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Global research output in antimicrobial resistance among uropathogens: A bibliometric analysis (2002–2016)

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ABSTRACT

Objectives: Antimicrobial resistance (AMR) among uropathogens contributes to treatment failure. Research in AMR among uropathogens is important to establish treatment options. This study assessed global research trends in AMR among uropathogens.

Methods: SciVerse Scopus was used to retrieve relevant documents for the period 2002–2016. Only journal articles were included in the analysis. Analysis of author keywords was carried out using VOSviewer.

Results: A total of 1087 journal articles were retrieved with an *h*-index of 50. The number of publications increased noticeably in the past decade. Analysis of subject areas of retrieved documents showed that 275 (25.3%) articles were in molecular biology/genetics/microbiology/immunology, 197 (18.1%) were in pharmacological/therapeutic approaches for treatment of urinary tract infections and 615 (56.6%) were in epidemiology/public health. Terms such as multidrug-resistant and extended-spectrum β-lactamases (ESBLs) appeared more frequently in documents published in the period 2012–2016. The mean number of authors per article was 5.3. Most active authors in this field were from Japan. The USA ranked first with 148 documents (13.6%), followed by India (97; 8.9%) and Iran (84; 7.7%). The top productive institution was Tehran University of Medical Sciences (21 publications), followed by Kobe University in Japan (20 publications). The *Journal of Antimicrobial Chemotherapy* ranked first with 33 publications.

Conclusion: Research in AMR among uropathogens showed a noticeable increase in the past decade. Reports of increasing incidence of resistance among uropathogens were published from different parts of the world. Empirical therapy should be based on updated research in AMR.

1. Introduction

Antimicrobial resistance (AMR) is a worldwide problem that poses a serious threat to treatment success for a wide range of infections [1]. AMR also poses an economic burden owing to longer duration of treatment, additional laboratory tests and the use of expensive medications to treat infections [2,3]. Actions needed to control the problem of AMR are the responsibility of governments, healthcare providers, researchers and the public. Research, awareness, knowledge and up-to-date information regarding AMR are important in minimising this phenomenon and in updating therapeutic guidelines appropriate for various types of infections [4–11].

Urinary tract infections (UTIs), both hospital- and community-acquired, are common in all age groups in both sexes, particularly in females owing to certain physiological features unique to females [12,13]. It has been reported that ca. 150 million people are diagnosed annually with UTI, leading to the loss of billions of dollars [14]. Poor hygiene and low socioeconomic status are predisposing factors for UTI [15]. Several pathogens have been implicated in UTIs, such as *Escherichia coli*, *Klebsiella* spp., *Proteus mirabilis*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Staphylococcus saprophyticus* [16].

Analysis of the published literature on AMR among uropathogens is important for developing new empirical and therapeutic guidelines for the treatment of UTIs. Furthermore, analysis of the published literature is important in order to understand global and regional changes in AMR. Many review articles have been published regarding UTIs and AMR among uropathogens [16–19], but none has discussed or analysed global research output and

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trends in this regard. Therefore, the aim of this study was to analyse global research output in AMR among uropathogens. Specifically, national and international contributions to AMR-related literature among uropathogens were analysed. This study is the first to discuss research growth and trends in AMR among uropathogens and may be used as baseline information for future comparison and assessment.

2. Methods

Details regarding how data were retrieved are shown in the flow chart illustrated in Appendix A. SciVerse Scopus was selected to perform this study because it has a larger number of indexed journals than Web of Science and has 100% coverage of Medline [20,21]. In Scopus, the time of the study was set from 2002–2016. Different scenarios were used in the search query and these scenarios were based on the title search of keywords related to UTI and/or uropathogens and AMR. In the search query, quotation marks were used along with certain phrases to indicate that the exact phrase is needed and not any related words. The asterisk was also used with certain keywords to retrieve related words. For example, when the term *resist** was used, Scopus will retrieve words such as *resist*ant and *resist*ance. The validity of the overall search strategy was checked by manual investigation of 10 randomly selected documents from each year to check for the presence of false-positive results, which were then excluded using the Boolean 'NOT TITLE' in the overall search strategy as seen in Appendix A. Articles pertaining to veterinary data were also excluded because the focus of this study was on AMR in humans rather than animals. The finalised list of retrieved documents was analysed and the following bibliometric indicators were presented: types of retrieved documents and languages used in publications; growth of publications and citation analysis; frequent terms in author keywords of retrieved documents; top cited articles; authorship analysis; top productive countries; international collaboration; top productive institutions/organisations; and preferred journals for publications. Analysis of certain parameters, such as frequent terms in author keywords and geographical distribution, was made on three time intervals (2002–2006, 2007–2011 and 2012–2016) to show the temporal changes in type and content of research activity pertaining to AMR among uropathogens.

Bibliometric indicators were obtained directly from Scopus, which provides an easy-to-use analytic format for most bibliometric indicators presented in the current study. For growth analysis, annual growth rate (AGR) was calculated using the equation: AGR = [(ending value − beginning value)/beginning value] × 100. All bibliometric indicators were obtained directly from Scopus, which allows for ranking of countries, institutions, authors and journals. Stratification of productivity for each country was based on either gross domestic product (GDP) or population size obtained from World Bank data [22].

Scopus also allows for limiting or exclusion of certain results and this process can help in determining the level of international collaboration and Hirsh index (*h*-index) along with the total citations for any country or institution. The tool used to visualise and map bibliometric indicators was VOSviewer [23]. For the most frequently encountered terms in author keywords, a minimum of five occurrences was set as the threshold.

3. Results

3.1. Types of documents and languages

A total of 1087 journal articles were retrieved. The most common type of documents was research articles (938; 86.3%), followed by review articles (48; 4.4%). All types of retrieved documents are shown in Table 1. English (866; 79.7%) was the most common language, followed by Spanish (56; 5.2%) and Japanese (28; 2.6%). A list of different languages encountered in the retrieved documents is shown in Table 2. It should be emphasised here that language analysis was obtained directly from Scopus and was not made through manual investigation of each article. A second important point is that some articles had two abstracts written in two different languages; therefore, the total number listed in Table 2 exceeds the total number of retrieved documents. Analysis of subject areas of retrieved documents showed that 275 (25.3%) articles were in molecular biology/genetics/microbiology/immunology, 197 (18.1%) were in pharmacological/therapeutic approaches for treatment of UTIs and 615 (56.6%) were in epidemiology/public health.

Table 1
Types of retrieved documents in antimicrobial resistance among uropathogens (2002–2016).

Document type	*n*	% (*N* = 1087)
Article	938	86.3
Review	48	4.4
Letter	45	4.1
Note	20	1.8
Article in press	12	1.1
Conference paper	11	1.0
Editorial	8	0.7
Short survey	5	0.5

n, number of retrieved documents.

3.2. Growth of publications and citation analysis

The number of published documents showed a noticeable increase in the past decade. The maximum number of publications recorded was 124, which were obtained in 2015. The average annual number of publications was 72 documents per year. The AGR of publications showed a noticeable increase in 2008 (26.0%) and 2014 (28.4%). Retrieved documents received 12 193 citations with an *h*-index of 50. The median (interquartile range) number of citations was 3 (0–12), whilst the mean ± standard deviation was 11.2 ± 23.5 and the range was (0–350). Total citations for each year and total cumulative citations are shown in Table 3.

3.3. Analysis of most frequently encountered author keywords

The most frequently encountered author keywords were analysed using VOSviewer. The analysis included frequently encountered antimicrobial agents, micro-organisms and AMR-related terms. The analysis was made for three time intervals of the study period to show temporal changes in type of antimicrobial

Table 2
Languages used in retrieved documents in antimicrobial resistance among uropathogens (2002–2016) (*N* = 1087)[a].

Language	*n*	% (*N* = 1087)	Language	*n*	%	Language	*n*	%
English	866	79.7	Korean	9	0.8	Dutch	1	0.1
Spanish	56	5.2	Persian	9	0.8	Norwegian	1	0.1
Japanese	28	2.6	Romanian	5	0.5	Slovak	1	0.1
Chinese	21	1.9	Italian	4	0.4	Ukrainian	1	0.1
Turkish	21	1.9	Serbian	4	0.4	Urdu	1	0.1
French	19	1.7	Bulgarian	3	0.3			
German	19	1.7	Croatian	2	0.2			
Portuguese	13	1.2	Czech	2	0.2			
Polish	11	1.0	Greek	2	0.2			
Russian	10	0.9	Hebrew	2	0.2			

n, number of retrieved documents.
[a] Some articles had two abstracts written in two different languages; therefore, the total number exceeds the number of retrieved documents.

Table 3
Growth of publications and citations on antimicrobial resistance among uropathogens (2002–2016).

Year	*n*	% (*N* = 1087)	AGR	Citations	Cumulative citations
2002	44	4.0	–	1169	1169
2003	41	3.8	−6.8	1387	2556
2004	45	4.1	9.8	859	3415
2005	46	4.2	2.2	1202	4617
2006	45	4.1	−2.2	1014	5631
2007	50	4.6	11.1	930	6561
2008	63	5.8	26.0	938	7499
2009	63	5.8	0	1038	8537
2010	66	6.1	4.8	741	9278
2011	77	7.1	16.7	666	9944
2012	86	7.9	11.7	813	10 757
2013	95	8.7	10.5	666	11 423
2014	122	11.2	28.4	421	11 844
2015	124	11.4	1.6	247	12 091
2016	120	11.0	−3.2	102	12 193

n, number of retrieved documents; AGR, annual growth rate.

agents and micro-organisms being studied. The results are shown in Table 4. In the last interval of the study period (2012–2016), antimicrobial agents such as tigecycline, GAR-936, carbapenems and third-generation cephalosporins were being tested for activity against uropathogens, which was not seen in the earlier intervals. The types of micro-organisms being frequently encountered in the last interval (2012–2016) were similar to those studied at earlier time intervals but with more emphasis on new resistant strains of *E. coli* such as *E. coli* sequence type 131 (ST131). In the last time interval, certain AMR-related terms appeared more often in author keywords. Such terms included multidrug resistance, extended-spectrum β-lactamases (ESBLs), carbapenemases and others (Table 4). The growth of research publications in ESBLs among uropathogens is shown in Fig. 1.

3.4. Top cited articles

The top ten cited articles for the three intervals of the study period are presented in Tables 5A–C. The purpose of investigating top cited articles for three separate intervals was to show the changes and variations in the interest of researchers and readers with time in the field of uropathogen AMR. For the interval 2002–2006, the top cited articles discussed mainly themes related to epidemiology and prevalence as well resistance of *E. coli* to fluoroquinolones and trimethoprim/sulfamethoxazole. For the second interval (2007–2011), the main themes of the ten top cited articles were again epidemiology and the development of fluoroquinolone resistance in *E. coli*. In the last time interval (2012–2016), the main themes of the top cited articles were new strains of *E. coli*, resistance of uropathogens to cephalosporins, molecular biology and genetics of microbial resistance, and epidemiological studies.

One of the most commonly cited articles during the study period was an article that received 356 citations and was published in the *Journal of Antimicrobial Chemotherapy* in 2003. The article was a survey in 17 countries to investigate the prevalence and susceptibility of pathogens causing community-acquired acute uncomplicated UTIs and the authors concluded that AMR was lowest in the Nordic countries and Austria and highest in Portugal and Spain [24]. The authors repeated their study after several years (ECO.SENS study) and published the results in the *International Journal of Antimicrobial Agents* in 2012 [25]. The authors of the follow-up study concluded that in 2003 no isolates with ESBL were found; however, in the study carried out in 2012, 11 isolates were identified as having either CTX-M or AmpC β-lactamases.

Of particular interest among the top cited articles was an article that received 198 citations which was published in *Annals of Clinical Microbiology and Antimicrobials* in 2007 [26]. The article determined the distribution and antibiotic susceptibility patterns of bacterial strains isolated from patients with community-acquired UTIs in India as well as identification of ESBLs among different uropathogens. The authors concluded that production of ESBLs among uropathogens was increasing. A total of 168 articles (15.5%) of the retrieved documents discussed the issue of emerging ESBLs. The growth of publications regarding ESBLs among uropathogens showed a significant noticeable but gradual increase during the study period. Fig. 1 shows that the number of publications regarding ESBLs from 2002–2006 was low and showed a fluctuating increase from 2007–2011. However, a sharp linear upward increase was seen from 2012–2016. A total of 103 articles (9.5%) regarding multidrug resistance among uropathogens were retrieved for the overall study period. The growth of publications in multidrug resistance showed a similar pattern to that of ESBLs.

3.5. Authorship analysis and top productive authors

Retrieved articles included 71 (6.5%) single authored publications, whilst the remaining 1016 (93.5%) were multi-authored publications. The mean number of authors per article was 5.3. Authors with a minimum productivity of 10 publications are shown in a network visualisation map (Fig. 2). The number of active authors with a minimum productivity of 10 publications is 31 researchers. Active authors were grouped in two clusters, a large cluster with 27 researchers and a small cluster with 4 researchers.

Table 4
Most frequent terms in encountered author keywords in the assigned study period.

2002–2006	2007–2011	2012–2016
Antimicrobial agents		
Fluoroquinolones/quinolones, ciprofloxacin, nitrofurantoin, aminoglycosides, SXT, levofloxacin, trimethoprim	Fluoroquinolones/quinolones, ciprofloxacin, ampicillin, fosfomycin, SXT, gentamicin, nitrofurantoin	Ciprofloxacin, fosfomycin, nitrofurantoin, fluoroquinolones/ quinolones, carbapenems, cefazolin, SXT, amikacin, cefepime, third-generation cephalosporins, tigecycline, GAR-936
Micro-organisms		
Escherichia coli, Enterobacteriaceae, *Pseudomonas aeruginosa*, *Enterococcus*, *Enterococcus faecalis*	*E. coli*, Enterobacteriaceae, *Klebsiella pneumoniae*, enterococci, *E. faecalis*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*	*E. coli*, Enterobacteriaceae, *P. aeruginosa*, *K. pneumoniae*, *E. faecalis*, *Enterococcus faecium*, *E. coli* ST131, MRSA, *P. mirabilis*, *Acinetobacter baumannii*, *Citrobacter*, enterococci, *S. aureus*
Resistance-related terms		
Multidrug resistance (*P. aeruginosa*)	ESBL, cross-resistance, biofilm	ESBL, multidrug resistance, biofilm, fluoroquinolone resistance, carbapenem-resistant Enterobacteriaceae, *K. pneumoniae* carbapenemase (KPC), AmpC β-lactamase, β-lactamases, CTX-M (β-lactamases), vancomycin-resistant enterococci

SXT, trimethoprim/sulfamethoxazole; ST, sequence type; MRSA, methicillin-resistant *S. aureus*; ESBL, extended-spectrum β-lactamase.
Terms are written in order of decreasing number of occurrences in the retrieved articles.

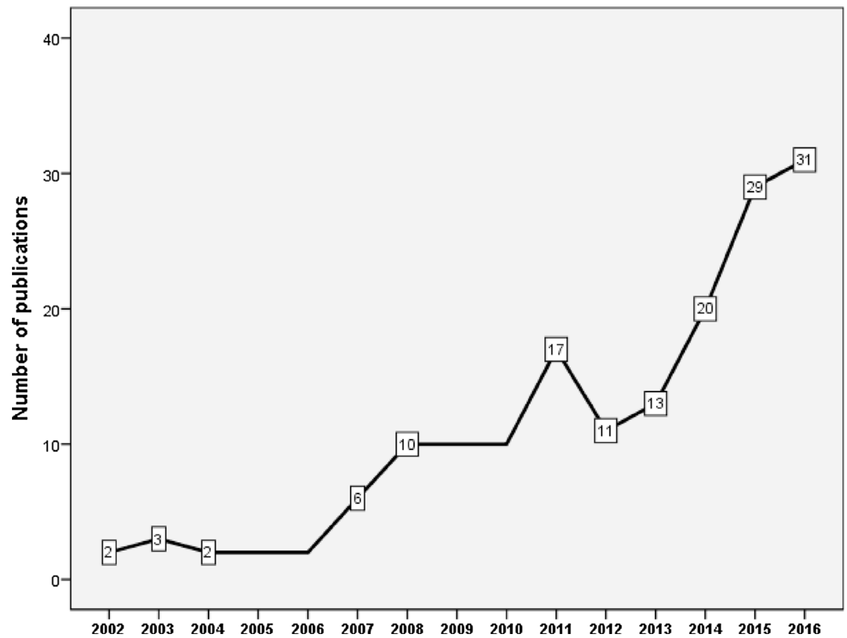

Fig. 1. Growth of publications in antimicrobial resistance among uropathogens producing extended-spectrum β-lactamases (ESBLs) (2002–2016).

Table 5A
Top ten cited articles in antimicrobial resistance (AMR) among uropathogens (2002–2006).

Author(s)	Title	Reference	Cited by (*n*)
Kahlmeter G.	An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS project	[24]	356
Karlowsky J.A., Kelly L.J., Thornsberry C., Jones M.E., Sahm D.F.	Trends in antimicrobial resistance among urinary tract infection isolates of *Escherichia coli* from female outpatients in the United States	[47]	221
Komp Lindgren P., Karlsson Å., Hughes D.	Mutation rate and evolution of fluoroquinolone resistance in *Escherichia coli* isolates from patients with urinary tract infections	[48]	182
Arslan H., Azap O.K., Ergönül O., Timurkaynak F.	Risk factors for ciprofloxacin resistance among *Escherichia coli* strains isolated from community-acquired urinary tract infections in Turkey	[49]	165
Farrell D.J., Morrissey I., De Rubeis D., Robbins M., Felmingham D.	A UK multicentre study of the antimicrobial susceptibility of bacterial pathogens causing urinary tract infection	[50]	152
Raz R., Chazan B., Kennes Y., Colodner R., Rottensterich E., Dan M., et al.	Empiric use of trimethoprim–sulfamethoxazole (TMP-SMX) in the treatment of women with uncomplicated urinary tract infections, in a geographical area with a high prevalence of TMP–SMX-resistant uropathogens	[51]	137
Zhanel G.G., Hisanaga T.L., Laing N.M., DeCorby M.R., Nichol K.A., Weshnoweski B., et al.	Antibiotic resistance in *Escherichia coli* outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA)	[52]	136
Zhanel G.G., Hisanaga T.L., Laing N.M., DeCorby M.R., Nichol K.A., Palatnik L.P., et al.	Antibiotic resistance in outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA)	[53]	128
Kerrn M.B., Klemmensen T., Frimodt-Møller N., Espersen F.	Susceptibility of Danish *Escherichia coli* strains isolated from urinary tract infections and bacteraemia, and distribution of *sul* genes conferring sulphonamide resistance	[54]	107
Karlowsky J.A., Hoban D.J., DeCorby M.R., Laing N.M., Zhanel G.G.	Fluoroquinolone-resistant urinary isolates of *Escherichia coli* from outpatients are frequently multidrug resistant: results from the North American Urinary Tract Infection Collaborative Alliance–Quinolone Resistance Study	[55]	101

The sizes of circles in the large cluster are almost equal, suggesting that all authors in the large cluster had equal research productivity.

3.6. Top productive countries and international collaboration

The geographical distribution of retrieved publications is shown in Fig. 3. The distribution showed that publications regarding AMR among uropathogens were focused in Europe, certain parts of the Mediterranean region, certain parts of Southeast Asia, and North America. The remaining parts of the world showed few or scattered publications (Fig. 3). The top ten productive countries in the field of AMR among uropathogens at different time intervals are shown in Table 6. The list of top ten countries changed with time, suggestive of either increased research activity in specific countries or increased medical encounter of AMR among uropathogens in these countries. Pakistan and Taiwan showed up in the active top ten list in the last time interval (2012–2016) but were not in earlier intervals. India has moved up in the ranking order with time and ranked second in the last time interval (2012–2016).

The top ten productive countries for the overall study period are shown in Table 7. The USA ranked first with 148 documents (13.6%), followed by India (97; 8.9%) and Iran (84; 7.7%). The top ten productive countries were from different world regions such as

Table 5B
Top ten cited articles in AMR among uropathogens (2007–2011).

Author(s)	Title	Reference	Cited by (*n*)
Akram M., Shahid M., Khan A.U.	Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India	[26]	198
Johnson J.R., Menard M., Johnston B., Kuskowski M.A., Nichol K., Zhanel G.G.	Epidemic clonal groups of *Escherichia coli* as a cause of antimicrobial-resistant urinary tract infections in Canada, 2002–2004	[56]	181
Schito G.C., Naber K.G., Botto H., Palou J., Mazzei T., Gualco L., et al.	The ARESC study: an international survey on the antimicrobial resistance of pathogens involved in uncomplicated urinary tract infections	[57]	148
Hillier S., Roberts Z., Dunstan F., Butler C., Howard A., Palmer S.	Prior antibiotics and risk of antibiotic-resistant community-acquired urinary tract infection: a case–control study	[58]	77
Manges A.R., Smith S.P., Lau B.J., Nuval C.J., Eisenberg J.N.S., Dietrich P.S., et al	Retail meat consumption and the acquisition of antimicrobial resistant *Escherichia coli* causing urinary tract infections: a case–control study	[59]	66
van der Starre W.E., van Nieuwkoop C., Paltansing S., van't Wout J.W., Groeneveld G.H., Becker M.J., et al.	Risk factors for fluoroquinolone-resistant *Escherichia coli* in adults with community-onset febrile urinary tract infection	[60]	64
Kothari A., Sagar V.	Antibiotic resistance in pathogens causing community-acquired urinary tract infections in India: a multicenter study	[61]	64
Butler C.C., Dunstan F., Heginbothom M., Mason B., Roberts Z., Hillier S., et al.	Containing antibiotic resistance: decreased antibiotic-resistant coliform urinary tract infections with reduction in antibiotic prescribing by general practices	[62]	60
Randrianirina F., Soares J.L., Carod J.F., Ratsima E., Thonnier V., Combe P., et al.	Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in Antananarivo, Madagascar	[63]	57
Cheng C.-H., Tsai M.-H., Huang Y.-C., Su L.-H., Tsau Y.-K., Lin C.-J., et al.	Antibiotic resistance patterns of community-acquired urinary tract infections in children with vesicoureteral reflux receiving prophylactic antibiotic therapy	[64]	56

Table 5C
Top ten cited articles in AMR among uropathogens (2012–2016)

Author(s)	Title	Reference	Cited by (*n*)
Kahlmeter G., Poulsen H.O.	Antimicrobial susceptibility of *Escherichia coli* from community-acquired urinary tract infections in Europe: the ECO·SENS study revisited	[25]	93
Lu P.-L., Liu Y.-C., Toh H.-S., Lee Y.-L., Liu Y.-M., Ho C.-M., et al.	Epidemiology and antimicrobial susceptibility profiles of Gram-negative bacteria causing urinary tract infections in the Asia-Pacific region: 2009–2010 results from the Study for Monitoring Antimicrobial Resistance Trends (SMART)	[65]	74
Banerjee R., Johnston B., Lohse C., Porter S.B., Clabots C., Johnson J.R.	*Escherichia coli* sequence type 131 is a dominant, antimicrobial- resistant clonal group associated with healthcare and elderly hosts	[66]	63
Neuner E.A., Sekeres J., Hall G.S., van Duin D.	Experience with fosfomycin for treatment of urinary tract infections due to multidrug-resistant organisms	[67]	63
Linhares I., Raposo T., Rodrigues A., Almeida A.	Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten-year surveillance study (2000–2009)	[68]	59
Edlin R.S., Shapiro D.J., Hersh A.L., Copp H.L.	Antibiotic resistance patterns of outpatient pediatric urinary tract infections	[69]	46
Zilberberg M.D., Shorr A.F.	Secular trends in Gram-negative resistance among urinary tract infection hospitalizations in the United States, 2000–2009	[70]	45
Sorlozano A., Jimenez-Pacheco A., de Dios Luna Del Castillo J., Sampedro A., Martinez-Brocal A., Miranda-Casas C., et al.	Evolution of the resistance to antibiotics of bacteria involved in urinary tract infections: a 7-year surveillance study	[71]	39
Carmeli Y., Armstrong J., Laud P.J., Newell P., Stone G., Wardman A., et al.	Ceftazidime–avibactam or best available therapy in patients with ceftazidime-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* complicated urinary tract infections or complicated intra-abdominal infections (REPRISE): a randomised, pathogen-directed, phase 3 study	[72]	33
Schmiemann G., Gágyor I., Hummers-Pradier E., Bleidorn J.	Resistance profiles of urinary tract infections in general practice — an observational study	[73]	31

North America, Asia, the Middle East, Europe and Latin America. International collaboration (intercountry collaboration) among the top ten productive countries ranged from 2.4% for Iran up to 46.7% for Canada (Table 8). When research productivity among the top ten productive countries was stratified by GPD, Iran ranked first with 213.7 publications per one trillion GDP, whilst China ranked tenth with 2.9 publications per one trillion GDP. When productivity was stratified by population size, Iran ranked first with 100 publications per 100 million people and China ranked tenth with 2.4 publications per 100 million people (Table 9).

3.7. Top productive institutions/organisations and preferred journals

The top ten productive institutions in AMR among uropathogens are shown in Table 10. The top productive institution was Tehran University of Medical Sciences (21 publications), followed by Kobe University in Japan (20 publications). The top ten list included four Japanese institutions and three Iranian institutions. It is noteworthy that none of the top ten institutions were from the USA even though it was the most productive country; this is due to the large number of institutions in the USA, so that even if every one of them published just one article, the total number of publications would be high. In other countries, the number of institutions is lower, thus several publications come from the same institute. Regarding the *h*-index, the publications by Kobe University had the highest *h*-index (8).

The top ten preferred journals for publishing articles in AMR among uropathogens are shown in Table 11. The *Journal of Antimicrobial Chemotherapy* ranked first with 33 publications and the *International Journal of Antimicrobial Agents* ranked second

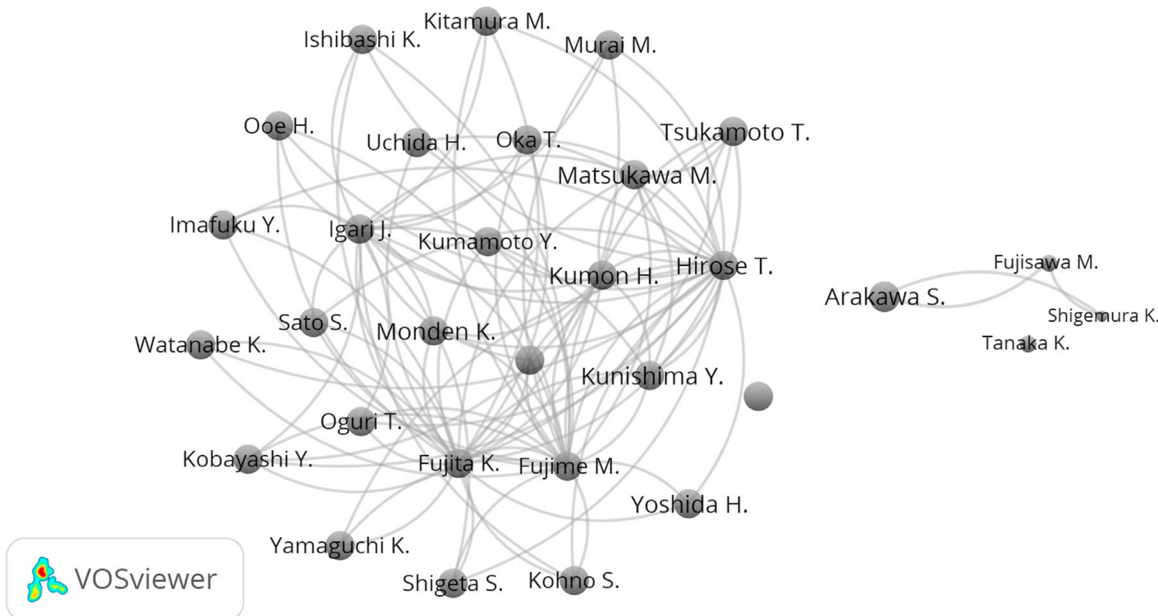

Fig. 2. Network visualisation map of authorship collaboration in antimicrobial resistance among uropathogens during the period 2002–2006.

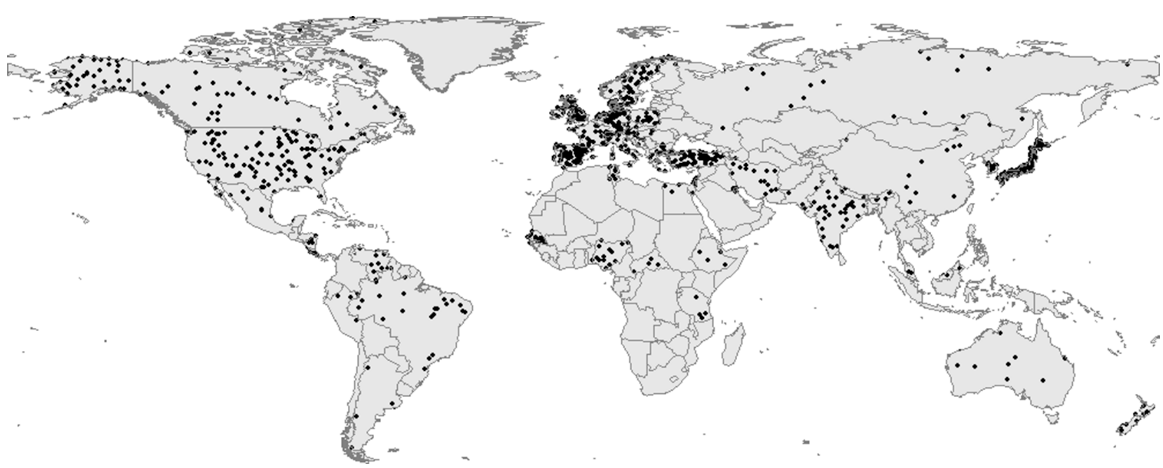

Fig. 3. Geographical distribution of publications in antimicrobial resistance among uropathogens (2002–2016). Each dot represents 0.5 publications.

with 32 publications. Two specialised urology journals were among the top ten preferred journals. Four journals in the top ten list were issued from the USA and two from each of the UK, Japan and India.

Table 6
Top productive countries in antimicrobial resistance among uropathogens during three different time intervals.

2002–2006			2007–2011			2012–2016		
Country	*n*	% (*N* = 1087)	Country	*n*	%	Country	*n*	%
USA	38	3.5	USA	34	3.1	USA	76	7.0
Japan	19	1.7	Iran	22	2.0	India	75	6.9
Spain	14	1.3	Turkey	20	1.8	Iran	58	5.3
Turkey	14	1.3	South Korea	15	1.4	Turkey	25	2.3
Canada	13	1.2	China	14	1.3	Brazil	22	2.0
Germany	11	1.0	India	13	1.2	UK	19	1.7
UK	10	0.9	Japan	12	1.1	Pakistan	18	1.7
India	9	0.8	UK	12	1.1	China	17	1.6
Sweden	7	0.6	Spain	10	0.9	Taiwan	17	1.6
Brazil	6	0.6	Italy	9	0.8	Spain	14	1.3
France	6	0.6	Mexico	9	0.8			

n, number of retrieved documents.

4. Discussion

In this bibliometric study, the growth of publications and research trends in AMR among uropathogens were assessed and analysed. This study showed that there was a noticeable increase in publications, suggesting that the AMR problem is increasing and that new antibiotics might be needed to treat UTIs in the future. In most UTI cases, treatment is empirical and therefore research identifying antibiotic susceptibility patterns is extremely important in every country and even in different regions within the same country [15]. The growth of AMR among uropathogens threatens the success of empirical treatment of millions of cases of community-acquired UTI with the subsequent loss of extra expenditure and human suffering [27]. It should be emphasised here that the problem of AMR among uropathogens is increasing and might reach a situation in which antibiotics such as fosfomycin become ineffective in the treatment of UTIs [28].

The relatively high *h*-index of the retrieved publications is an indication of the large number of readers such as clinicians and researchers who are interested in this topic. Furthermore, the diversity of journal names publishing in this topic indicates that

Table 7
Top productive countries in antimicrobial resistance among uropathogens (2002–2016).

Rank	Country	*n*	% (*N* = 1087)	*h*-index
1	USA	148	13.6	32
2	India	97	8.9	10
3	Iran	84	7.7	14
4	Turkey	59	5.4	13
5	Japan	44	4.0	9
6	UK	41	3.8	17
7	Spain	38	3.5	12
8	Brazil	35	3.2	10
9	China	33	3.0	7
10	Canada	29	2.7	14

n, number of retrieved documents.

editors consider this topic as an important microbiological, clinical, pharmacological and public health issue. Furthermore, the retrieved publications originated from different regions of the world, which is an important indication of the global dimension of AMR among uropathogens. None of the countries in the African region showed up in the top productive list during the different intervals of the study period. The more dangerous infections and health conditions such as malaria, tuberculosis, malnutrition, internal conflicts and human immunodeficiency virus (HIV) are a true burden in Africa and most financial support and research is directed toward these topics [29]. This might have led to research being focused on the above mentioned diseases rather than AMR in UTIs.

The development of AMR among uropathogens, particularly in *E. coli*, could be attributed to irrational use of antibiotics, such as over-the-counter use of antibiotics in developing countries where

Table 8
International collaboration in top ten productive countries in antimicrobial resistance among uropathogens (2002–2016).

Rank	Country	*n*	% (*N* = 1087)	*h*-index	No. of articles with intracountry collaboration[a]	%	No. of articles with intercountry collaboration[b]	%
1	USA	148	13.6	32	103	69.6	45	30.4
2	India	97	8.9	10	90	92.8	7	7.2
3	Iran	84	7.7	14	82	97.6	2	2.4
4	Turkey	59	5.4	13	57	96.6	2	3.4
5	Japan	44	4.0	9	42	95.5	2	4.5
6	UK	41	3.8	17	31	75.6	10	24.4
7	Spain	38	3.5	12	36	94.7	2	5.3
8	Brazil	35	3.2	10	31	88.6	4	11.4
9	China	35	3.2	7	28	80.0	7	20.0
10	Canada	30	2.8	14	16	53.3	14	46.7

n, number of retrieved documents.
[a] Intracountry collaboration refers to articles in which all authors had the same country affiliation.
[b] Intercountry collaboration (international collaboration) refers to articles in which authors had different country affiliations.

Table 9
Top ten productive countries in antimicrobial resistance among uropathogens stratified by GDP or population size (2002–2016).

Rank	Country	No. of publications	% (*N* = 1087)	No. of publications per one trillion USD GDP	No. of publications per 100 million people
1	USA	148	13.6	10.0	45.8
2	India	97	8.9	42.9	7.3
3	Iran	84	7.7	213.7	100
4	Turkey	59	5.4	68.8	73.8
5	Japan	44	4.0	9.0	34.9
6	UK	41	3.8	15.7	1.5
7	Spain	38	3.5	28.8	82.6
8	Brazil	35	3.2	19.4	16.9
9	China	33	3.0	2.9	2.4
10	Canada	29	2.7	18.7	80.6

GDP, gross domestic product; USD, US dollars.

Table 10
Top productive institutions/organisations in antimicrobial resistance among uropathogens (2002–2016).

Rank	Institution/organisation	*n*	% (*N* = 1087)	*h*-index	Country
1	Tehran University of Medical Sciences	21	1.9	5	Iran
2	Kobe University	20	1.8	8	Japan
3	University of Occupational and Environmental Health	12	1.1	5	Japan
4	Sapporo Medical University School of Medicine	12	1.1	6	Japan
5	University of Manitoba	10	0.9	6	Canada
6	Shahid Beheshti University of Medical Sciences	10	0.9	6	Iran
7	Universidade de São Paulo–USP	9	0.8	3	Brazil
8	National Taiwan University Hospital	9	0.8	6	Taiwan
9	Toho University School of Medicine	8	0.7	3	Japan
10	Islamic Azad University	8	0.7	2	Iran

n, number of retrieved documents.

Table 11
Preferred journals for publishing documents in antimicrobial resistance among uropathogens (2002–2016).

Rank	Journal	Country	*n*	% (*N* = 1087)	IF
1	*Journal of Antimicrobial Chemotherapy*	UK	33	3.0	4.27
2	*International Journal of Antimicrobial Agents*	Netherlands	32	2.9	4.097
3	*Antimicrobial Agents and Chemotherapy*	USA	21	1.9	4.415
4	*Journal of Chemotherapy*	UK	16	1.5	N/A
5	*European Journal of Clinical Microbiology and Infectious Diseases*	Germany	12	1.1	2.857
6	*Japanese Journal of Antibiotics*	Japan	11	1.0	0.31
6	*Journal of Urology*	USA	11	1.0	4.7
8	*Journal of Clinical Microbiology*	USA	10	0.9	2.44
8	*Clinical Infectious Diseases*	USA	9	0.8	5.39
8	*Enfermedades Infecciosas y Microbiología Clínica*	Spain	9	0.8	1.51
8	*International Journal of Pharma and Bio Sciences*	India	9	0.8	0.36
8	*Japanese Journal of Chemotherapy*	Japan	9	0.8	N/A
8	*Journal of Clinical and Diagnostic Research*	India	9	0.8	0.65
8	*Journal of Infection in Developing Countries*	Italy	9	0.8	1.2
8	*Korean Journal of Urology*	Korea	9	0.8	N/A

n, number of retrieved documents.
IF, impact factor (as issued by Journal Citation Report, 2016); N/A, no data regarding IF were available.

pharmacy regulations do not impose strict dispensing on antibiotics [30,31]. Containment of antibiotic resistance is a global challenge that requires promoting the rational use of antibiotics and more strict dispensing practices of antibiotics in developing countries [31]. Furthermore, pharmaceutical companies need to invest more resources to develop new-generation antibiotics. Such new-generation antibiotics should be based on the advanced understanding of molecular and genetic mechanisms responsible for antibiotic resistance [32].

The top active list of institutions included three Iranian academic institutions, suggesting that Iranian researchers and academics perceive this issue as a serious problem in Iran. A recent study from Iran showed that the percentage of multidrug resistance in *E. coli* urine isolates was 68% in inpatients and 61% in outpatients [33]. Another study in Iran showed that almost 59–66% of uropathogenic *E. coli* strains were resistant to amikacin, trimethoprim/sulfamethoxazole, tetracycline and cefalotin, and nearly one-half of them were resistant to nalidixic acid and cefalexin [34]. Studies from Iran indicated that virulent strains and those producing ESBLs are generally more resistant to antibiotics than avirulent and non-ESBL-producing strains [35].

This study showed that bacterial ESBLs are the main mechanism involved in the development of resistance among uropathogens. ESBL-producing bacteria showed resistance to penicillin, cephalosporin and β-lactam antibiotics [36]. Uropathogens belonging to the Enterobacteriaceae are known to produce ESBLs and carbapenemases, consequently leading to multidrug resistance [37]. It has been found that there is a significant association between the ESBL-producing ability of *E. coli* and it ability to form a biofilm, which renders the bacteria more resistant to antibiotics [38]. The current study showed that there was a focus on fosfomycin in the last interval of the study period. Studies have shown that Enterobacteriaceae such as *E. coli* and *Klebsiella pneumoniae* that were ESBL-producers and multidrug-resistant showed high susceptibility to fosfomycin and it can be a good option for treating UTIs [39]. Data retrieved in the current study showed that quinolone resistance was commonly reported. Quinolone resistance in *E. coli* is mainly mediated by point mutation in DNA gyrase or topoisomerase IV as well as plasmid-mediated quinolone resistance (PMQR) genes such as *qnr*, *aac(6′)-Ib*-cr, *qepA* and *oqxAB* [40–42].

International collaboration in AMR among uropathogens was relatively weak. This was expected given that AMR patterns differ from one country to another and each country needs to establish its own surveillance research studies to establish empirical antibiotic therapy guidelines for each country. Furthermore, the bulk of retrieved documents were in the field of epidemiology and public health, which does not require research collaboration like molecular biology or genetics. Despite that, international collaboration is highly needed in research pertaining to molecular and genetic mechanisms of antibiotic resistance, since understanding such mechanisms is of global value for researchers and the pharmaceutical industry. Developing new pharmaceuticals to overcome antibiotic resistance is a global need, and research collaboration will help to elucidate molecular microbial targets to develop these new pharmaceuticals.

This study is the first bibliometric study to assess AMR among uropathogens in a bibliometric manner. However, it has several limitations that are inherent to the nature of bibliometrics and to the database selected for data analysis. Such limitations have been discussed in previous bibliometric studies [43–46] and include the potential for false-negative results. However, if such false-negative results did exist, they will have little effect on the overall results given the use of the last scenario in which we used the related keywords both in title and abstract.

5. Conclusions

Research in AMR among uropathogens had witnessed a noticeable increase in the past decade. Research results obtained from different countries regarding AMR among uropathogens should be updated and made available to clinicians to develop suitable empirical therapy for UTIs. Global data on AMR among uropathogens need to be converted to an action plan to face this growing health challenge. Such a plan needs to include antibiotic surveillance studies in regions and countries where no data regarding AMR are yet available. Developing countries need to invest in policies such as antibiotic stewardship to minimise growth of the AMR problem. Increasing reports about resistance among uropathogens suggest that urgent action from pharmaceutical companies and from healthcare providers is needed to face the future consequences of this problem.

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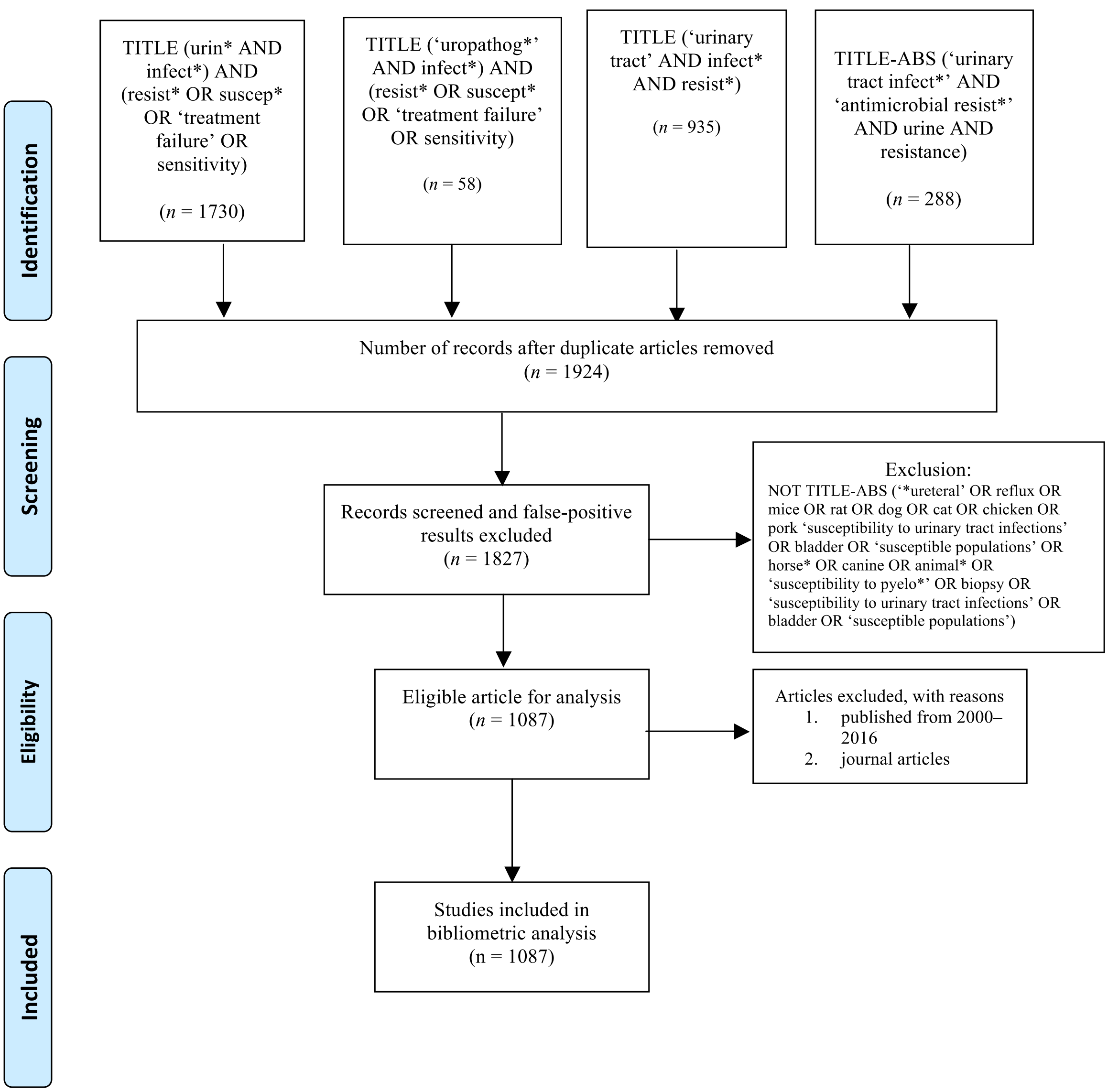
Competing interests

None declared.

Ethical approval

Not required.

Appendix A. Research strategy for articles regarding antimicrobial resistance (AMR) among uropathogens



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