *pmr*A, *pmr*B, *lpx*A, *lpx*C, and *lpx*D	Unknown
57	2018	2015-2016	Cao et al (69)	1112	6	No	Yes	No	No	No	No	*mcr*-1, *bla*TEM-1B, *bla*CTX-M14, *bla*CTX-M132, *bla*CTX-M55, *bla*CTX-M123, *fos*A3, *fos*A, *aph*(4)-Ia,	*mcr*-1

												*sul*2, k2*oqx*A, *oqx*B, *aad*A2	
58	2018	2014-2016	Aghapour et al (70)	900	30	No	Yes	No	No	No	No	*mcr*-1,*crr*B	None
59	2018	2016-2017	Yonchanghu et al (71)	6497	49	No	No	No	No	No	No	*mcr*-3	*mcr*-3
60	2018	2015-2016	Moubareck et al (72)	13025	89	No	Yes	No	No	No	No	*bla*OXA-48-like, *bla*NDM	*bla*OXA-48-like
61	2018	2010-2013	Lomonaco et al (73)	10	7	No	Yes	No	No	No	Yes	*arm*A, *rmt*, *aad*A, *aac*(3)-, *aph*(3'')-Ib, *aph*(6)-Id, *aac*(6')-Ib, *aac*(6')-Ib-cr, *bla*CTX-M-15, *bla*SHV-, *bla*OXA-1, *bla*OXA-10, *bla*OXA-48, *bla*NDM-1, *bla*TEM-1, *bla*CMY-, *cml*A5, *cat*A1, *qnr*, *ble*, *mph, mrx, arr, sul,* *tet*(A), *dfr*A, *mgr*B, *pmr*B	*bla*CTX-M-15
62	2018	2014-2016	Li et al (74)	7249	7	No	Yes	No	No	No	Yes	*mcr*-1, *bla*NDM-5, *bla*KPC, *bla*CTX-	*bla*KPC, *bla*NDM

												M-65 and *bla*TEM-1B, *aph*(4)-Ia, *str*A, *str*B, *aad*A5, *aac*(3)-Iid, *oqx*A, *oqx*B, *fos*A, *mph*(A), *sul*1, *sul*2, *tet*(A), *dfr*A17	
63	2018	None	Okdah et al (75)	57	55	Yes	No	No	Yes	No	No	*mcr*-1	*mcr*-1
64	2018	2007-2016	Mustapha et al (76)	42	18	No	No	No	No	No	No	*pmr*A	*pmr*AB
65	2019	2017-2018	Hameed et al (77)	146	16	No	Yes	No	No	No	No	*mcr*-1	*mcr*-1
66	2019	2011-2017	Menekse et al (78)	210	60	Yes	Yes	No	No	No	No	NDM-1	OXA-48
67	2019	2017-2018	Messeron et al (79)	200	38	No	Yes	No	No	No	No	*mcr*-1	*mcr*-1
68	2019	2017	Cheong et al (80)	252	13	Yes	Yes	Yes	Yes	No	Yes	*pmr*A, *pmr*B, *pho*P, *pho*Q	*pho*Q
Europe													
69	2011	unknown	Wareham et al (81)	6	5	No	No	No	Yes	No	No	Unknown	Unknown
70	2011	unknown	Vila-farres et al (82)	15	13	No	No	Yes	No	No	No	none	None
71	2012	2010-2012	Capone et al (83)	97	89	No	Yes	Yes	No	No	No	*bla*KPC-3,VIM-1, CTX-M 1	*bla*KPC-3
72	2013	2009-2012	Huttner et al (84)	54	24	No	Yes	No	No	No	No	unknown	Unknown
73	2013	2008-2009	Camacho et al (85)	26	1	No	Yes	No	No	No	No	*omp*K36 porin, *mgr*B, *suf*B, *slt* gene, *bla*DHA-1	*bla*DHA-1
74	2013	None	Cannatelli et al (86)	2	1	Yes	No	No	Yes	No	No	*mgr*B	None
75	2013	2012	Tamayo et al (87)	66	16	Yes	No	No	No	No	No	*ipx*A,*ipx*D	*ipx*A
76	2014	2013-2014	Monaco et al (88)	197	191	No	Yes	No	No	No	No	*bla*KPC, *bla*NDM, *bla*VIM, and *bla*OXA-48	*bla*KPC
77	2014	2011-2012	Gaibani et al (89)	17	8	No	Yes	No	Yes	No	No	KPC3, *mgr*B	KPC3
78	2014	2008-2011	Agodi et al (90)	26	15	Yes	No	No	No	No	Yes	*bla*-OXA-	None

												51	
79	2014	2011	Cannateli et al (91)	2	1	Yes	No	No	No	No	No	*pmr*A,*pmr* B, *pmr*K	None
80	2014	None	Olivgeris et al (92)	254	28	No	Yes	No	Yes	No	Yes	None	None
81	2015	2014-2015	Hasman et al (93)	534	417	No	Yes	No	No	No	No	*mcr*-1, *aad*A5, *bla*CMY-2, *bla*CTX-M-55, *bla*TEM-1B, *cat*A1, *dfr*A17, *flo*R, *fos*A, *mph*(A), *rmt*B, *str*A, *str*B, *sul*1, *sul*2, *tet*(A)	*mcr*-1 gene
82	2015	2013	Olaitan et al (30)	267	2	No	No	No	No	No	No	*bla*CTX-M-2, mutant *pmr*B gene	*pmr*B gene
83	2015	Unknown	Wand et al (94)	12	11	No	Yes	No	No	No	No	*lpx*A, *lpx*C , *px*D, *pmr*B	*pmr*B
84	2015	Unknown	Formosa et al (95)	2	1	No	Yes	No	No	No	No	*lpx*A, *lpx*C, *msb*A, *pmr*A, *pmr*B, *pmr*D, *pho*P, *pho*Q, *arn*T, *mgr*B	*mgr*B
85	2015	unknown	Farre´s et al (96)	256	128	No	Yes	No	No	No	No	*lpx*D	*lpx*D
86	2015	2009-2013	Dafopoulou et al (97)	61	58	No	No	No	Yes	No	Yes	None	None
87	2015	2012-2014	Parisi et al (98)	399	97	Yes	No	No	No	No	Yes	NDM, OXA-48, KPC	CPKP
88	2015	2012-2014	Oikonoma et al (99)	1228	86	Yes	No	No	No	No	Yes	*ipx*A, *ipx*C	*pmr*A and *pmr*C
89	2016	2012-2015	Godbole et al (100)	24480	15	No	Yes	No	No	No	No	*mcr*-1, *bla*TEM-1,	*mcr*-1

90	2016	unknown	Gue´rin et al (101)	124	71	No	Yes	No	No	No	No	*bla*CTX-M-27, *bla*CTX-M-14, *bla*CMY-2, *qnr*S1 *pho*P, *pho*Q	Unknown
91	2016	2010-2012	Wintersdorff et al (102)	122	6	No	No	No	No	No	No	*mcr*-1, *qnr*A, *qnr*B, *qnr*S, CTX-M-2a, CTX-M-9a	*mcr*-1
92	2016	Unknown	Boll et al (103)	15	4	No	No	No	No	No	No	*lpx*A, *lpx*C, *lpx*D, *pon*A, *mrc*A	Unknown
93	2016	2014	Jayol et al (104)	972	42	No	Yes	No	No	No	No	*mgr*B, OXA-48, NDM, KPC, CTX-M-15, VIM, IMP	*bla* OXA-48
94	2016	None	Lopez-roja et al (105)	11	8	No	No	No	No	No	No	*pmr*A	None
95	2016	None	Wand et al (106)	6	5	Yes	No	No	No	No	No	*pho*P, *pho*Q, *pmr*D, *pmr*K, *pag*P, *smv*R, and *smv*A	*pmr*K, *pmr*D
96	2016	Unknown	Mavroidi et al (107)	135	19	No	Yes	No	No	No	No	*mgr*B, *bla*KPC	*bla*-KPC
97	2017	2015	Vourli et al (108)	117	108	No	Yes	No	No	No	No	*bla*OXA-51-like	Unknown
98	2017	None	Coppi et al (109)	74	61	No	No	Yes	No	No	No	*mcr*-1, *mcr*-2	*mcr*-1
99	2017	2015	Dona et al (110)	36	3	No	No	No	No	No	No	*mcr*-1, *mcr*-2	*mcr*-1
100	2017	1996-2016	Jayol et al (111)	25	24	No	Yes	No	Yes	No	No	Unknown	Unknown
101	2017	2014-2015	Otter et al (112)	40	25	No	No	No	No	Yes	No	*mgr*B, *pho*Q, NDM-1	*mgr*B

102	2017	2012-2015	Prim et al (113)	13579	91	Yes	Yes	No	No	No	No	*mcr*-1, *mcr*-2	*mcr*-1
103	2017	2014	Cannatelli et al (114)	10	4	Yes	No	No	No	No	No	*pmr*B, *mcr*-1	*pmr*B
104	2018	unknown	Lucas et al (115)	8	7	No	No	No	No	No	No	*pmr*A, *pmr*C, *ept*A	*ept*A
105	2018	unknown	Servat et al (116)	61	4	No	No	No	Yes	No	No	unknown	Unknown
106	2018	2016	Hannuksela et al (117)	176	93	No	Yes	No	No	No	No	*mcr*-1, *bla*TEM-1b, *bla*CMY-2, *qnr*B19, *dfr*A8, *str*A, *str*B, *sul*2, *flo*R	*mcr*-1
107	2018	2016	Principe et al (118)	3902	35	No	Yes	No	No	No	No	*mcr*-1, *bla* TEM	*mcr*-1
108	2018	2016-2017	Bianco et al (119)	19050	90	No	No	Yes	No	No	No	*mcr*-1	*mcr*-1,*mcr*-2
109	2018	None	Dortek et al (120)	17	9	No	No	No	No	No	No	*pmr*A, *pmr*B, *pmr*C	*pmr*C
110	2019	unknown	Girlich et al (121)	94	53	No	Yes	No	No	No	No	*pmr*B, *mgr*B, *mcr*-1, *mcr*-2, *mcr*-5, *mcr*-1.5, *mcr*-3.2, Δ*mgr*B	Unknown
North America													
111	2011	2010	Bogdanovich et al (122)	8	5	No	Yes	No	No	No	No	*bla*KPC-2	Unknown
112	2012	None	Jernigan et al (123)	12	10	Yes	No	No	No	No	No	None	None
113	2013	unknown	Snitkin et al (124)	37	4	No	No	No	No	No	No	*pmr*B, *ade*J, *fus*A, *pmr*A, *ade*B, *asp*S, *csu*E, NIA, *kdp*B, *p*IF, *hut*H, *feo*B, *wca*J, *ptk*, *lys*S, *rps*B,	*pmr*B

												*rel*A	
114	2013	2010-2011	Hong et al (125)	12	9	Yes	No	No	No	No	No	*bla*KPC-2, *bla*SHV-12, and *bla*TEM-1	None
115	2013	None	Lee et al (126)	2	1	Yes	No	No	No	No	No	None	None
116	2013	None	Oleksuik et al (127)	18	6	No	No	Yes	No	No	No	None	None
117	2013	Unknown	Napier et al (128)	10	6	Yes	Yes	No	No	No	No	*pmr*B	*pmr*B
118	2013	2010-2011	Hindler et al (129)	107	15	No	No	No	Yes	No	No	Unknown	Unknown
119	2013	Unknown	Lesho et al (130)	28	14	No	Yes	No	No	No	No	*pmr*A, *pmr*B, *pmr*C	*pmr*B, *pmr*A1
120	2015	2007-2014	Qureshi et al (131)	38	20	No	Yes	No	No	No	No	*bla*OXA-23, *bla*OXA-40, *bla*OXA-58	Unknown
121	2015	2012-2013	Bradford et al (132)	19719	309	Yes	No	No	No	No	No	OXA-48, KPC, CTX-M, SHV, and VEB	KPC
122	2016	2011-2014	Rojas et al (133)	246	31	No	Yes	No	No	No	No	*bla*KPC-2, *bla*KPC-3, *bla*NDM-1	*bla*KPC-3
123	2016	2008-2015	Walkty et al (134)	5571	12	No	Yes	No	No	No	No	*mcr*-1, *mcr*-2	*mcr*-1
124	2016	2011-2014	Rojas et al (135)	264	41	No	No	Yes	No	No	No	*mgr*B, *mcr*-1	*mgr*B
125	2017	2012-2014	Gallet et al (136)	32	19	No	No	No	No	No	No	*bla*KPC, *mgr*B, *pho*PQ, *pmr*CAB, *crab*	*mgr*B
126	2017	2011-2016	Duin et al (137)	137	12	No	Yes	No	No	No	No	*bla*KPC, *bla*NDM, *bla*VIM, *bla*IMP, and *bla*OXA-48	*bla*KPC-2, *bla*KPC-3
127	2017	None	Zhang et al (138)	25	18	Yes	No	No	Yes	No	No	*pmr*A, *pmr*B, *lpx*A, *lpx*C and *lpx*D	None

128	2018	2011-2016	Richter et al (139)	28512	128	Yes	No	No	No	No	No	None	None
129	2018	2016	Zhung et al (140)	134	22	No	No	No	Yes	No	No	*mcr*-4	*mcr* genes
						Africa							
130	2011	2005-2008	Maalej et al (141)	150	7	Yes	Yes	No	Yes	No	No	Unknown	Unknown
131	2017	Unknown	Sekyere et al (142)	63	44	No	Yes	No	No	No	No	*bla*NDM-1, *bla*OXA-232, *bla*GES-5, CNP−‡‡‡, CNP+§§§, *bla*NDM-5, CNP+	*bla*NDM-1
132	2017	2015-2016	Mansour et al (143)	940	7	No	Yes	No	No	No	No	*mgr*B, *bla*OXA-48-like, *bla*OXA-204, *bla*CMY-4, *bla*NDM-1, *bla*CMY-16, *bla*CTX-M-15	*bla* OXA-48
						South America							
133	2014	1996-2013	Rodriguez et al (144)	641	512	No	No	No	No	Yes	No	None	None
134	2015	unknown	Jayol et al (145)	2	1	No	Yes	No	No	No	No	*mgr*B, *bla*CTX-M-15	Unknown
135	2016	2011-2012	Carrillho et al (146)	127	27	No	Yes	No	No	No	No	OMPK35, OMPK36, *bla*OXA-9, *pmr*A, *pmr*B, *mgr*B, *yci*M, *ipx*M, *fos*A	Unknown
136	2016	2010-2014	Rossi et al (147)	33765	1346	No	No	No	Yes	No	Yes	*bla*-KPC	*bla*-KPC
137	2016	Unknown	Leite et al (148)	20	7	No	No	Yes	No	No	No	*bla*OXA-51-like, *bla*OXA-23-like, *bla*OXA-143-like,	*bla*OXA-51-like, *car*O

138	2017	unknown	Esposito et al (149)	109	86	No	Yes	No	No	No	No	*bla*IMP, *bla*VIM, *bla*NDM, *opm*33-36, *car*O *mcr*-1, *pmr*B, *pho*Q, *mgr*B,	Unknown
139	2017	None	Jayole et al	152	33	No	No	Yes	No	No	No	*pho*P, *crr*b	None
Others													
140	2014	Unknown	Poirel et al (150)	47	13	No	Yes	No	No	No	No	*mgr*B, KPC-2, KPC-3, CTX-M-2, CTX-M-15	Unknown
141	2014	2012-2013	Olaitan et al (151)	869	35	No	No	No	No	No	No	*mgr*B, *pho*P, *pho*Q, *pmr*B	Unknown
142	2016	Unknown	Nordmann et al (152)	88	52	Yes	No	Yes	No	No	No	*mcr*-1	Unknown
143	2018	2014-2016	Wise et al (153)	44407	934	No	Yes	Yes	No	No	No	*mcr*-1, *mcr*-1.2, *mcr*-1.5, *mcr*-3.1, *mcr*-5	*mcr*-1

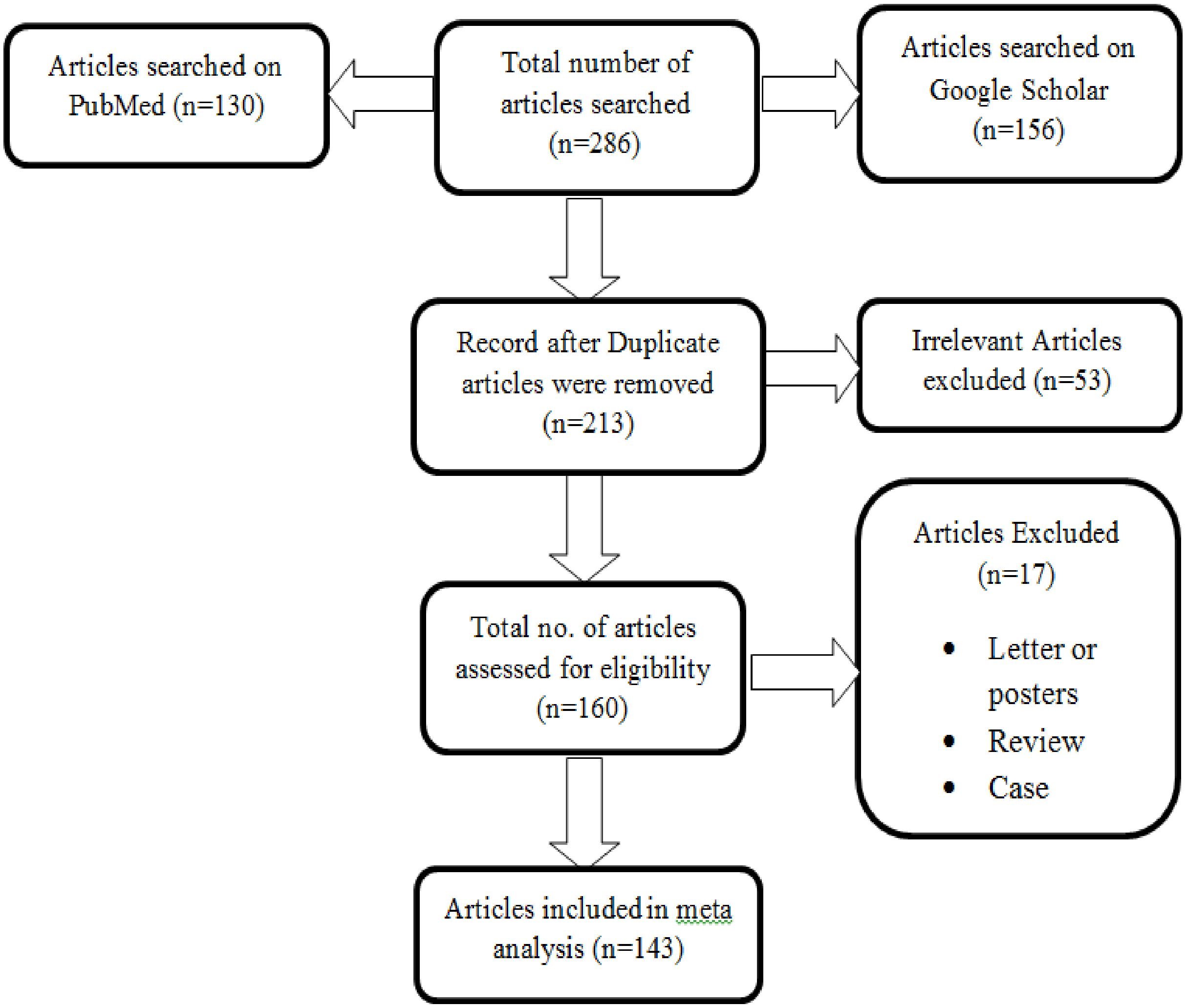

Figure 1: Article selection flowchart by PRISMA guidelines.

RESULTS

Distribution of articles describing Colistin Resistance Worldwide

A total of 286 studies resulted from search on different electronic databases. From which 143 articles were reviewed from five different continents of World i-e 68 (48%) from Asia, 42 (29%) from Europe, 19 (13%) from North America, 3 (2%) from Africa, 7 (5%) from South America, while 4 (3%) all together from different countries of different continents. No studies were found from Australia, Antarctica and Oceania (Table 2 and Figure 2). Maximum number of studies was published from 2015-2017 years (Figure 3).

Prevalence of colistin resistant isolates isolated from human clinical samples in different regions of the World

There were mainly four isolates responsible for Colistin resistance in clinical samples including *Acinetobacter baumannii*, *Klebsiella pneumoniae, Escherichia coli* and *Pseudomonas aeruginosa.* Among them *Klebsiella pneumoniae* showed highest rate of Colistin resistance about 39% followed by *Acinetobacter baumannii* (26%), *Escherichia coli* (24%) and *Pseudomonas aeruginosa* (11%) (Table 3). Highest rate of colistin resistance was found in Asia by *Klebsiella pneumoniae* (32%), by *Escherichia coli* (25%), by *Acinetobacter baumannii* (25%), *Pseudomonas aeruginosa* (18%). In Europe Colistin resistance by *Klebsiella pneumoniae* was 49%, by *Acinetobacter baumannii* (29%), by *Escherichia coli* (22%), and no resistance was found by *Pseudomonas aeruginosa*. Lowest rate of colistin resistance was found in Africa (Table 3).

Table 2: Distribution of published articles in different regions of the World.

Year	Asia	Europe	North America	Africa	South America	Others	Annual Total Publication
2009-2011	4 (6)	2 (5)	1 (5)	1 (25)	0 (0)	0 (0)	8 (6)
2012-2014	9 (13)	10 (23)	8 (42)	0 (0)	1 (14)	2 (50)	30 (21)
2015-2017	35 (51)	23 (53)	8 (42)	2 (67)	6 (86)	1 (25)	75 (52)
2018-2019	20 (29)	7 (16)	2 (11)	0 (0)	0 (0)	1 (25)	30 (21)
Region Wide	68 (48)	42 (29)	19 (13)	3 (2)	7 (5)	4 (3)	143

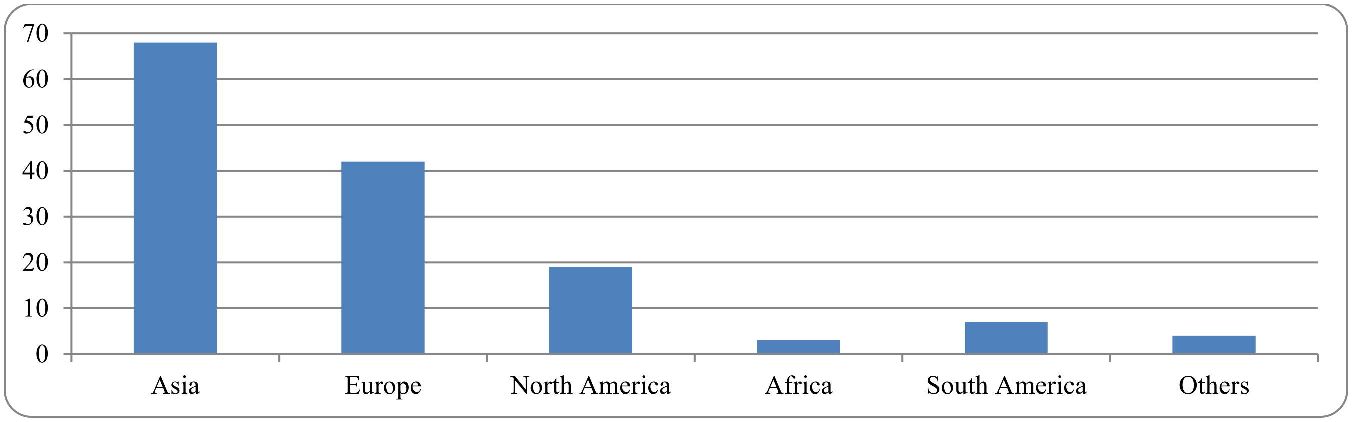

Figure 2: Graphical representation of published articles in different countries.

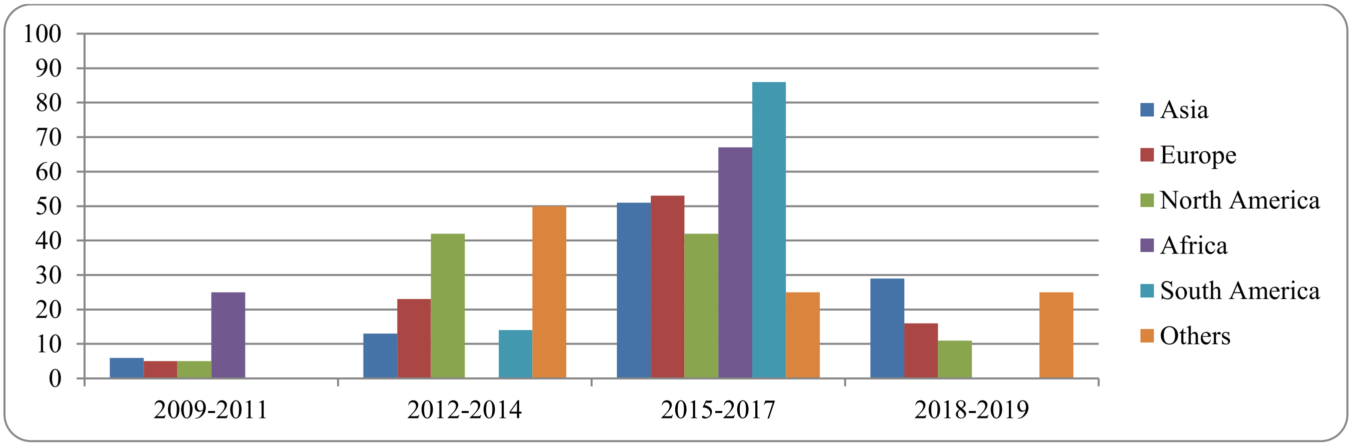

Figure 3: Annual Publication (%) of articles in different regions of the World.

Table 3: Year-wise distribution of bacterial isolates causing Colistin resistance.

Continents	Year	*Acinetobacter baumannii*	*Pseudomonas aeruginosa*	*Klebsiella pneumonia*	*Escherichia coli*
Asia	2009-2011	1 (2)	2 (9)	1 (1)	0 (0)
	2012-2014	6 (11)	2 (9)	4 (5)	1 (2)
	2015-2017	12 (22)	11 (48)	15 (19)	17 (35)
	2018-2019	7 (13)	4 (17)	14 (18)	8 (16)
Europe	2009-2011	2 (4)	0 (0)	0 (0)	0 (0)
	2012-2014	2 (4)	0 (0)	8 (10)	0 (0)
	2015-2017	8 (15)	0 (0)	12 (15)	9 (18)

	2018-2019	2 (4)	0 (0)	4 (5)	2 (4)
North America	2009-2011	0 (0)	0 (0)	1 (1)	0 (0)
	2012-2014	6 (11)	1 (4)	3 (4)	0 (0)
	2015-2017	2 (4)	0 (0)	5 (6)	3 (6)
	2018-2019	1 (2)	1 (4)	2 (3)	1 (2)
Africa	2009-2011	0 (0)	0 (0)	1 (1)	1 (2)
	2012-2014	0 (0)	0 (0)	0 (0)	0 (0)
	2015-2017	1 (2)	0 (0)	2 (3)	1 (2)
	2018-2019	0 (0)	0 (0)	0 (0)	0 (0)
South America	2009-2011	0 (0)	0 (0)	0 (0)	0 (0)
	2012-2014	0 (0)	0 (0)	0 (0)	0 (0)
	2015-2017	2 (4)	1 (4)	4 (5)	3 (6)
	2018-2019	0 (0)	0 (0)	0 (0)	0 (0)
Others	2009-2011	0 (0)	0 (0)	0 (0)	1 (2)
	2012-2014	0 (0)	0 (0)	2 (3)	0 (0)
	2015-2017	1 (2)	1 (4)	1 (1)	1 (2)
	2018-2019	0 (0)	0 (0)	1 (1)	1 (2)

Prevalence of laboratory detection methods for estimating Colistin Resistance

The most common phenotypic detection methods used to estimate Colistin resistance was MIC, Disc Diffusion, Broth Micro-dilution, E-Test, Agar Dilution and VITEK. Among them Disc Diffusion test was mostly used (42% studies) followed by MIC (24% studies), E test (14% studies), Broth Micro-dilution (13% studies) and VITEK (11% studies). Agar dilution test was used only in 6 (4%) studies (Table 4). Molecular detection tests were also performed which shows genes that are responsible for Colistin resistance. The most prevalent genes were *pmr*ABC, *mcr-1*, *pho*PQ, *blaKPC*, *mgrB*, *bla* OXA-48 (Table 4).

Prevalence of Colistin resistance and their distribution in different regions of the World

From available data, over-all pooled proportion of colistin resistance in different regions of the World was 0.21 (CI 95%: 0.20-0.21). Heterogeneity was (I^2= 99.54%, $p < 0.001$), ES was 0 (z=62.53, $p < 0.001$). The pooled proportion of Colistin resistance in Asia was 0.23 (CI 95%: 0.20-0.21), in Europe was 0.36 (CI 95%: 0.33-0.34), in North America was 0.06 (CI 95%: 0.04-0.05), in Africa was 0.40 (CI 95%: 0.06-0.23), in South America was 0.76 (CI 95%: 0.06-0.41), and in other regions was 0.23 (CI 95%: 0.10-0.17). Heterogeneity for these regions with $p < 0.001$ was 99.35% (Asia), 99.72% (Europe), 97.06% (North America), 98.64% (Africa), 99.78% (South America), and 97.88% (Others). ES was 0 with $p < 0.001$ and Z= 32.41 (Asia), 42.47 (Europe), 8.56 (North America), 2.72 (Africa), 2.28 (South America) and 5.16 (others) (Figure 4).

Table 4: Proportion estimates of Colistin Resistance.

Study	ES	95% Conf. Interval		% Weight
		Asia		
Suh et al., 2009 (15)	0.07	0.04	0.11	1.13
Gill et al., 2011 (16)	0.38	0.32	0.46	0.52
Lee et al., 2011 (17)	0.07	0.05	0.12	1.09
Park et al., 2011 (7)	0.21	0.11	0.38	0.17
Hamzeh et al., 2012 (18)	0.93	0.89	0.95	1.17
Bahador et al., 2013 (19)	0.05	0.02	0.12	0.88
Choi et al., 2013 (20)	0.45	0.36	0.54	0.36
Huangki et al., 2013 (21)	0.73	0.67	0.78	0.72
Lee et al., 2013 (22)	0.35	0.29	0.42	0.60
Naparstek et al., 2014 (23)	0.07	0.02	0.18	0.52

Lee et al., 2014 (24)	0.50	0.15	0.85	0.02
Kim et al., 2014 (25)	0.80	0.38	0.96	0.03
Guven et al., 2014 (26)	0.02	0.01	0.04	1.52
Mansoor et al., 2015 (27)	0.36	0.33	0.40	1.04
Choi et al., 2015 (28)	0.50	0.19	0.81	0.02
Nhung et al., 2015 (29)	0.58	0.39	0.76	0.09
Olaitan et al., 2015 (30)	0.40	0.12	0.77	0.02
Qadeer et al., 2016 (31)	0.47	0.43	0.51	0.96
Bashir et al., 2016 (32)	0.00	0.00	0.01	1.67
Mu et al., 2016 (33)	0.25	0.05	0.70	0.02
Goli et al., 2016 (34)	0.68	0.58	0.76	0.36
Sonnevend et al., 2016 (35)	0.11	0.06	0.20	0.53
Crawford et al., 2016 (36)	0.70	0.40	0.89	0.05
Yilmaz et al., 2016 (37)	0.52	0.39	0.64	0.20
Bashie et al., 2016 (32)	0.00	0.00	0.01	1.67
Cheng et al., 2016 (38)	0.65	0.46	0.81	0.11
Ni et al., 2016 (39)	0.29	0.21	0.38	0.40
Zhaong et al., 2016 (40)	0.11	0.07	0.17	0.79
Sato et al., 2016 (41)	0.01	0.00	0.02	1.64
Ye et al., 2016 (42)	0.04	0.01	0.11	0.90
Crawford et al., 2016 (43)	0.70	0.40	0.89	0.05
Kumar et al., 2016 (44)	0.08	0.06	0.09	1.57
Qamar et al., 2017 (45)	0.28	0.23	0.34	0.71
Aydin et al., 2017 (46)	0.07	0.06	0.08	1.57
Thong et al., 2017 (47)	0.97	0.84	0.99	0.62
Cizmeci et al., 2017 (48)	0.25	0.17	0.36	0.32
Hua et al., 2017 (49)	0.50	0.09	0.91	0.01
Soudeiha et al., 2017 (50)	0.19	0.13	0.28	0.46
Luo et al., 2017 (51)	0.03	0.02	0.04	1.62
Haeili et al., 2017 (52)	0.87	0.68	0.95	0.18
Hu et al., 2017 (53)	0.02	0.01	0.05	1.46
Tada et al., 2017 (54)	0.22	0.09	0.45	0.10
Juhaz et al., 2017 (55)	0.01	0.00	0.02	1.65
Tada et al., 2017 (56)	0.25	0.05	0.70	0.02
Chew et al., 2017 (57)	0.63	0.52	0.73	0.27
Chung et al., 2017 (58)	0.50	0.15	0.85	0.02
Wang et al., 2017 (59)	0.20	0.14	0.26	0.65
Miwi et al., 2017 (60)	0.12	0.06	0.21	0.51
Singh et al., 2018 (61)	0.10	0.07	0.16	0.93
Luxmi et al., 2018 (62)	0.24	0.21	0.27	1.19
Forde et al., 2018 (63)	0.00	0.00	0.02	1.65
Eiamphungporn et al., 2018 (64)	0.71	0.66	0.76	0.80
Farshadzadeh et al., 2018 (65)	0.50	0.22	0.78	0.03
Lu et al., 2018 (66)	0.04	0.02	0.10	1.02
Guducuoglu et al., 2018 (67)	0.69	0.42	0.87	0.06
Haeili et al., 2018 (68)	0.60	0.23	0.88	0.02
Cao et al., 2018 (69)	0.01	0.00	0.01	1.67
Aghapour et al., 2018 (70)	0.03	0.02	0.05	1.59

Yonchanghu et al., 2018 (71)	0.01	0.01	0.01	1.68
Moubareck et al., 2018 (72)	0.01	0.01	0.01	1.68
Lomonaco et al., 2018 (73)	0.70	0.40	0.89	0.05
Li et al., 2018 (74)	0.00	0.00	0.00	1.68
Okdah et al., 2018 (75)	0.96	0.88	0.99	0.84
Mustapha et al., 2018 (76)	0.43	0.29	0.58	0.15
Hameed et al., 2019 (77)	0.11	0.07	0.17	0.79
Menekse et al., 2019 (78)	0.29	0.23	0.35	0.63
Messeron et al., 2019 (79)	0.19	0.14	0.25	0.73
Cheong et al., 2019 (80)	0.05	0.03	0.09	1.27
Europe				
Wareham et al., 2011 (81)	0.83	0.44	0.97	0.04
Vila-farres et al., 2011 (82)	0.87	0.62	0.96	0.12
Capone et al., 2012 (83)	0.92	0.85	0.96	0.72
Huttner et al., 2013 (84)	0.44	0.32	0.58	0.19
Camacho et al., 2013 (85)	0.04	0.01	0.19	0.49
Cannatelli et al., 2013 (86)	0.50	0.09	0.91	0.01
Tamayo et al., 2013 (87)	0.24	0.16	0.36	0.29
Monaca et al., 2014 (88)	0.97	0.94	0.99	1.34
Gaibani et al., 2014 (89)	0.47	0.26	0.69	0.06
Agodi et al., 2014 (90)	0.58	0.39	0.74	0.10
Cannateli et al., 2014 (91)	0.50	0.09	0.91	0.01
Olivgeris et al., 2014 (92)	0.11	0.08	0.15	1.02
Hasman et al., 2015 (93)	0.78	0.74	0.81	1.09
Olaitan et al., 2015 (30)	0.01	0.00	0.03	1.61
Wand et al., 2015 (94)	0.92	0.65	0.99	0.14
Formosa et al., 2015 (95)	0.50	0.09	0.91	0.01
Farre’s et al., 2015 (96)	0.50	0.44	0.56	0.63
Dafopoulou et al., 2015 (97)	0.95	0.87	0.98	0.73
Parisi et al., 2015 (98)	0.24	0.20	0.29	0.94
Oikonoma et al., 2015 (99)	0.07	0.06	0.09	1.55
Godbole et al., 2016 (100)	0.00	0.00	0.00	1.69
Gue’rin et al., 2016 (101)	0.57	0.48	0.66	0.39
Wintersdorff et al., 2016 (102)	0.05	0.02	0.10	1.02
Boll et al., 2016 (103)	0.27	0.11	0.52	0.07
Jayol et al., 2016 (104)	0.04	0.03	0.06	1.57
Lopez-roja et al., 2016 (105)	0.73	0.43	0.90	0.05
Wand et al., 2016 (106)	0.83	0.44	0.97	0.04
Mavroidi et al., 2016 (107)	0.14	0.09	0.21	0.67
Vourli et al., 2017 (108)	0.92	0.86	0.96	0.83
Coppi et al., 2017 (109)	0.82	0.72	0.89	0.39
Dona et al., 2017 (110)	0.08	0.03	0.22	0.36
Jayol et al., 2017 (111)	0.96	0.80	0.99	0.47
Otter et al., 2017 (112)	0.63	0.47	0.76	0.15
Prim et al., 2017 (113)	0.01	0.01	0.01	1.68
Cannatelli et al., 2017 (114)	0.40	0.17	0.69	0.04
Lucas et al., 2018 (115)	0.88	0.53	0.98	0.07
Servat et al., 2018 (116)	0.07	0.03	0.16	0.62

Hannuksela et al., 2018 (117)	0.53	0.45	0.60	0.49
Principe et al., 2018 (118)	0.01	0.01	0.01	1.68
Bianco et al., 2018 (119)	0.00	0.00	0.01	1.68
Dortek et al., 2018 (120)	0.53	0.31	0.74	0.06
Girlich et al., 2019 (121)	0.56	0.46	0.66	0.31
North America				
Bogdanovich et al 2011 (122)	0.63	0.31	0.86	0.03
Jerigan et al., 2012 (123)	0.83	0.55	0.95	0.08
Snitkin et al., 2013 (124)	0.11	0.04	0.25	0.31
Hong et al., 2013 (125)	0.75	0.47	0.91	0.06
Lee et al., 2013 (126)	0.50	0.09	0.91	0.01
Oleksuik et al., 2013 (127)	0.33	0.16	0.56	0.08
Napier et al., 2013 (128)	0.60	0.31	0.83	0.04
Hindler et al., 2013 (129)	0.14	0.09	0.22	0.58
Lesho et al., 2013 (130)	0.50	0.33	0.67	0.10
Qureshi et al., 2015 (131)	0.53	0.37	0.68	0.14
Bradford et al., 2015 (132)	0.02	0.01	0.02	1.68
Rojas et al., 2016 (133)	0.13	0.09	0.17	0.96
Walkty et al., 2016 (134)	0.00	0.00	0.00	1.68
Rojas et al., 2016 (135)	0.16	0.12	0.20	0.91
Gallet et al., 2017 (136)	0.59	0.42	0.74	0.12
Duin et al., 2017 (137)	0.09	0.05	0.15	0.84
Zhang et al., 2017 (138)	0.72	0.52	0.86	0.11
Richter et al., 2018 (139)	0.00	0.00	0.01	1.68
Zhung et al., 2018 (140)	0.16	0.11	0.24	0.61
Africa				
Maalej et al., 2011 (141)	0.05	0.02	0.09	1.12
Sekyere et al., 2017 (142)	0.70	0.58	0.80	0.25
Mansour et al., 2017 (143)	0.01	0.00	0.02	1.66
South America				
Rodriguez et al., 2014 (144)	0.80	0.77	0.83	1.18
Jayol et al., 2015 (145)	0.50	0.09	0.91	0.01
Carrillho et al., 2016 (146)	0.21	0.15	0.29	0.52
Rossi et al., 2016 (147)	0.04	0.04	0.04	1.68
Leite et al., 2016 (148)	0.35	0.18	0.57	0.08
Esposito et al., 2017 (149)	0.79	0.70	0.86	0.47
Jayole et al., 2017	0.22	0.16	0.29	0.58
Others				
Poirel et al., 2014 (150)	0.28	0.17	0.42	0.20
Olaitan et al., 2014 (151)	0.04	0.03	0.06	1.57
Nordmann et al., 2016 (152)	0.59	0.49	0.69	0.30
Wise et al., 2018 (153)	0.02	0.02	0.02	1.68

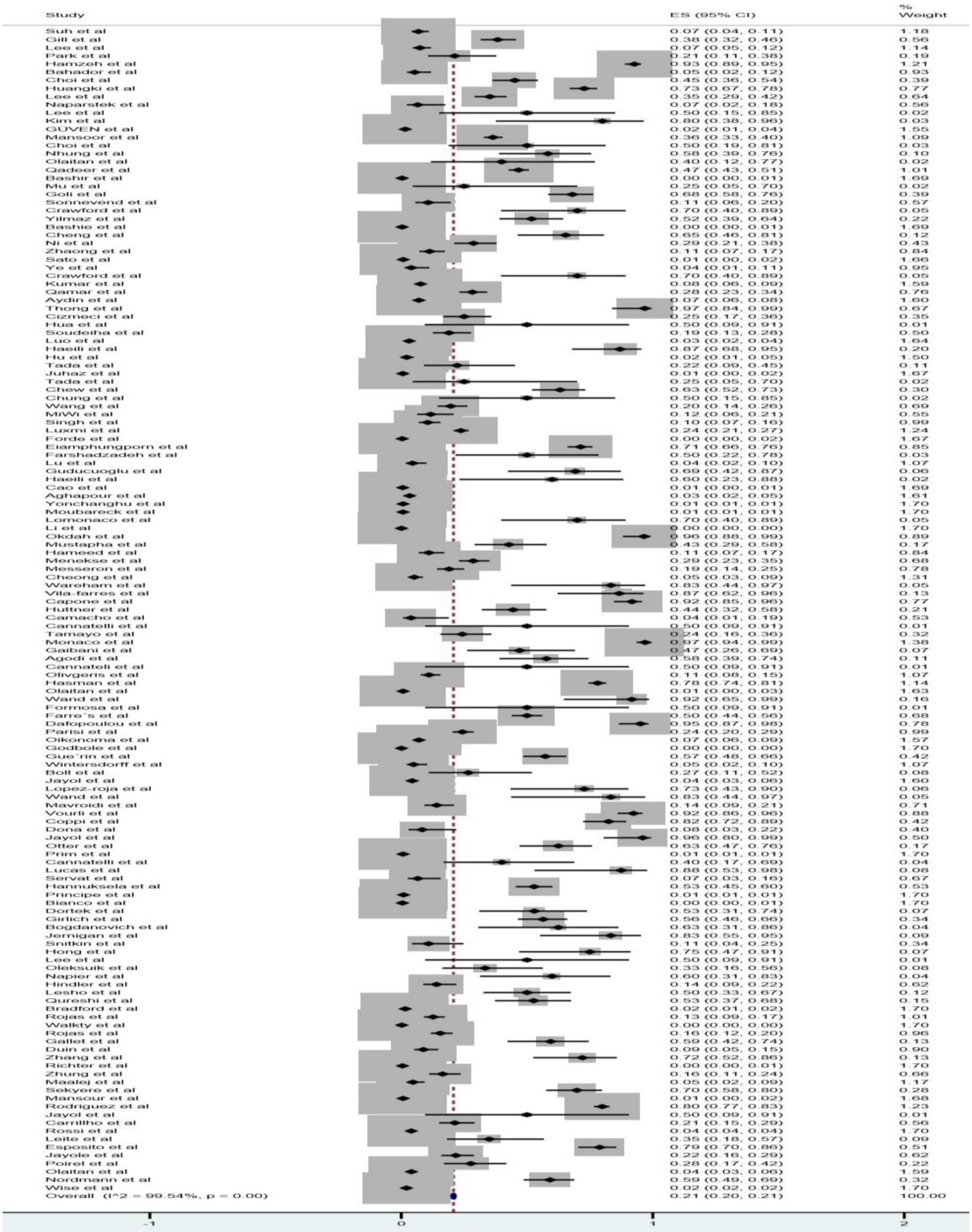

Figure 4: Proportion estimates of Colistin resistance Worldwide. The proportion estimates of colistin resistance have been donated by midpoint of each horizontal line segment. Rhombic mark donates the pooled proportion of all the included studies

DISCUSSION

It is necessary to evaluate the prevalence of colistin resistance in different regions of the world to raise the awareness of multidrug resistant bacteria. Different studies from Asia indicated that there were highest rate of colistin resistance in this region. Colistin resistance had been seen in countries including India (13.8%) (154), Singapore (30%) (155), Philippines (50%) (154), China (92.7%) (156), Iran (11.6%) (157), Korea (27.9%) (158), Turkey (27.5%) (159), Thailand (7.3%) (160) and Pakistan (15%) (161). The bacterial isolate *Klebsiella pneumoniae* was the most prevalent colistin resistance isolate (162). The present study evaluated total 143 studies, according to this study the highest rate of colistin resistance was also found in Asia in *Klebsiella pneumonia*e isolates because large number of studies 48% was conducted in this region. In Asia, *Klebsiella pneumoniae* show highest rate of colistin resistance between years 2015-2017. The rates of *Acinetobacter baumannii, Escherichia coli* and *Pseudomonas aeruginosa* colistin resistant isolates are also high in Asia between years 2015-2017.

There were different studies showing rates of colistin resistance in European countries. European countries like United Kingdom reported 3.1% colistin resistance in *Pseudomonas aeruginosa* (163). Spain reported 19.1% strains were resistant to colistin (164). In Romania rates of colistin resistance were 17% in *E.coli* and 11% in *Klebsiella* spp. (165). Rome and Italy reported 36.1% colistin resistance strains of *Klebsiella pneumonia* (83). In this present study about 29% of studies were collected from Europe showing high rates of colistin resistance in *Klebsiella pneumoniae* between years 2015-2017.

A study indicated rates of colistin resistance in isolates of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* was less than 5.5% in North American countries (166). However rates of colistin resistance were high in isolates of *Klebsiella pneumoniae.* In Denmark no resistance to colistin had been observed in *Pseudomonas aeruginosa* isolates (167). Isolates like *Acinetobacter baumannii*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa, Escherichia coli,* and *Enterobacter* spp showed colistin resistance in Canada (168). And the rate of colistin resistant *Acinetobacter baumannii* were about 4% in Argentina (169). According to the present study, about 13% studies were collected from North America. In North America the most prevalent colistin resistant isolate was *Klebsiella pneumoniae* followed by *Acinetobacter baumannii* and highest rate of resistance was found between years 2012-2017.

Studies from South American countries like Chile and Brazil showed 9% rates of colistin resistance for *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (170). In present study only 5% studies were conducted from South America and most prevalent colistin resistant isolate was *Klebsiella pneumoniae* from years 2015-2017. Studies from African countries like South Africa and Nigeria showed less than 10% colistin resitance (171). A study from Tunisia showed 1.2% colistin resistance for *Klebsiella pneumoniae,* 1.5% for *E. cloacae* and 0.09% for *Escherichia coli* (172). Zimbabwe study reported 53% colistin resistance in isolates of *Pseudomonas aeruginosa* (173). According to this study only 2% studies were conducted in this region and highest rate of colistin resistance was found in *Klebsiella pneumoniae* isolate from years 2015-2017.

Different studies also indicated that the genes that were responsible for causing colistin resistance were *lpxA, lpxC*, or *lpxD* in *Acinetobacter baumannii* (174). In *Pseudomonas aeruginosa PmrAB, PhoPQ* regulatory genes involved in colistin resistance (175) and *mgrB* (86), *bla*KPC (176) were the genes responsible for colistin resistance in *Klebsiella pneumoniae*. According to this present study the most prevalent genes were *pmr*ABC, *mcr-1*, *phoPQ, bla*KPC, *mgrB,* responsible for causing resistance to colistin. Among them *mcr-1* was the most prevalent one. After that *pmr*ABC were most prevalent. The prevalence of *mcr-1* gene was high in Asia followed by Europe. This study contributes to understanding the extent of colistin resistance in isolates of *Acinetobacter baumannii*, *Klebsiella pneumoniae, Escherichia coli* and *Pseudomonas aeruginosa.* Due to various clinical implications the prevalence of colistin resistance should not be minimized. There are many reasons contributing resistance to colistin from 143 studies in different regions of the World. With this limited available information it is difficult to minimize the problem of resistance.

CONCLUSION AND RECOMMENDATIONS

This meta-analysis performed to show rates of colistin resistance in different regions of the World. These studies show frequency of colistin resistance in various continents of the World year wise. No study is present describing colistin resistance in Oceania continent. Bacterial isolates including *Acinetobacter baumannii*, *Klebsiella pneumoniae, Escherichia coli* and *Pseudomonas aeruginosa* showed highest rate of resistance. There is a need for appropriate and regular surveillance program that addresses the issue of resistance to this antibiotic. Implementation of effective measures including active surveillance activation, highlighting coherent antibiotic strategies in hospitals with hand hygiene to control and stop the spread of colistin resistance in communities and hospitals is required.

DECLARATION

This study is part of BS thesis of Sumaya Mobin.

LIST OF ABBREVIATION

Lipopolysacchrides (LPS), Extended-spectrum β-lactamase (ESBL), multidrug-resistant (MDR), New Delhi metallo-ß-lactamase-1 (NDM-1), Epsilometric test (E-Test), Minimum inhibitory concentration (MIC), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), Meta-analysis Proportion (*Metaprop*).

AVAILABILITY OF DATA AND MATERIALS

The data sets analyzed during the current study are available from the corresponding author

AUTHORS' CONTRIBUTIONS

SA: designed the study, designed the analysis, SM: Data collection and Manuscript write-up, and IA: manuscript write up, NA: Helped with data collection, AR; data collection.

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

1. Okeke IN, Lamikanra A, Edelman R. Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries. Emerging infectious diseases. 1999;5(1):18 https://doi.org/10.3201%2Feid0501.990103.
2. Biswas S, Brunel J-M, Dubus J-C, Reynaud-Gaubert M, Rolain J-M. Colistin: an update on the antibiotic of the 21st century. Expert review of anti-infective therapy. 2012;10(8):917-34 https://doi.org/10.1586/eri.12.78.
3. Koyama Y. A new antibiotic'colistin'produced by spore-forming soil bacteria. J Antibiot. 1950;3:457-8 https://doi.org/10.1016/S0922-338X(97)82994-7.
4. Petrosillo N, Taglietti F, Granata G. Treatment options for colistin resistant Klebsiella pneumoniae: present and future. Journal of clinical medicine. 2019;8(7):934 https://doi.org/10.3390/jcm8070934.
5. Poirel L, Jayol A, Nordmann P. Polymyxins: antibacterial activity, susceptibility testing, and resistance mechanisms encoded by plasmids or chromosomes. Clinical microbiology reviews. 2017;30(2):557-96 https://doi.org/10.1128/CMR.00064-16.
6. Aghapour Z, Gholizadeh P, Ganbarov K, Bialvaei AZ, Mahmood SS, Tanomand A, et al. Molecular mechanisms related to colistin resistance in Enterobacteriaceae. Infection and drug resistance. 2019:965-75 doi/full/10.2147/IDR.S199844.
7. Park YK, Choi JY, Shin D, Ko KS. Correlation between overexpression and amino acid substitution of the PmrAB locus and colistin resistance in Acinetobacter baumannii. International journal of antimicrobial agents. 2011;37(6):525-30 https://doi.org/10.1016/j.ijantimicag.2011.02.008.
8. Kim Y, Bae IK, Lee H, Jeong SH, Yong D, Lee K. In vivo emergence of colistin resistance in Acinetobacter baumannii clinical isolates of sequence type 357 during colistin treatment. Diagnostic microbiology and infectious disease. 2014;79(3):362-6 https://doi.org/10.1016/j.diagmicrobio.2014.03.027.
9. Ito-Kagawa M, Koyama Y. Selective cleavage of a peptide antibiotic, colistin by colistinase. The Journal of antibiotics. 1980;33(12):1551-5 https://doi.org/10.7164/antibiotics.33.1551.
10. López-Rojas R, Domínguez-Herrera J, McConnell MJ, Docobo-Peréz F, Smani Y, Fernández-Reyes M, et al. Impaired virulence and in vivo fitness of colistin-resistant Acinetobacter baumannii. Journal of Infectious Diseases. 2011;203(4):545-8 https://doi.org/10.1093/infdis/jiq086.
11. Falgenhauer L, Waezsada S-E, Yao Y, Imirzalioglu C, Käsbohrer A, Roesler U, et al. Colistin resistance gene mcr-1 in extended-spectrum β-lactamase-producing and carbapenemase-producing Gram-negative bacteria in Germany. The Lancet infectious diseases. 2016;16(3):282-3 https://doi.org/10.1016/S1473-3099(16)00009-8.
12. Pamp SJ, Gjermansen M, Johansen HK, Tolker-Nielsen T. Tolerance to the antimicrobial peptide colistin in Pseudomonas aeruginosa biofilms is linked to metabolically active cells, and depends on the pmr and mexAB-oprM genes. Molecular microbiology. 2008;68(1):223-40 https://doi.org/10.1111/j.1365-2958.2008.06152.x.
13. Nation RL, Velkov T, Li J. Colistin and polymyxin B: peas in a pod, or chalk and cheese? Clinical infectious diseases. 2014;59(1):88-94 https://doi.org/10.1093/cid/ciu213.

14. Abrar S, Hussain S, Khan RA, Ul Ain N, Haider H, Riaz S. Prevalence of extended-spectrum-β-lactamase-producing Enterobacteriaceae: first systematic meta-analysis report from Pakistan. Antimicrobial Resistance & Infection Control. 2018;7(1):1-11 https://doi.org/10.1186/s13756-018-0309-1.
15. Suh J-Y, Son JS, Chung DR, Peck KR, Ko KS, Song J-H. Nonclonal emergence of colistin-resistant Klebsiella pneumoniae isolates from blood samples in South Korea. Antimicrobial agents and chemotherapy. 2010;54(1):560-2 https://doi.org/10.1128/AAC.00762-09.
16. Gill MM, Usman J, Kaleem F, Hassan A, Khalid A, Anjum R, et al. Frequency and antibiogram of multi-drug resistant Pseudomonas aeruginosa. J Coll Physicians Surg Pak. 2011;21(9):531-4 https://doi.org/10.12669%2Fpjms.35.6.930.
17. Lee J-Y, Song J-H, Ko KS. Identification of nonclonal Pseudomonas aeruginosa isolates with reduced colistin susceptibility in Korea. Microbial Drug Resistance. 2011;17(2):299-304 https://doi.org/10.1089/mdr.2010.0145.
18. Hamzeh AR, Al Najjar M, Mahfoud M. Prevalence of antibiotic resistance among Acinetobacter baumannii isolates from Aleppo, Syria. American journal of infection control. 2012;40(8):776-7 https://doi.org/10.1016/j.ajic.2011.09.019.
19. Bahador A, Taheri M, Pourakbari B, Hashemizadeh Z, Rostami H, Mansoori N, et al. Emergence of rifampicin, tigecycline, and colistin-resistant Acinetobacter baumannii in Iran; spreading of MDR strains of novel International Clone variants. Microbial Drug Resistance. 2013;19(5):397-406 https://doi.org/10.1089/mdr.2012.0233.
20. Choi M-J, Ko KS. Mutant prevention concentrations of colistin for Acinetobacter baumannii, Pseudomonas aeruginosa and Klebsiella pneumoniae clinical isolates. Journal of Antimicrobial Chemotherapy. 2014;69(1):275-7 https://doi.org/10.1093/jac/dkt315.
21. Ku Y-H, Lee M-F, Chuang Y-C, Chen C-C, Yu W-L. In vitro activity of colistin sulfate against Enterobacteriaceae producing extended-spectrum β-lactamases. Journal of Microbiology, Immunology and Infection. 2015;48(6):699-702 https://doi.org/10.1016/j.jmii.2013.11.005.
22. Lee SY, Shin JH, Lee K, Joo MY, Park KH, Shin MG, et al. Comparison of the Vitek 2, MicroScan, and Etest methods with the agar dilution method in assessing colistin susceptibility of bloodstream isolates of Acinetobacter species from a Korean university hospital. Journal of Clinical Microbiology. 2013;51(6):1924-6 https://doi.org/10.1128/JCM.00427-13.
23. Naparstek L, Carmeli Y, Navon-Venezia S, Banin E. Biofilm formation and susceptibility to gentamicin and colistin of extremely drug-resistant KPC-producing Klebsiella pneumoniae. Journal of antimicrobial chemotherapy. 2014;69(4):1027-34 https://doi.org/10.1093/jac/dkt487.
24. Lee J-Y, Na IY, Park YK, Ko KS. Genomic variations between colistin-susceptible and-resistant Pseudomonas aeruginosa clinical isolates and their effects on colistin resistance. Journal of Antimicrobial Chemotherapy. 2014;69(5):1248-56 https://doi.org/10.1093/jac/dkt531.
25. Kim SY, Choi HJ, Ko KS. Differential expression of two-component systems, pmrAB and phoPQ, with different growth phases of Klebsiella pneumoniae in the presence or absence of colistin. Current microbiology. 2014;69(1):37-41 https://doi.org/10.1007/s00284-014-0549-0.
26. Güven T, Yilmaz G, Güner HR, KALEM AK, Eser F, TAŞYARAN MA. Increasing resistance of nosocomial Acinetobacter baumannii: are we going to be defeated? Turkish journal of medical sciences. 2014;44(1):73-8 10.3906/sag-1211-21.
27. Mansoor K, Tanvir SB, Shariq A, Hussain A, Farooqi BJ, Ahmed S, et al. Frequency and susceptibility pattern of Multidrug Resistant Pseudomonas aeruginosa in isolates of patients from a tertiary care hospital of Karachi, Pakistan. Eur J Biotechnol Bio Sci. 2015;2(5):33-6 https://doi.org/10.12669%2Fpjms.333.12416.
28. Choi M-J, Ko KS. Loss of hypermucoviscosity and increased fitness cost in colistin-resistant Klebsiella pneumoniae sequence type 23 strains. Antimicrobial agents and chemotherapy. 2015;59(11):6763-73 https://doi.org/10.1128/AAC.00952-15.
29. Nhung PH, Miyoshi-Akiyama T, Phuong DM, Shimada K, Anh NQ, Binh NG, et al. Evaluation of the Etest method for detecting colistin susceptibility of multidrug-resistant Gram-negative isolates in Vietnam. Journal of Infection and Chemotherapy. 2015;21(8):617-9 https://doi.org/10.1016/j.jiac.2015.04.002.
30. Olaitan AO, Dia NM, Gautret P, Benkouiten S,

Belhouchat K, Drali T, et al. Acquisition of extended-spectrum cephalosporin-and colistin-resistant Salmonella enterica subsp. enterica serotype Newport by pilgrims during Hajj. International journal of antimicrobial agents. 2015;45(6):600-4 https://doi.org/10.1016/j.ijantimicag.2015.01.010.

31. Qadeer A, Akhtar A, Ain QU, Saadat S, Mansoor S, Assad S, et al. Antibiogram of medical intensive care unit at tertiary care hospital setting of Pakistan. Cureus. 2016;8(9) 10.7759/cureus.809.
32. Bashir T, Ahmed A. Colistin resistance among gram negative organisms; an evolving problem from tertiary care hospital, Pakistan 2014. American Journal of Microbiology. 2016 https://doi.org/10.3844/ajmsp.2016.29.31.
33. Mu X, Wang N, Li X, Shi K, Zhou Z, Yu Y, et al. The effect of colistin resistance-associated mutations on the fitness of Acinetobacter baumannii. Frontiers in microbiology. 2016;7:1715 https://doi.org/10.3389/fmicb.2016.01715.
34. Goli HR, Nahaei MR, Rezaee MA, Hasani A, Kafil HS, Aghazadeh M. Emergence of colistin resistant Pseudomonas aeruginosa at Tabriz hospitals, Iran. Iranian journal of microbiology. 2016;8(1):62 PMCID: PMC4833742.
35. Sonnevend Á, Ghazawi A, Alqahtani M, Shibl A, Jamal W, Hashmey R, et al. Plasmid-mediated colistin resistance in Escherichia coli from the Arabian Peninsula. International Journal of Infectious Diseases. 2016;50:85-90.
36. Crawford MA, Timme R, Lomonaco S, Lascols C, Fisher DJ, Sharma SK, Strain E, Allard MW, Brown EW, McFarland MA, Croley T. Genome sequences of multidrug-resistant, colistin-susceptible and-resistant Klebsiella pneumoniae clinical isolates from Pakistan. Genome Announcements. 2016 Dec 29;4(6):10-128. https://doi.org/10.1128/genomea.01419-16.
37. Yilmaz GR, Dizbay M, Guven T, Pullukcu H, Tasbakan M, Guzel OT, et al. Risk factors for infection with colistin-resistant gram-negative microorganisms: a multicenter study. Annals of Saudi medicine. 2016;36(3):216-22 https://doi.org/10.5144/0256-4947.2016.216.
38. Cheng Y-H, Lin T-L, Lin Y-T, Wang J-T. Amino acid substitutions of CrrB responsible for resistance to colistin through CrrC in Klebsiella pneumoniae. Antimicrobial agents and chemotherapy. 2016;60(6):3709-16 https://doi.org/10.1128/AAC.00009-16.
39. Ni W, Li Y, Guan J, Zhao J, Cui J, Wang R, Liu Y. Effects of efflux pump inhibitors on colistin resistance in multidrug-resistant Gram-negative bacteria. Antimicrobial agents and chemotherapy. 2016 May;60(5):3215-8. https://doi.org/10.1128/aac.00248-16
40. Zhong L-L, Zhang Y-F, Doi Y, Huang X, Zhang X-F, Zeng K-J, et al. Coproduction of MCR-1 and NDM-1 by colistin-resistant Escherichia coli isolated from a healthy individual. Antimicrobial agents and chemotherapy. 2017;61(1):e01962-16 https://doi.org/10.1128/AAC.01962-16.
41. Sato T, Fukuda A, Suzuki Y, Shiraishi T, Honda H, Shinagawa M, et al. Pathogenic lineage of mcr-negative colistin-resistant Escherichia coli, Japan, 2008–2015. Emerging Infectious Diseases. 2016;22(12):2223 https://doi.org/10.3201%2Feid2212.161117.
42. Ye H, Li Y, Li Z, Gao R, Zhang H, Wen R, et al. Diversified mcr-1-harbouring plasmid reservoirs confer resistance to colistin in human gut microbiota. MBio. 2016;7(2):e00177-16 https://doi.org/10.1128/mBio.00177-16.
43. Crawford MA, Timme R, Lomonaco S, Lascols C, Fisher DJ, Sharma SK, et al. Genome sequences of multidrug-resistant, colistin-susceptible and-resistant Klebsiella pneumoniae clinical isolates from Pakistan. Genome Announcements. 2016;4(6):e01419-16 https://doi.org/10.1128/genomeA.01419-16.
44. Kumar M, Gupta A, Sahoo RK, Jena J, Debata NK, Subudhi E. Functional genome screening to elucidate the colistin resistance mechanism. Scientific reports. 2016;6(1):1-7 DOI: 10.1038/srep23156.
45. Qamar S, Shaheen N, Shakoor S, Farooqi J, Jabeen K, Hasan R. Frequency of colistin and fosfomycin resistance in carbapenem-resistant Enterobacteriaceae from a tertiary care hospital in Karachi. Infection and drug resistance. 2017;10:231 doi/full/10.2147/IDR.S136777.
46. Aydın M, Ergönül Ö, Azap A, Bilgin H, Aydın G, Çavuş S, et al. Rapid emergence of colistin resistance and its impact on fatality among healthcare-associated infections. Journal of Hospital Infection. 2018;98(3):260-3 https://doi.org/10.1016/j.jhin.2017.11.014.
47. Berglund B, Hoang NTB, Tärnberg M, Le NK, Svartström O, Khu DTK, et al. Insertion sequence

transpositions and point mutations in mgrB causing colistin resistance in a clinical strain of carbapenem-resistant Klebsiella pneumoniae from Vietnam. International Journal of Antimicrobial Agents. 2018;51(5):789-93 https://doi.org/10.1016/j.ijantimicag.2017.11.012.

48. Cizmeci Z, Aktas E, Otlu B, Acikgoz O, Ordekci S. Molecular characterization of carbapenem-resistant Enterobacteriaceae yields increasing rates of NDM-1 carbapenemases and colistin resistance in an OXA-48-endemic area. Journal of Chemotherapy. 2017;29(6):344-50 https://doi.org/10.1080/1120009X.2017.1323149.

49. Hua X, Liu L, Fang Y, Shi Q, Li X, Chen Q, et al. Colistin resistance in Acinetobacter baumannii MDR-ZJ06 revealed by a multiomics approach. Frontiers in cellular and infection microbiology. 2017;7:45 https://doi.org/10.3389/fcimb.2017.00045.

50. Soudeiha MA, Dahdouh EA, Azar E, Sarkis DK, Daoud Z. In vitro evaluation of the colistin-carbapenem combination in clinical isolates of A. baumannii using the checkerboard, Etest, and time-kill curve techniques. Frontiers in cellular and infection microbiology. 2017;7:209 https://doi.org/10.3389/fcimb.2017.00209.

51. Luo Q, Yu W, Zhou K, Guo L, Shen P, Lu H, et al. Molecular epidemiology and colistin resistant mechanism of mcr-positive and mcr-negative clinical isolated Escherichia coli. Frontiers in microbiology. 2017;8:2262 https://doi.org/10.3389/fmicb.2017.02262.

52. Haeili M, Javani A, Moradi J, Jafari Z, Feizabadi MM, Babaei E. MgrB alterations mediate colistin resistance in Klebsiella pneumoniae isolates from Iran. Frontiers in microbiology. 2017;8:2470 https://doi.org/10.3389/fmicb.2017.02470.

53. Hu Y, Wang Y, Sun Q, Huang Z, Wang H, Zhang R, et al. Colistin-resistance gene mcr-1 in children’s gut flora. Int J Antimicrob Agents. 2017;50:593-7 https://doi.org/10.1016/j.ijantimicag.2017.06.011.

54. Tada T, Nhung PH, Shimada K, Tsuchiya M, Phuong DM, Anh NQ, et al. Emergence of colistin-resistant Escherichia coli clinical isolates harboring mcr-1 in Vietnam. International Journal of Infectious Diseases. 2017;63:72-3 https://doi.org/10.1016/j.ijid.2017.07.003.

55. Juhász E, Iván M, Pintér E, Pongrácz J, Kristóf K. Colistin resistance among blood culture isolates at a tertiary care centre in Hungary. Journal of global antimicrobial resistance. 2017;11:167-70 https://doi.org/10.1016/j.jgar.2017.08.002.

56. Tada T, Uechi K, Nakasone I, Shimada K, Nakamatsu M, Kirikae T, et al. Emergence of a colistin-resistant Escherichia coli clinical isolate harboring mcr-1 in Japan. International Journal of Infectious Diseases. 2017;63:21-2 https://doi.org/10.1016/j.ijid.2017.07.023.

57. Chew KL, La M-V, Lin RT, Teo JW. Colistin and polymyxin B susceptibility testing for carbapenem-resistant and mcr-positive Enterobacteriaceae: comparison of Sensititre, MicroScan, Vitek 2, and Etest with broth microdilution. Journal of clinical microbiology. 2017;55(9):2609-16 https://doi.org/10.1128/JCM.00268-17.

58. Chung ES, Lee J-Y, Rhee J-Y, Ko KS. Colistin resistance in Pseudomonas aeruginosa that is not linked to arnB. Journal of medical microbiology. 2017;66(6):833-41 https://doi.org/10.1099/jmm.0.000456.

59. Wang X, Liu Y, Qi X, Wang R, Jin L, Zhao M, et al. Molecular epidemiology of colistin-resistant Enterobacteriaceae in inpatient and avian isolates from China: high prevalence of mcr-negative Klebsiella pneumoniae. International journal of antimicrobial agents. 2017;50(4):536-41 https://doi.org/10.1016/j.ijantimicag.2017.05.009.

60. Wi YM, Choi J-Y, Lee J-Y, Kang C-I, Chung DR, Peck KR, et al. Emergence of colistin resistance in Pseudomonas aeruginosa ST235 clone in South Korea. International journal of antimicrobial agents. 2017;49(6):767-9 https://doi.org/10.1016/j.ijantimicag.2017.01.023.

61. Singh S, Pathak A, Kumar A, Rahman M, Singh A, Gonzalez-Zorn B, et al. Emergence of chromosome-borne colistin resistance gene mcr-1 in clinical isolates of Klebsiella pneumoniae from India. Antimicrobial agents and chemotherapy. 2018;62(2):e01885-17 https://doi.org/10.1128/AAC.01885-17.

62. Luxmi S, Javed S. Frequency of Carbapenem, Colistin and Tigecycline Resistant Enterobacteriacae in Medical ICU of a Tertiary Care Hospital in Karachi. Journal of Pioneering Medical Sciences. 2018;8(1):2.

63. Forde BM, Zowawi HM, Harris PN, Roberts L, Ibrahim E, Shaikh N, et al. Discovery of mcr-1-mediated colistin resistance in a highly virulent Escherichia coli lineage. Msphere. 2018;3(5):e00486-

18 https://doi.org/10.1128/mSphere.00486-18.

64. Eiamphungporn W, Yainoy S, Jumderm C, Tan-Arsuwongkul R, Tiengrim S, Thamlikitkul V. Prevalence of the colistin resistance gene mcr-1 in colistin-resistant Escherichia coli and Klebsiella pneumoniae isolated from humans in Thailand. Journal of global antimicrobial resistance. 2018;15:32-5 https://doi.org/10.1016/j.jgar.2018.06.007.

65. Farshadzadeh Z, Taheri B, Rahimi S, Shoja S, Pourhajibagher M, Haghighi MA, et al. Growth rate and biofilm formation ability of clinical and laboratory-evolved colistin-resistant strains of Acinetobacter baumannii. Frontiers in microbiology. 2018;9:153 DOI=10.3389/fmicb.2018.00153.

66. Lu Y, Feng Y, McNally A, Zong Z. The occurence of colistin-resistant hypervirulent Klebsiella pneumoniae in china. Frontiers in microbiology. 2018 Oct 25;9:412334. https://doi.org/10.3389/fmicb.2018.02568

67. Guducuoglu H, Gursoy NC, Yakupogullari Y, Parlak M, Karasin G, Sunnetcioglu M, et al. Hospital outbreak of a colistin-resistant, NDM-1-and OXA-48-producing Klebsiella pneumoniae: high mortality from pandrug resistance. Microbial Drug Resistance. 2018;24(7):966-72 https://doi.org/10.1089/mdr.2017.0173.

68. Haeili M, Kafshdouz M, Feizabadi MM. Molecular mechanisms of colistin resistance among pandrug-resistant isolates of Acinetobacter baumannii with high case-fatality rate in intensive care unit patients. Microbial Drug Resistance. 2018;24(9):1271-6 https://doi.org/10.1089/mdr.2017.0397.

69. Cao L, Li X, Xu Y, Shen J. Prevalence and molecular characteristics of mcr-1 colistin resistance in Escherichia coli: isolates of clinical infection from a Chinese University Hospital. Infection and drug resistance. 2018;11:1597 https://doi.org/10.2147%2FIDR.S166726.

70. Aghapour Z, Hasani A, Aghazadeh M, Rezaee MA, Ganbarov K, Pourlak T, et al. Genes involved in colistin resistance of gram-negative isolates in the northwest of Iran. Gene Reports. 2019;14:81-6 https://doi.org/10.1016/j.genrep.2018.12.001.

71. Xu Y, Zhong L-L, Srinivas S, Sun J, Huang M, Paterson DL, et al. Spread of MCR-3 colistin resistance in China: an epidemiological, genomic and mechanistic study. EBioMedicine. 2018;34:139-57 https://doi.org/10.1016/j.ebiom.2018.07.027.

72. Moubareck CA, Mouftah SF, Pál T, Ghazawi A, Halat DH, Nabi A, et al. Clonal emergence of Klebsiella pneumoniae ST14 co-producing OXA-48-type and NDM carbapenemases with high rate of colistin resistance in Dubai, United Arab Emirates. International journal of antimicrobial agents. 2018;52(1):90-5 https://doi.org/10.1016/j.ijantimicag.2018.03.003.

73. Lomonaco S, Crawford MA, Lascols C, Timme RE, Anderson K, Hodge DR, et al. Resistome of carbapenem-and colistin-resistant Klebsiella pneumoniae clinical isolates. PLoS One. 2018;13(6):e0198526 https://doi.org/10.1371/journal.pone.0198526.

74. Li Y, Sun Q-l, Shen Y, Zhang Y, Yang J-w, Shu L-b, et al. Rapid increase in prevalence of carbapenem-resistant Enterobacteriaceae (CRE) and emergence of colistin resistance gene mcr-1 in CRE in a hospital in Henan, China. Journal of clinical microbiology. 2018;56(4):e01932-17 https://doi.org/10.1128/JCM.01932-17

75. Okdah L, Le Page S, Olaitan AO, Dubourg G, Hadjadj L, Rolain J-M. New therapy from old drugs: synergistic bactericidal activity of sulfadiazine with colistin against colistin-resistant bacteria, including plasmid-mediated colistin-resistant mcr-1 isolates. International journal of antimicrobial agents. 2018;51(5):775-83 https://doi.org/10.1016/j.ijantimicag.2018.01.027.

76. Mustapha MM, Li B, Pacey MP, Mettus RT, McElheny CL, Marshall CW, et al. Phylogenomics of colistin-susceptible and resistant XDR Acinetobacter baumannii. Journal of Antimicrobial Chemotherapy. 2018;73(11):2952-9 https://doi.org/10.1093/jac/dky290.

77. Hameed F, Khan MA, Muhammad H, Sarwar T, Bilal H, Rehman TU. Plasmid-mediated mcr-1 gene in Acinetobacter baumannii and Pseudomonas aeruginosa: first report from Pakistan. Revista da Sociedade Brasileira de Medicina Tropical. 2019;52 https://doi.org/10.1590/0037-8682-0237-2019.

78. Menekşe Ş, Çağ Y, Işık ME, Şahin S, Hacıseyitoğlu D, Can F, et al. The effect of colistin resistance and other predictors on fatality among patients with bloodstream infections due to Klebsiella pneumoniae in an OXA-48 dominant region. International Journal of Infectious Diseases. 2019;86:208-11 https://doi.org/10.1016/j.ijid.2019.06.008.

79. Masseron A, Poirel L, Ali BJ, Syed MA, Nordmann

P. Molecular characterization of multidrug-resistance in Gram-negative bacteria from the Peshawar teaching hospital, Pakistan. New microbes and new infections. 2019;32:100605 https://doi.org/10.3390/antibiotics11010048.

80. Cheong HS, Kim SY, Wi YM, Peck KR, Ko KS. Colistin heteroresistance in Klebsiella pneumoniae isolates and diverse mutations of PmrAB and PhoPQ in resistant subpopulations. Journal of Clinical Medicine. 2019;8(9):1444 https://doi.org/10.3390/jcm8091444.

81. Wareham D, Gordon N, Hornsey M. In vitro activity of teicoplanin combined with colistin versus multidrug-resistant strains of Acinetobacter baumannii. Journal of antimicrobial chemotherapy. 2011;66(5):1047-51 https://doi.org/10.1128/AAC.00922-10.

82. Vila-Farres X, De La Maria CG, López-Rojas R, Pachón J, Giralt E, Vila J. In vitro activity of several antimicrobial peptides against colistin-susceptible and colistin-resistant Acinetobacter baumannii. Clinical Microbiology and Infection. 2012;18(4):383-7 https://doi.org/10.1111/j.1469-0691.2011.03581.x.

83. Capone A, Giannella M, Fortini D, Giordano A, Meledandri M, Ballardini M, et al. High rate of colistin resistance among patients with carbapenem-resistant Klebsiella pneumoniae infection accounts for an excess of mortality. Clinical Microbiology and Infection. 2013;19(1):E23-E30 https://doi.org/10.1111/1469-0691.12070.

84. Huttner B, Haustein T, Uçkay I, Renzi G, Stewardson A, Schaerrer D, et al. Decolonization of intestinal carriage of extended-spectrum β-lactamase-producing Enterobacteriaceae with oral colistin and neomycin: a randomized, double-blind, placebo-controlled trial. Journal of Antimicrobial Chemotherapy. 2013;68(10):2375-82 https://doi.org/10.1093/jac/dkt174.

85. López-Camacho E, Gómez-Gil R, Tobes R, Manrique M, Lorenzo M, Galván B, et al. Genomic analysis of the emergence and evolution of multidrug resistance during a Klebsiella pneumoniae outbreak including carbapenem and colistin resistance. Journal of Antimicrobial Chemotherapy. 2014;69(3):632-6 https://doi.org/10.1093/jac/dkt419.

86. Cannatelli A, D'Andrea MM, Giani T, Di Pilato V, Arena F, Ambretti S, et al. In vivo emergence of colistin resistance in Klebsiella pneumoniae producing KPC-type carbapenemases mediated by insertional inactivation of the PhoQ/PhoP mgrB regulator. Antimicrobial agents and chemotherapy. 2013;57(11):5521-6 https://doi.org/10.1128/AAC.01480-13.

87. Tamayo M, Santiso R, Otero F, Bou G, Lepe JA, McConnell MJ, et al. Rapid determination of colistin resistance in clinical strains of Acinetobacter baumannii by use of the micromax assay. Journal of Clinical Microbiology. 2013;51(11):3675-82 DOI: 10.1128/JCM.01787-13..

88. Monaco M, Giani T, Raffone M, Arena F, Garcia-Fernandez A, Pollini S, et al. Colistin resistance superimposed to endemic carbapenem-resistant Klebsiella pneumoniae: a rapidly evolving problem in Italy, November 2013 to April 2014. Eurosurveillance. 2014;19(42):20939 https://doi.org/10.2807/1560-7917.ES2014.19.42.20939.

89. Gaibani P, Lombardo D, Lewis RE, Mercuri M, Bonora S, Landini MP, et al. In vitro activity and post-antibiotic effects of colistin in combination with other antimicrobials against colistin-resistant KPC-producing Klebsiella pneumoniae bloodstream isolates. Journal of Antimicrobial Chemotherapy. 2014;69(7):1856-65 https://doi.org/10.1093/jac/dku065.

90. Agodi A, Voulgari E, Barchitta M, Quattrocchi A, Bellocchi P, Poulou A, et al. Spread of a carbapenem-and colistin-resistant Acinetobacter baumannii ST2 clonal strain causing outbreaks in two Sicilian hospitals. Journal of Hospital Infection. 2014;86(4):260-6 https://doi.org/10.1016/j.jhin.2014.02.001.

91. Cannatelli A, Di Pilato V, Giani T, Arena F, Ambretti S, Gaibani P, et al. In vivo evolution to colistin resistance by PmrB sensor kinase mutation in KPC-producing Klebsiella pneumoniae is associated with low-dosage colistin treatment. Antimicrobial agents and chemotherapy. 2014;58(8):4399-403 https://doi.org/10.1128/AAC.02555-14.

92. Papadimitriou-Olivgeris M, Christofidou M, Fligou F, Bartzavali C, Vrettos T, Filos K, et al. The role of colonization pressure in the dissemination of colistin or tigecycline resistant KPC-producing Klebsiella pneumoniae in critically ill patients. Infection. 2014;42(5):883-90 https://doi.org/10.1007/s15010-014-0653-x.

93. Hasman H, Hammerum AM, Hansen F, Hendriksen RS, Olesen B, Agersø Y, et al. Detection of mcr-1

encoding plasmid-mediated colistin-resistant Escherichia coli isolates from human bloodstream infection and imported chicken meat, Denmark 2015. Eurosurveillance. 2015;20(49):30085 https://doi.org/10.2807/1560-7917.ES.2015.20.49.30085.

94. Wand ME, Bock LJ, Bonney LC, Sutton JM. Retention of virulence following adaptation to colistin in Acinetobacter baumannii reflects the mechanism of resistance. Journal of Antimicrobial Chemotherapy. 2015;70(8):2209-16 https://doi.org/10.1093/jac/dkv097.
95. Formosa C, Herold M, Vidaillac C, Duval R, Dague E. Unravelling of a mechanism of resistance to colistin in Klebsiella pneumoniae using atomic force microscopy. Journal of Antimicrobial Chemotherapy. 2015;70(8):2261-70 https://doi.org/10.1093/jac/dkv118.
96. Vila-Farrés X, Ferrer-Navarro M, Callarisa AE, Martí S, Espinal P, Gupta S, et al. Loss of LPS is involved in the virulence and resistance to colistin of colistin-resistant Acinetobacter nosocomialis mutants selected in vitro. Journal of Antimicrobial Chemotherapy. 2015;70(11):2981-6 https://doi.org/10.1093/jac/dkv244.
97. Dafopoulou K, Zarkotou O, Dimitroulia E, Hadjichristodoulou C, Gennimata V, Pournaras S, et al. Comparative evaluation of colistin susceptibility testing methods among carbapenem-nonsusceptible Klebsiella pneumoniae and Acinetobacter baumannii clinical isolates. Antimicrobial agents and chemotherapy. 2015;59(8):4625-30 https://doi.org/10.1128/AAC.00868-15.
98. Parisi SG, Bartolini A, Santacatterina E, Castellani E, Ghirardo R, Berto A, et al. Prevalence of Klebsiella pneumoniae strains producing carbapenemases and increase of resistance to colistin in an Italian teaching hospital from January 2012 to December 2014. BMC infectious diseases. 2015;15(1):1-10 https://doi.org/10.1186/s12879-015-0996-7.
99. Oikonomou O, Sarrou S, Papagiannitsis C, Georgiadou S, Mantzarlis K, Zakynthinos E, et al. Rapid dissemination of colistin and carbapenem resistant Acinetobacter baumannii in Central Greece: mechanisms of resistance, molecular identification and epidemiological data. BMC infectious diseases. 2015;15(1):1-6 https://doi.org/10.1186/s12879-015-1297-x.
100. Doumith M, Godbole G, Ashton P, Larkin L, Dallman T, Day M, et al. Detection of the plasmid-mediated mcr-1 gene conferring colistin resistance in human and food isolates of Salmonella enterica and Escherichia coli in England and Wales. Journal of Antimicrobial Chemotherapy. 2016;71(8):2300-5 https://doi.org/10.1093/jac/dkw093.
101. Guérin F, Isnard C, Sinel C, Morand P, Dhalluin A, Cattoir V, et al. Cluster-dependent colistin hetero-resistance in Enterobacter cloacae complex. Journal of Antimicrobial Chemotherapy. 2016;71(11):3058-61 https://doi.org/10.1093/jac/dkw260.
102. Von Wintersdorff CJ, Wolffs PF, van Niekerk JM, Beuken E, van Alphen LB, Stobberingh EE, et al. Detection of the plasmid-mediated colistin-resistance gene mcr-1 in faecal metagenomes of Dutch travellers. Journal of Antimicrobial Chemotherapy. 2016;71(12):3416-9 https://doi.org/10.1093/jac/dkw328.
103. Boll JM, Crofts AA, Peters K, Cattoir V, Vollmer W, Davies BW, et al. A penicillin-binding protein inhibits selection of colistin-resistant, lipooligosaccharide-deficient Acinetobacter baumannii. Proceedings of the National Academy of Sciences. 2016;113(41):E6228-E37 https://doi.org/10.1073/pnas.1611594113.
104. Jayol A, Poirel L, Dortet L, Nordmann P. National survey of colistin resistance among carbapenemase-producing Enterobacteriaceae and outbreak caused by colistin-resistant OXA-48-producing Klebsiella pneumoniae, France, 2014. Eurosurveillance. 2016;21(37):30339 https://doi.org/10.2807/1560-7917.ES.2016.21.37.30339.
105. López-Rojas R, García-Quintanilla M, Labrador-Herrera G, Pachón J, McConnell MJ. Impaired growth under iron-limiting conditions associated with the acquisition of colistin resistance in Acinetobacter baumannii. International journal of antimicrobial agents. 2016;47(6):473-7 https://doi.org/10.1016/j.ijantimicag.2016.03.010.
106. Wand ME, Bock LJ, Bonney LC, Sutton JM. Mechanisms of increased resistance to chlorhexidine and cross-resistance to colistin following exposure of Klebsiella pneumoniae clinical isolates to chlorhexidine. Antimicrobial agents and chemotherapy. 2017;61(1):e01162-16 https://doi.org/10.1128/AAC.01162-16.
107. Mavroidi A, Katsiari M, Likousi S, Palla E, Roussou Z, Nikolaou C, et al. Characterization of ST258 colistin-resistant, Bla KPC-producing Klebsiella

pneumoniae in a Greek hospital. Microbial drug resistance. 2016;22(5):392-8 https://doi.org/10.1089/mdr.2015.0282.

108. Vourli S, Dafopoulou K, Vrioni G, Tsakris A, Pournaras S. Evaluation of two automated systems for colistin susceptibility testing of carbapenem-resistant Acinetobacter baumannii clinical isolates. Journal of Antimicrobial Chemotherapy. 2017;72(9):2528-30 https://doi.org/10.1093/jac/dkx186.

109. Coppi M, Cannatelli A, Antonelli A, Baccani I, Di Pilato V, Sennati S, et al. A simple phenotypic method for screening of MCR-1-mediated colistin resistance. Clinical Microbiology and Infection. 2018;24(2):201. e1-. e3 https://doi.org/10.1016/j.cmi.2017.08.011.

110. Donà V, Bernasconi OJ, Kasraian S, Tinguely R, Endimiani A. A SYBR® Green-based real-time PCR method for improved detection of mcr-1-mediated colistin resistance in human stool samples. Journal of global antimicrobial resistance. 2017;9:57-60 https://doi.org/10.1016/j.jgar.2017.01.007.

111. Jayol A, Saly M, Nordmann P, Ménard A, Poirel L, Dubois V. Hafnia, an enterobacterial genus naturally resistant to colistin revealed by three susceptibility testing methods. Journal of Antimicrobial Chemotherapy. 2017;72(9):2507-11 https://doi.org/10.1093/jac/dkx154.

112. Otter JA, Doumith M, Davies F, Mookerjee S, Dyakova E, Gilchrist M, et al. Emergence and clonal spread of colistin resistance due to multiple mutational mechanisms in carbapenemase-producing Klebsiella pneumoniae in London. Scientific reports. 2017;7(1):1-8 https://doi.org/10.1038/s41598-017-12637-4.

113. Prim N, Turbau M, Rivera A, Rodríguez-Navarro J, Coll P, Mirelis B. Prevalence of colistin resistance in clinical isolates of Enterobacteriaceae: A four-year cross-sectional study. Journal of Infection. 2017;75(6):493-8 https://doi.org/10.1016/j.jinf.2017.09.008.

114. Cannatelli A, Giani T, Aiezza N, Di Pilato V, Principe L, Luzzaro F, et al. An allelic variant of the PmrB sensor kinase responsible for colistin resistance in an Escherichia coli strain of clinical origin. Scientific reports. 2017;7(1):1-6 https://doi.org/10.1038/s41598-017-05167-6.

115. Deveson Lucas D, Crane B, Wright A, Han M-L, Moffatt J, Bulach D, et al. Emergence of high-level colistin resistance in an Acinetobacter baumannii clinical isolate mediated by inactivation of the global regulator H-NS. Antimicrobial agents and chemotherapy. 2018;62(7):e02442-17 https://doi.org/10.1128/AAC.02442-17.

116. Martínez-Servat S, Yero D, Huedo P, Marquez R, Molina G, Daura X, et al. Heterogeneous colistin-resistance phenotypes coexisting in Stenotrophomonas maltophilia isolates influence colistin susceptibility testing. Frontiers in microbiology. 2018;9:2871 https://doi.org/10.3389/fmicb.2018.02871.

117. Gröndahl-Yli-Hannuksela K, Lönnqvist E, Kallonen T, Lindholm L, Jalava J, Rantakokko-Jalava K, et al. The first human report of mobile colistin resistance gene, mcr-1, in Finland. Apmis. 2018;126(5):413-7 https://doi.org/10.1111/apm.12834.

118. Principe L, Piazza A, Mauri C, Anesi A, Bracco S, Brigante G, et al. Multicenter prospective study on the prevalence of colistin resistance in Escherichia coli: relevance of mcr-1-positive clinical isolates in Lombardy, Northern Italy. Infection and drug resistance. 2018;11:377 https://doi.org/10.2147%2FIDR.S160489.

119. Del Bianco F, Morotti M, Pedna M, Farabegoli P, Sambri V. Microbiological surveillance of plasmid mediated colistin resistance in human Enterobacteriaceae isolates in Romagna (Northern Italy): August 2016–July 2017. International Journal of Infectious Diseases. 2018;69:96-8 https://doi.org/10.1016/j.ijid.2018.02.006.

120. Dortet L, Potron A, Bonnin RA, Plesiat P, Naas T, Filloux A, et al. Rapid detection of colistin resistance in Acinetobacter baumannii using MALDI-TOF-based lipidomics on intact bacteria. Scientific reports. 2018;8(1):1-5 https://doi.org/10.1590/0037-8682-0237-2019.

121. Girlich D, Naas T, Dortet L. Comparison of the superpolymyxin and ChromID colistin R screening media for the detection of colistin-resistant Enterobacteriaceae from spiked rectal swabs. Antimicrobial agents and chemotherapy. 2019;63(1):e01618-18 https://doi.org/10.1128/AAC.01618-18.

122. Bogdanovich T, Adams-Haduch JM, Tian G-B, Nguyen MH, Kwak EJ, Muto CA, et al. Colistin-resistant, Klebsiella pneumoniae carbapenemase (KPC)–producing Klebsiella pneumoniae belonging to the international epidemic clone ST258. Clinical

infectious diseases. 2011;53(4):373-6 https://doi.org/10.1093/cid/cir401.

123. Jernigan MG, Press EG, Nguyen MH, Clancy CJ, Shields RK. The combination of doripenem and colistin is bactericidal and synergistic against colistin-resistant, carbapenemase-producing Klebsiella pneumoniae. Antimicrobial agents and chemotherapy. 2012;56(6):3395-8 https://doi.org/10.1128/AAC.06364-11.

124. Snitkin ES, Zelazny AM, Gupta J, Palmore TN, Murray PR, Segre JA, et al. Genomic insights into the fate of colistin resistance and Acinetobacter baumannii during patient treatment. Genome research. 2013;23(7):1155-62 doi:10.1101/gr.154328.112.

125. Hong JH, Clancy CJ, Cheng S, Shields RK, Chen L, Doi Y, et al. Characterization of porin expression in Klebsiella pneumoniae carbapenemase (KPC)-producing K. pneumoniae identifies isolates most susceptible to the combination of colistin and carbapenems. Antimicrobial agents and chemotherapy. 2013;57(5):2147-53 https://doi.org/10.1128/AAC.02411-12.

126. Lee HJ, Bergen PJ, Bulitta JB, Tsuji B, Forrest A, Nation RL, et al. Synergistic activity of colistin and rifampin combination against multidrug-resistant Acinetobacter baumannii in an in vitro pharmacokinetic/pharmacodynamic model. Antimicrobial agents and chemotherapy. 2013;57(8):3738-45 https://doi.org/10.1128/AAC.00703-13.

127. Oleksiuk LM, Nguyen MH, Press EG, Updike CL, O'Hara JA, Doi Y, et al. In vitro responses of Acinetobacter baumannii to two-and three-drug combinations following exposure to colistin and doripenem. Antimicrobial agents and chemotherapy. 2014;58(2):1195-9 https://doi.org/10.1128/AAC.01779-13.

128. Napier BA, Burd EM, Satola SW, Cagle SM, Ray SM, McGann P, et al. Clinical use of colistin induces cross-resistance to host antimicrobials in Acinetobacter baumannii. MBio. 2013;4(3):e00021-13 https://doi.org/10.1128/mBio.00021-13.

129. Hindler JA, Humphries RM. Colistin MIC variability by method for contemporary clinical isolates of multidrug-resistant Gram-negative bacilli. Journal of clinical microbiology. 2013;51(6):1678-84 https://doi.org/10.1128/JCM.03385-12.

130. Lesho E, Yoon E-J, McGann P, Snesrud E, Kwak Y, Milillo M, et al. Emergence of colistin-resistance in extremely drug-resistant Acinetobacter baumannii containing a novel pmrCAB operon during colistin therapy of wound infections. The Journal of infectious diseases. 2013;208(7):1142-51 https://doi.org/10.1093/infdis/jit293.

131. Qureshi ZA, Hittle LE, O'Hara JA, Rivera JI, Syed A, Shields RK, et al. Colistin-resistant Acinetobacter baumannii: beyond carbapenem resistance. Clinical infectious diseases. 2015;60(9):1295-303 https://doi.org/10.1093/cid/civ048.

132. Bradford PA, Kazmierczak KM, Biedenbach DJ, Wise MG, Hackel M, Sahm DF. Correlation of β-lactamase production and colistin resistance among Enterobacteriaceae isolates from a global surveillance program. Antimicrobial agents and chemotherapy. 2016;60(3):1385-92 https://doi.org/10.1128/AAC.01870-15.

133. Rojas LJ, Salim M, Cober E, Richter SS, Perez F, Salata RA, et al. Colistin resistance in carbapenem-resistant Klebsiella pneumoniae: laboratory detection and impact on mortality. Clinical Infectious Diseases. 2017;64(6):711-8 https://doi.org/10.1093/cid/ciw805.

134. Walkty A, Karlowsky JA, Adam HJ, Lagacé-Wiens P, Baxter M, Mulvey MR, et al. Frequency of MCR-1-mediated colistin resistance among Escherichia coli clinical isolates obtained from patients in Canadian hospitals (CANWARD 2008-2015). Canadian Medical Association Open Access Journal. 2016;4(4):E641-E5 DOI: https://doi.org/10.9778/cmajo.20160080.

135. Rojas LJ, Marshall S, Cober E, Richter SS, Perez F, Salata R, et al., editors. Molecular Analysis of Colistin Resistance Among Klebsiella pneumoniae Producing K pneumoniae Carbapenemase: Heterogeneity of Genetic Mechanisms. Open Forum Infectious Diseases; 2016: Oxford University Press https://doi.org/10.1093/ofid/ofw172.50.

136. Cienfuegos-Gallet AV, Chen L, Kreiswirth BN, Jiménez JN. Colistin resistance in carbapenem-resistant Klebsiella pneumoniae mediated by chromosomal integration of plasmid DNA. Antimicrobial agents and chemotherapy. 2017;61(8):e00404-17 https://doi.org/10.1128/AAC.00404-17.

137. Van Duin D, Lok JJ, Earley M, Cober E, Richter SS, Perez F, et al. Colistin versus ceftazidime-avibactam in the treatment of infections due to carbapenem-resistant Enterobacteriaceae. Clinical Infectious

Diseases. 2018;66(2):163-71 https://doi.org/10.1093/cid/cix783.

138. Zhang W, Aurosree B, Gopalakrishnan B, Balada-Llasat J-M, Pancholi V, Pancholi P. The role of LpxA/C/D and pmrA/B gene systems in colistin-resistant clinical strains of Acinetobacter baumannii. Frontiers in Laboratory Medicine. 2017;1(2):86-91 https://doi.org/10.1016/j.flm.2017.07.001.
139. Richter SE, Miller L, Uslan DZ, Bell D, Watson K, Humphries R, et al. Risk factors for colistin resistance among gram-negative rods and Klebsiella pneumoniae isolates. Journal of Clinical Microbiology. 2018;56(9):e00149-18 https://doi.org/10.1128/JCM.00149-18.
140. Zhang J, Chen L, Wang J, Butaye P, Huang K, Qiu H, et al. Molecular detection of colistin resistance genes (mcr-1 to mcr-5) in human vaginal swabs. BMC Research Notes. 2018;11(1):1-4 https://doi.org/10.1186/s13104-018-3255-3.
141. Maalej S, Meziou M, Rhimi F, Hammami A. Comparison of disc diffusion, Etest and agar dilution for susceptibility testing of colistin against Enterobacteriaceae. Letters in applied microbiology. 2011;53(5):546-51 https://doi.org/10.1111/j.1472-765X.2011.03145.x.
142. Osei Sekyere J, Amoako DG. Carbonyl cyanide m-chlorophenylhydrazine (CCCP) reverses resistance to colistin, but not to carbapenems and tigecycline in multidrug-resistant Enterobacteriaceae. Frontiers in microbiology. 2017;8:228 https://doi.org/10.3389/fmicb.2017.00228.
143. Mansour W, Haenni M, Saras E, Grami R, Mani Y, Khalifa ABH, et al. Outbreak of colistin-resistant carbapenemase-producing Klebsiella pneumoniae in Tunisia. Journal of global antimicrobial resistance. 2017;10:88-94 https://doi.org/10.1016/j.jgar.2017.03.017.
144. Rodríguez CH, Nastro M, Calvo JL, Fariña ME, Dabos L, Famiglietti A. In vitro activity of colistin against Stenotrophomonas maltophilia. Journal of Global Antimicrobial Resistance. 2014;2(4):316-7 https://doi.org/10.1016/j.jgar.2014.04.004.
145. Jayol A, Poirel L, Villegas M-V, Nordmann P. Modulation of mgrB gene expression as a source of colistin resistance in Klebsiella oxytoca. International journal of antimicrobial agents. 2015;46(1):108-10 https://doi.org/10.1016/j.ijantimicag.2015.02.015.
146. De Maio Carrillho CM, Gaudereto JJ, Martins RCR, de Castro Lima VAC, de Oliveira LM, Urbano MR, et al. Colistin-resistant Enterobacteriaceae infections: clinical and molecular characterization and analysis of in vitro synergy. Diagnostic Microbiology and Infectious Disease. 2017;87(3):253-7 https://doi.org/10.1016/j.diagmicrobio.2016.11.007.
147. Rossi F, Girardello R, Cury AP, Di Gioia TSR, Almeida JNd, Duarte AJdS. Emergence of colistin resistance in the largest university hospital complex of São Paulo, Brazil, over five years☆. Brazilian Journal of Infectious Diseases. 2017;21:98-101 https://doi.org/10.1016/j.bjid.2016.09.011.
148. Leite GC, Oliveira MS, Perdigao-Neto LV, Rocha CKD, Guimaraes T, Rizek C, et al. Antimicrobial combinations against pan-resistant Acinetobacter baumannii isolates with different resistance mechanisms. PloS one. 2016;11(3):e0151270 https://doi.org/10.1371/journal.pone.0151270.
149. Esposito F, Fernandes MR, Lopes R, Muñoz M, Sabino CP, Cunha MP, et al. Detection of colistin-resistant MCR-1-positive Escherichia coli by use of assays based on inhibition by EDTA and zeta potential. Journal of Clinical Microbiology. 2017;55(12):3454-65 https://doi.org/10.1128/JCM.00835-17.
150. Poirel L, Jayol A, Bontron S, Villegas M-V, Ozdamar M, Türkoglu S, et al. The mgrB gene as a key target for acquired resistance to colistin in Klebsiella pneumoniae. Journal of Antimicrobial Chemotherapy. 2015;70(1):75-80 https://doi.org/10.1093/jac/dku323.
151. Olaitan AO, Diene SM, Kempf M, Berrazeg M, Bakour S, Gupta SK, et al. Worldwide emergence of colistin resistance in Klebsiella pneumoniae from healthy humans and patients in Lao PDR, Thailand, Israel, Nigeria and France owing to inactivation of the PhoP/PhoQ regulator mgrB: an epidemiological and molecular study. International journal of antimicrobial agents. 2014;44(6):500-7 https://doi.org/10.1016/j.ijantimicag.2014.07.020.
152. Nordmann P, Jayol A, Poirel L. A universal culture medium for screening polymyxin-resistant Gram-negative isolates. Journal of clinical microbiology. 2016;54(5):1395-9 https://doi.org/10.1128/JCM.00446-16.
153. Wise MG, Estabrook MA, Sahm DF, Stone GG, Kazmierczak KM. Prevalence of mcr-type genes among colistin-resistant Enterobacteriaceae collected in 2014-2016 as part of the INFORM global surveillance program. PloS one.

2018;13(4):e0195281 https://doi.org/10.1371/journal.pone.0195281.

154. Turnidge J, Bell J, Jones R, editors. Emergence of colistin-resistant Klebsiella spp., and Enterobacter spp. in the Asia-Pacific (APAC) region: a SENTRY antimicrobial surveillance program report (2006). Conf Antimicrob Agents Chemother American Society for Microbiology, Washington, DC; 2007. https://doi.org/10.1185/03007995.2015.1018989

155. Tan T, Ng S. The in-vitro activity of colistin in gram-negative bacteria. Singapore medical journal. 2006;47(7):621. PMID: 16810437

156. Chen S, Hu F, Zhang X, Xu X, Liu Y, Zhu D, et al. Independent emergence of colistin-resistant Enterobacteriaceae clinical isolates without colistin treatment. Journal of clinical microbiology. 2011;49(11):4022. doi: 10.1128/JCM.01233-11

157. Vakili B, Fazeli H, Shoaei P, Yaran M, Ataei B, Khorvash F, et al. Detection of colistin sensitivity in clinical isolates of Acinetobacter baumannii in Iran. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2014;19(Suppl 1):S67. PMID: 25002899; PMCID: PMC4078383.

158. Ko KS, Suh JY, Kwon KT, Jung S-I, Park K-H, Kang CI, et al. High rates of resistance to colistin and polymyxin B in subgroups of Acinetobacter baumannii isolates from Korea. Journal of Antimicrobial Chemotherapy. 2007;60(5):1163-7. doi: 10.1093/jac/dkm305.

159. Eser OK, Ergin A, Hascelik G. Antimicrobial resistance and existence of metallo-beta-lactamase in Acinetobacter species isolated from adult patients. Mikrobiyoloji bulteni. 2009;43(3):383-90. PMID: 19795613

160. Punpanich W, Tantichattanon W, Wongwatcharapaiboon S, Treeratweeraphong V. In vitro susceptibility pattern of cephalosporin-resistant Gram-negative bacteria. J Med Assoc Thai. 2008;91(Suppl 3):S21-7. PMID: 19255989

161. Imtiaz W, Syed Z, Rafaque Z, Andrews SC, Dasti JI. Analysis of antibiotic resistance and virulence traits (genetic and phenotypic) in Klebsiella pneumoniae clinical isolates from Pakistan: identification of significant levels of carbapenem and colistin resistance. Infection and drug resistance. 2021;14:227. doi: 10.2147/IDR.S293290.

162. Bialvaei AZ, Samadi Kafil H. Colistin, mechanisms and prevalence of resistance. Current medical research and opinion. 2015;31(4):707-21. doi: 10.1185/03007995.2015.1018989.

163. Pitt T, Sparrow M, Warner M, Stefanidou M. Survey of resistance of Pseudomonas aeruginosa from UK patients with cystic fibrosis to six commonly prescribed antimicrobial agents. Thorax. 2003;58(9):794-6. doi: 10.1136/thorax.58.9.794.

164. Arroyo L, Garcia-Curiel A, Pachon-Ibanez M, Llanos A, Ruiz M, Pachon J, et al. Reliability of the E-test method for detection of colistin resistance in clinical isolates of Acinetobacter baumannii. Journal of clinical microbiology. 2005;43(2):903-5. doi: 10.1128/JCM.43.2.903-905.2005

165. Miftode E, Dorneanu O, Leca D, Teodor A, Mihalache D, Filip O, et al. Antimicrobial resistance profile of E. coli and Klebsiella spp. from urine in the Infectious Diseases Hospital Iaşi. Revista Medico-Chirurgicala a Societatii de Medici si Naturalisti din Iasi. 2008;112(2):478-82. PMID: 19295023

166. Keen III EF, Robinson BJ, Hospenthal DR, Aldous WK, Wolf SE, Chung KK, et al. Prevalence of multidrug-resistant organisms recovered at a military burn center. Burns. 2010;36(6):819-25. doi: 10.1016/j.burns.2009.10.013.

167. Li J, Nation RL, Turnidge JD, Milne RW, Coulthard K, Rayner CR, et al. Colistin: the re-emerging antibiotic for multidrug-resistant Gram-negative bacterial infections. The Lancet infectious diseases. 2006;6(9):589-601. DOI: 10.1016/S1473-3099(06)70580-1

168. Walkty A, DeCorby M, Nichol K, Karlowsky J, Hoban D, Zhanel G. In vitro activity of colistin (polymyxin E) against 3,480 isolates of gram-negative bacilli obtained from patients in Canadian hospitals in the CANWARD study, 2007-2008. Antimicrobial agents and chemotherapy. 2009;53(11):4924-6. doi: 10.1128/AAC.00786-09.

169. Hernan RC, Karina B, Gabriela G, Marcela N, Carlos V, Angela F. Selection of colistin-resistant Acinetobacter baumannii isolates in postneurosurgical meningitis in an intensive care unit with high presence of heteroresistance to colistin. Diagnostic microbiology and infectious disease. 2009;65(2):188-91. doi: 10.1016/S1473-3099(06)70580-1.

170. Falagas ME, Rafailidis PI, Matthaiou DK. Resistance to polymyxins: mechanisms, frequency and treatment options. Drug resistance updates. 2010;13(4-5):132-8. doi: 10.1016/j.drup.2010.05.002.

171. Ahmed NH, Baba K, Clay C, Lekalakala R, Hoosen AA. In vitro activity of tigecycline against clinical isolates of carbapenem resistant Acinetobacter baumannii complex in Pretoria, South Africa. BMC research notes. 2012;5(1):1-4. doi: 10.1186/1756-0500-5-215.

172. Maalej SM, Meziou MR, Mahjoubi F, Hammami A. Epidemiological study of Enterobacteriaceae resistance to colistin in Sfax (Tunisia). Médecine et maladies infectieuses. 2012;42(6):256-63. doi: 10.1016/j.medmal.2012.04.008.

173. Igumbor E, Gwanzura L, Chirara M, Obi C, Muza D. Antibiotic sensitivity and plasmid profiles of Pseudomonas aeruginosa. The Central African Journal of Medicine. 2000;46(11):296-300. PMID: 12002119

174. Moffatt JH, Harper M, Harrison P, Hale JD, Vinogradov E, Seemann T, et al. Colistin resistance in Acinetobacter baumannii is mediated by complete loss of lipopolysaccharide production. Antimicrobial agents and chemotherapy. 2010;54(12):4971-7. doi: 10.1128/AAC.00834-10.

175. Haagensen JA, Klausen M, Ernst RK, Miller SI, Folkesson A, Tolker-Nielsen T, et al. Differentiation and distribution of colistin-and sodium dodecyl sulfate-tolerant cells in Pseudomonas aeruginosa biofilms. Journal of bacteriology. 2007;189(1):28-37. doi: 10.1128/JB.00720-06.

176. Cannatelli A, Giani T, D'Andrea MM, Di Pilato V, Arena F, Conte V, et al. MgrB inactivation is a common mechanism of colistin resistance in KPC-producing Klebsiella pneumoniae of clinical origin. Antimicrobial agents and chemotherapy. 2014;58(10):5696-703. doi: 10.1128/AAC.03110-14.