Systematic Review

Antimicrobial Resistance in Libya: A Systematic Literature Review of Two Decades

Ahmed Atia[1], Bushra Hosien[2], Howida Belhaj[2]

[1]Department of Anaesthesia and Intensive Care, Faculty of Medical Technology, The University of Tripoli, Tripoli, Libya, [2]Department of Medical Laboratories, The University of Tripoli Alahlia, Janzur, Libya

Abstract

Background: In low- and middle-income countries, antimicrobial resistance (AMR) imposes a significant burden on patients and health-care systems. Due to a lack of data, the overall impact of AMR in Libya is not well known or documented. As a result, this study presents the results of a review of available data on AMR in Libya over the past 20 years (from 2002 to 2021) to aid understanding of the current AMR situation in this portion of the continent. **Methods:** Articles related to the topic were researched using databases and search engines such as PubMed, Google Scholar, and ResearchGate websites. These articles were selected based on predetermined inclusion and exclusion criteria. The total number of tested isolates for each of the reported *Bacterial* spp. was used to calculate antibiotic resistance to a specific bacterium. **Results:** Studies published in the past 20 years, representing reports of 18,160 AMR tests, showed that Urinary Tract Infection (UTI) was the most reported clinical diagnosis in Libya (61.3%). Out of 43 articles, *Staphylococcus aureus* was the most common Gram-positive bacteria documented in (31, 61.3%) studies, and was most common in 59.78% of skin infections. Whereas, *Pseudomonas* spps., were the most common Gram-negative bacteria presented in (23, 53.48%) studies, and were commonly isolated in respiratory infection (9.39%). Among Gram-negative bacteria, *Pseudomonas* spp. reported a high resistance percentage for penicillin beta-lactam antibiotic, i.e., piperacillin (10.4%) and to the first-generation cephalosporins antibiotics, i.e., cefazolin (7.7%). However, they are susceptible to metronidazole, vancomycin, and colistin. Gram-positive bacteria, *S. aureus* shows high resistance to oxacillin, followed by gentamycin and cefoxitin (8.5%, 8.3%, and 8.3%, respectively). Effective antibiotics against *S. aureus* were azithromycin, clarithromycin, and metronidazole, whose susceptibility was 99.9% each, while 1% of *S. aureus* were vancomycin-resistant *S. aureus*. **Conclusion:** This study gives a comprehensive analysis of the state of AMR in Libya with respect to the most regularly prescribed antibiotics. The findings of the research show the alarmingly persistent occurrences of AMR in Libya, as well as the critical need to establish national action, plans to combat AMR and improve surveillance programs.

Keywords: Antibiotic, antimicrobial resistance, bacteria, Libya

Introduction

Antimicrobial resistance (AMR), which is currently projected to account for more than 1.2 million fatalities per year worldwide, is causing significant worry on a global scale.[1] AMR occurs when bacteria change in response to the use of antibiotics. It has been argued that AMR could kill 10 million people per year by 2050.[1] Although some have criticized these forecasts, the WHO, as well as many other organizations and scholars, concur that the development of AMR is a serious issue that requires a global, coordinated response.[2] As a result, AMR is one of the most significant obstacles to achieving the UN Sustainable Development Goals by 2030.[3]

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Antimicrobial medications (such as antibiotics) are overcome by bacteria through five primary biochemical pathways of resistance. These include antibiotic enzymatic alteration or destruction, antibiotic target site modification, antibiotic target mimicking with comparable biochemical functions or antibiotic target overproduction, antibiotic penetration

Address for correspondence: Dr. Ahmed Atia, Department of Anaesthesia and Intensive Care, Faculty of Medical Technology, The University of Tripoli, Tripoli, Libya.
E-mail: ah.atia@uot.edu.ly
ORCID: https://orcid.org/0000-0002-9951-1921

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reduction, and antibiotic removal from the cell through efflux pumps.[4]

AMR is a multi-dimensional concern in the sense that it affects biological, economic, ecological, social, and developmental aspects. Even though the variables influencing the emergence of AMR are complicated, it is undisputable that AMR is linked to the irrational or unsuitable use of antimicrobial medicines (more specifically antibiotics).[5]

The main factors exacerbating the issue of AMR in Libya include the unlimited access to antimicrobial drugs without prescription, and most of the available antibiotics might be of poor quality or counterfeit.[6] Poor infection prevention and control, as well as water, sanitation, and hygiene initiatives, can exacerbate the absence of drug regulation and quality control, promoting the spread of drug-resistant microbes.[7]

Antibiotic susceptibility testing (AST) is still the gold standard for diagnosing bacterial resistance and guiding doctors in the timely and appropriate treatment of bacterial infections.[8,9] Surveillance studies that generate epidemiological data on bacterial pathogens and related AMR rely heavily on AST results. These statistics serve as the foundation for AMR containment initiatives at the national, regional, and global levels.

Only a few reports and publications are available on the problem of AMR in Libya. One main review article published in 2013, and was conducted for the period 1970–2011 found little data available on AMR in Libya due to a lack of surveillance and published studies. According to that study, salmonella resistance rates peaked in the late 1970s and have remained high through 2011.[10] High prevalence rates of methicillin-resistant *Staphylococcus aureus* (MRSA) have been documented among *S. aureus* from patients with burns and surgical wound infections (54–68%).[10] In 2020, the COVID-19 pandemic further contributed to the increased spread of AMR due to the inappropriate use of antibiotics for the case management of patients.[11]

In general, the overall burden of AMR in Libya is not well understood or documented due to inadequate data. Therefore, this report presents the findings of a review of published data (from 2002 to 2021) on AMR in Libya to aid in understanding the current AMR situation in this part of the continent.

Methods

Data source and retrieval

Free-text web searches using PubMed, Google Scholar, and ResearchGate were searched for articles on AMR published in English from January 1, 2002, to December 31, 2021. The retrieving process and data inclusion were strictly followed PRISMA guidelines [Figure 1].[12]

To retrieve all relevant articles from the above-mentioned databases, relevant MeSH terms and keywords were applied. The following keywords and MeSH terms were used: "Antimicrobial Resistance and Libya," "Antimicrobial Susceptibility and Libya," "Bacteria Diagnostic Libya," "AMR/antibiotic and Libya," and "AMR/antibiotic prevalence and Libya." These search keywords were entered in the above-mentioned searching engine, respectively. All articles on

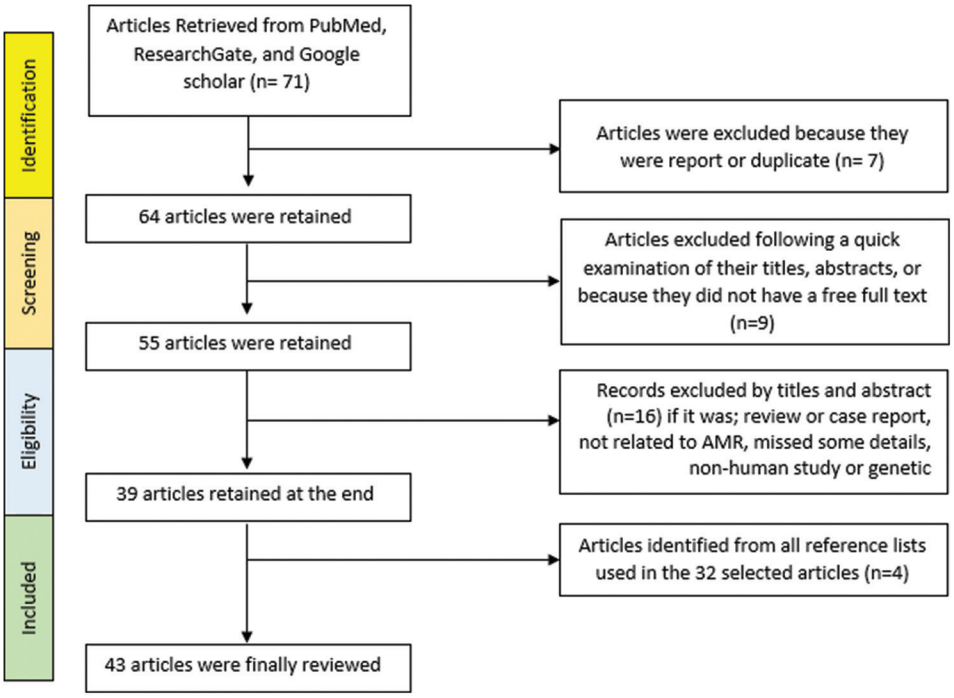

Figure 1: Illustration of the search and inclusion/exclusion process

AMR in Libya were then retrieved. The same search strategy was repeated for the second round of the search with the use of the same keywords but with the name of each Libyan city added next to it with each search.

Inclusion and exclusion criteria

For the identification of eligible articles, we used a predefined set of inclusion and exclusion criteria. Articles were retrieved if they met and fulfilled the following criteria for inclusion: published between 2002 and 2021; full text only available in English; reporting AMR research data in humans; conducted in Libya; free access to abstracts and full texts; providing information on the total number of studied isolates; and were observational studies (cross-sectional/longitudinal) that reported the proportion of bacterial pathogens and AMR. Conversely, any studies that did not comply with the above criteria were excluded. In addition, articles that did not provide information on the total number of studied isolates, studies conducted outside of Libya, studies conducted on nonhuman subjects, surveillance studies on antibiotic use/misuse, or molecular investigations of AMR molecular markers were all rejected. Furthermore, reference lists of potential research articles kept at this stage were examined for inclusion criteria, and those that met the criteria were added to the final list of potential research articles to be reviewed and included in this report.

Selection procedure

Of the initially retrieved 71 articles, seven were excluded because they were either a report or duplicate; nine articles were excluded because they did not fit in our review topic or lacked free full-text versions. At the next stage, a total of 16 articles were subsequently excluded because they were review or case report, not related to AMR, missed some details, and non-human studies or genetic investigations. A total of four articles were retained because they were identified from all their respective reference lists. This yielded a total of 43 articles that were analyzed in this review. A detailed description of all steps taken to select the final articles that were included in this report is shown in Figure 1.

Data extraction

Required data from the retained 43 papers were extracted in an Excel database 2016 that was designed for the purpose of this review report, and then further verified for consistency and quality of the data. The variables extracted included the author's name, year of publication, Libyan region, study design (hospital acquired or community acquired), type of sample, age group, number of specimens collected, number of positives (to estimate prevalence), and number of susceptible and resistant pathogens.

Data analysis

The total number of clinical bacterial isolates tested in each selected article was extracted using Microsoft Excel 2016, and the total number of isolates tested for susceptibility to the key antibiotics was calculated. The percentage of resistant bacterial isolates could then be calculated by subtracting the total number of tested isolates for each of the reported *Bacteria* spp.

Results

Reviewed articles and main data characteristics

This systematic review included a total of 71 articles that were reviewed from the three scientific databases; PubMed, Google Scholar, and ResearchGate as described above, and the selection process yielded a total number of 43 articles that met the inclusion criteria, representing reports of 18,160 AMR tests and were included in the analysis [Figure 1]. The characteristics of sample type, number of samples collected, type and proportion of bacterial species isolated and tested along sample source are described in Tables 1 and 2. The involved articles had tested for resistance to 64 different antimicrobial drugs involving 12 different microorganisms. The drug classes and major antimicrobial drugs assessed are shown in Table 3.

Samples from a total of 18,160 patients were analyzed in the selected local studies. The maximum number of the final selected articles were published in the year 2012 to 2021 (35/43, 81.4%), and the majority of the studies (16/43, 63.9%) were prospective studies [Table 1]. A high number of the reviewed articles were conducted in the west part of Libya (30/43, 69.7%), while the smallest number of studies were from the south district (4/43, 9.3%), with most of the studies (20/43, 46.5%) reported hospital-acquired infection [Table 1].

Data about the clinical diagnosis concerning bacterial pathogens are mentioned in Table 2. Out of 43 articles, Gram-negative bacteria were the most identified microorganism, with *Pseudomonas* spp. were presented in 23 articles, followed by *E. Coli, Klebsiella pneumoniae, Proteus*, and *Enterobacter* spp. (in 22, 19, 12, and 10 studies, respectively), while the lowest was *salmonella* in one study. On the other hand, *S. aureus* in 31 studies and *Streptococci* spp. in 9 studies, were the most frequent Gram-positive bacteria presented in these studies [Table 2].

Urinary Tract Infection (UTI) was the most testified clinical diagnosis with the highest number of isolates (11135/18160, 61.3%) of the total studies, followed by isolates from respiratory infection (3399/18160,18.7%), and from skin infection (455/18160,2.5%). Of the identified pathogens, *S. aureus* was the most common Gram-positive bacteria documented in (31, 61.3%) studies, and was most common in 59.78% of skin infections. Whereas, *Pseudomonas* spps., were the most common Gram-negative bacteria presented in (23, 53.48%) studies, and were commonly isolated in respiratory infection (9.39%).

Antibiotic resistance pattern

Among the commonly reported medical bacteria pathogens, nine Gram-negative bacteria (*Pseudomonas* spp., *Escherichia coli, Klebsiella* spp., *Proteus mirabilis, Enterobacter* spp,

Table 1: Characteristics of the articles included in the systematic review

Characteristics	Number of studies, *n* (%)	References
Publication year		
2002-2011	8 (18.6)	[13-20]
2012-2021	35 (81.4)	[22-55]
Study area		
East	9 (21)	[15,19,28,35,36,44,50,44,55]
West	30 (69.7)	[13,16-18,20-27,30-32,34,37-43,45-49,51,53]
South	4 (9.3)	[14,29,33,52]
Study design		
Cross sectional/case control	17 (39.5)	[13,18,21,28-30,33-37,49,51,55]
Prospective case study	16 (37.2)	[15-17,19,2022,23,25-27,38,39,45-48]
Retrospective case study	10 (23.3)	[14,24,31,32,40-44,50]
Type of infection		
Hospital acquired	20 (46.5)	[15,18-20,22-27,32,34,36,39,44,45,48,51-53]
Community acquired	14 (32.5)	[29,38,40-43,46,47,49,50,54,55]
Both	9 (21)	[13,14,17,28,30,31,33,35,37]
Age group		
Adult	9 (21)	[17,19,24-26,28,32,36,38]
Pediatrics and neonate	3 (7)	[20,23,27]
All age groups	4 (9.3)	[13,22,35,37]
Not mentioned	27 (62.7)	[30,31,33,34,39-55]

Table 2: Bacteria reported as number of studies (percentage of all studies) in different clinical diagnosis

Pathogen	Number of studies	UTI (*n*=11,135), *n* (%)	Skin (*n*=455), *n* (%)	Respiratory system (*n*=3399), *n* (%)	Vagina (*n*=48), *n* (%)	GIT (*n*=112), *n* (%)	Multi-sources (*n*=3011), *n* (%)	Total (*n*=18,160), *n* (%)
Gram-positive								
Staphylococcus aureus	31	1134 (10.18)	272 (59.78)	1241 (36.51)	20 (41.675)	-	1461 (48.52)	4128 (22.7)
Streptococci	9	68 (0.611)	-	706 (20.77)	30 (62.5)	-	7 (0.23)	811 (4.46)
TB	1	-	-	599 (17.62)	-	-	-	599 (3.29)
Gram-negative								
Pseudomonas	23	334 (2.99)	8 (1.76)	319 (9.39)	-	-	580 (19.26)	1241 (6.83)
Escherichia coli	22	5762 (51.75)	164 (36.04)	71 (2.09)	16 (33.3)	-	214 (7.11)	6227 (34.28)
Klebsiella pneumoniae	19	2045 (18.37)	2 (0.44)	877 (25.80)	4 (8.33)	-	333 (11.06)	3261 (17.95)
Proteus	12	926 (8.32)	8 (1.76)	29 (0.85)	-	-	19 (0.63)	982 (9.51)
Enterobacter spp.	10	249 (2.24)	-	83 (2.44)	14 (29.17)	-	10 (0.33)	356 (1.96)
Acinetobacter	6	11 (0.10)	-	14 (0.41)	-	-	191 (6.24)	216 (1.18)
Citrobacter	5	22 (0.20)	-	-	-	-	7 (0.23)	29 (0.15)
Shigella	2	-	1 (0.22)	-	-	1 (0.89)	-	2 (0.01)
Salmonella	1	-	-	-	-	19 (16.96)	-	19 (0.1)

TB: Tuberculosis, UTI: Urinary tract infection, GIT: Gastrointestinal tract infection

Acinetobacter baumannii, Acinetobacter spp*, Citrobacter* spp*, Shigella, and Salmonella*), and three Gram-positive bacteria species (*S. aureus, Streptococci* spp*, and Mycobacterium tuberculosis*) were identified in the 43 reviewed articles, and their AMR data are presented in Table 3. They were tested against 41 different antibiotics: ampicillin, cephalexin, cephaloridine, chloramphenicol, gentamicin, kanamycin, nalidixic acid, nitrofurantoin, tetracycline, cotrimoxazole, erythromycin, penicillin, amoxycillin, vancomycin, ciprofloxacin, fucidic acid, amikacin, noroxin, septrin, cephradin, co-amoxiclav, cephalothin, cefotaxime, streptomycin, sulphonamide, ticarcillin, cefazolin, ceftazidime, ticarcillin, imipenem, oxacillin, isoniazid, rifampicin, clindamycin, methicillin, ceftriaxone, cefepime, meropenem, tobramycin, levofloxacin.

Among all the 10 tested bacteria species, *S. aureus* remain the most tested bacteria in 31 studies shows high resistance to oxacillin, followed by amoxicillin and cefoxitin (8.5%, 8.3%, and 8.3%, respectively). Effective antibiotics against *S. aureus* were azithromycin, clarithromycin, and metronidazole, whose susceptibility was 99.9% each, while 1% of *S. aureus* were vancomycin-resistant *S. aureus* (VRSA) [Table 3]. In addition, out of 3458 tested *S. aureus* in eight studies against methicillin, 916 (26.5%) were confirmed MRSA.

Table 3: Antimicrobial resistance patterns among the identified bacteria in Libya, 2002-2021

Antibiotics	*Streptococci* spp.	*Staphylococcus aureus*	*Escherichia coli*	*Enterococci* spp.	*Pseudomonas* spp.	*Klebsiella* spp.	*Proteus* spp.	*Acinetobacter* spp.	*Citrobacter* spp.	*Salmonella*	*Shigella*	TB
Amikacin	2 (6.66)	463 (2.27)	55 (1.33)	0	95 (4.64)	320 (7.89)	11 (3.15)	124 (13.33)	0	0	0	0
Amoxicillin	0	1509 (7.40)	52 (1.26)	7 (2.62)	10 (0.49)	50 (1.23)	2 (0.57)	0	0	0	0	0
Ampicillin	0	241 (1.18)	836 (20.28)	0	143 (6.98)	182 (4.49)	21 (6.02)	140 (15.05)	0	0	0	0
Azithromycin	0	1 (0.004)	0	0	0	29 (0.71)	0	0	0	0	0	0
Aztreonam	0	16 (0.08)	0	0	4 (0.19)	12 (0.29)	0	12 (1.29)	0	0	0	0
Ceftazidime	0	0	0	0	49 (2.39)	203 (5.00)	0	0	0	0	0	0
Cefazolin	0	4 (0.02)	107 (2.59)	0	158 (7.71)	180 (4.44)	18 (5.16)	144 (51.48)	0	0	0	0
Cefepime	0	2 (0.01)	13 (0.32)	3 (1.12)	85 (4.15)	114 (2.81)	24 (6.88)	0	0	0	0	0
Cefixime	0	6 (0.03)	0	0	0	2 (0.05)	1 (0.29)	14 (1.51)	0	0	0	0
Cefoperazone	0	0	0	0	89 (4.35)	11 (0.27)	0	0	0	0	0	0
Cefotaxime	4 (13.3)	1397 (6.85)	99 (2.40)	32 (11.99)	145 (7.08)	67 (1.65)	0	135 (14.52)	0	0	0	0
Cefoxitin	0	1698 (8.33)	37 (0.89)	17 (6.37)	128 (6.25)	103 (2.54)	8 (2.29)	12 (1.29)	0	0	0	0
Ceftazidime	0	824 (4.04)	72 (1.75)	0	17 (0.83)	222 (5.47)	6 (1.72)	144 (15.48)	0	0	0	0
Ceftriaxone	0	18 (0.09)	14 (0.34)	3 (1.12)	105 (5.13)	127 (3.13)	7 (2.00)	10 (1.08)	2 (50)	0	0	0
Cefuroxime	0	19 (0.09)	0	6 (2.25)	118 (5.76)	164 (4.04)	32 (9.17)	2 (0.22)	0	0	0	0
Cephalexin	0	14 (0.07)	282 (6.83)	0	4 (0.19)	10 (0.25)	3 (0.86)	0	0	0	0	0
Cephaloridine	0	0	306 (7.42)	0	0	0	0	0	0	0	0	0
Cephalothin	0	0	28 (0.68)	7 (2.62)	10 (0.49)	60 (1.48)	11 (3.15)	0	2 (50)	0	0	0
Cephradine	0	0	6 (0.15)	0	6 (0.29)	24 (0.59)	0	0	0	0	0	0
Chloramphenicol	0	217 (1.06)	215 (5.21)	0	5 (0.24)	2 (0.05)	6 (1.72)	0	0	0	0	0
Ciprofloxacin	0	0	0	0	29 (1.42)	0	0	0	0	0	0	0
Ciprofloxacin	0	1014 (4.97)	75 (1.82)	12 (4.49)	11 (0.54)	92 (2.27)	12 (3.44)	43 (4.62)	0	12 (22.22)	0	0
Clarithromycin	0	1 (0.005)	0	0	0	0	0	0	0	0	0	0
Clindamycin	0	170 (0.83)	0	14 (5.24)	2 (0.09)	2 (0.05)	0	0	0	0	0	0
Co-amoxiclav	0	123 (0.60)	110 (2.67)	0	3 (0.15)	156 (3.85)	2 (0.57)	0	0	0	0	0
Colistin	0	0	0	0	3 (0.15)	154 (3.79)	0	0	0	0	0	0
Cotrimoxazole	0	1518 (7.45)	322 (7.81)	15 (5.62)	155 (7.57)	237 (5.84)	22 (6.30)	0	0	0	0	0
Daptomycin	0	2 (0.01)	0	0	0	0	0	0	0	0	0	0
Doxycycline	1 (3.33)	0	4 (0.09)	0	35 (1.71)	1 (0.025)	1 (0.29)	0	0	0	0	0
Ertapenem	0	0	0	2 (0.75)	8 (0.39)	17 (0.42)	2 (0.57)	0	0	0	0	0
Erythromycin	9 (30)	1515 (7.43)	47 (1.14)	25 (9.36)	2 (0.09)	0	3 (0.86)	0	0	0	0	0
Fusidic acid	2 (6.66)	87 (0.43)	0	2 (0.75)	0	0	0	0	0	0	0	0
Gentamycin	0	1687 (8.28)	43 (1.04)	16 (5.99)	79 (3.86)	271 (6.68)	18 (5.16)	112 (12.04)	0	0	0	0
Imipenem	2 (6.66)	1064 (5.22)	6 (0.15)	1 (0.37)	7 (0.34)	111 (2.74)	21 (6.02)	0	0	0	0	0
Isoniazid	0	0	0	0	0	0	0	0	0	0	0	10 (35.71)
Kanamycin	0	0	178 (4.32)	0	0	0	0	0	0	0	0	0
Levofloxacin	0	18 (0.09)	40 (0.97)	2 (0.75)	48 (2.34)	173 (4.26)	8 (2.29)	0	0	0	14 (51.85)	0
Linezolid	0	292 (1.43)	0	4 (1.49)	0	0	0	0	0	0	0	0
Meropenem	0	0	1 (0.02)	0	68 (3.32)	70 (1.73)	3 (0.86)	10 (1.08)	0	0	0	0

Contd...

Table 3: Contd...

Antibiotics	*Streptococci* spp.	*Staphylococcus aureus*	*Escherichia coli*	*Enterococci* spp.	*Pseudomonas* spp.	*Klebsiella* spp.	*Proteus* spp.	*Acinetobacter* spp.	*Citrobacter* spp.	*Salmonella*	*Shigella*	TB
Methicillin	0	368 (1.81)	0	0	0	0	0	0	0	0	0	0
Metronidazole	0	1 (0.005)	28 (0.68)	0	1 (0.05)	10 (0.25)	8 (2.29)	0	0	0	0	0
Minocycline	0	0	0	0	9 (0.44)	147 (3.62)	27 (7.74)	0	0	0	0	0
Moxifloxacin	0	9 (0.04)	0	7 (2.62)	0	0	0	0	0	0	0	0
Nalidixic acid	0	748 (3.67)	163 (3.95)	0	3 (0.15)	7 (0.17)	3 (0.86)	0	0	16 (29.63)	0	0
Nitrofurantoin	0	767 (3.76)	319 (7.74)	13 (4.87)	11 ((0.54)	97 (2.39)	25 (7.16)	0	0	0	0	0
Norfloxacin	0	0	39 (0.95)	0	7 (0.34)	11 (0.27)	2 (0.57)	0	0	0	0	0
Oxacillin	0	1740 (8.54)	0	15 (5.62)	0	0	0	0	0	0	0	0
Penicillin G	6 (20)	1380 (6.77)	124 (3.01)	32 (11.99)	3 (0.15)	1 (0.025)	6 (1.72)	0	0	0	0	0
Piperacillin	0	0	3 (0.07)	1 (0.37)	214 (10.45)	77 (1.89)	4 (1.15)	0	0	0	0	0
Polymyxin B	0	0	0	0	8 (0.39)	125 (3.08)	0	0	0	0	0	0
Rifampicin	0	44 (0.22)	0	2 (0.75)	31 (1.51)	8 (0.19)	4 (1.15)	14 (1.51)	0	0	0	4
Streptomycin	0	315 (1.55)	20 (0.49)	0	0	0	0	0	0	14 (25.92)	0	14 (50)
Teicoplanin	0	31 (0.15)	0	7 (2.62)	0	0	0	0	0	0	0	0
Tetracycline	0	859 (4.21)	335 (8.13)	17 (6.37)	47 (2.29)	15 (0.37)	28 (8.02)	0	0	12 (22.22)	1 (3.70)	0
Ticarcillin	0	0	127 (3.08)	0	21 (1.03)	218 (5.37)	0	0	0	0	0	0
Tobramycin	0	18 (0.049)	17 (0.41)	0	70 (3.42)	163 (4.02)	0	0	0	0	12 (44.44)	0
Vancomycin	4 (13.3)	185 (0.91)	0	5 (1.87)	2 (0.09)	12 (0.29)	0	14 (1.51)	0	0	0	0
Total	30	20385	4123	267	2048	4057	349	930	4	54	27	28

TB: Tuberculosis

Pseudomonas spp. were reported in 23 studies showing high resistance to a penicillin beta-lactam antibiotic, i.e., piperacillin (10.4%) and to the first-generation cephalosporines antibiotics, i.e., cefazolin (7.7%). However, they are susceptible to metronidazole (nearly 100%), vancomycin (99%), and colistin (99.8%). *E. coli* were reported in 22 studies showing high resistance to tetracycline, cotrimoxazole, and nitrofurantoin which are (8.1%, 7.8%, and 7.7%, respectively). Effective antibiotics against *E. coli* were meropenem, piperacillin, and doxycycline (nearly 100%). *Klebsiella* spp. were reported in 19 studies during the last two decades showing high resistance to amikacin (7.8%), gentamycin (6.7%), and cotrimoxazole (5.8%). However, they are 99–100% susceptible to penicillin G, doxycycline, and cefixime. *Proteus* spp. were reported in 12 studies showing the highest resistance to cefuroxime, and tetracycline antibiotics, i.e., minocycline. According to the reported studies, cefixime and doxycycline were the most efficient antibiotics against *Proteus* spp.

Enterobacter spp. were reported in 10 studies showing high resistance to penicillin G and cefotaxime (11.9%), while 100% of species were susceptible to imipenem and piperacillin. *Streptococci* spp. were reported in nine studies showing high resistance to penicillin G and erythromycin, and was almost susceptible to all tested antibiotics. Acinetobacter spp. were reported in 6 studies showing high resistance to the first and third-generation cephalosporins, i.e., cephazolin and ceftazidime (15.5%). The resistance pattern for carbapenems, i.e., meropenem were 98.9%. *Citrobacter* spp. were reported in five studies, showing high resistance to ceftriaxone and cephalothin. *Shigella* spp. were reported in two studies showing high resistance to tobramycin and levofloxacin, while tetracycline showed 100% susceptibility against the tested isolates. *Salmonella* spp. were reported in only one study showing high resistant to nalidixic acid, and streptomycin. *Mycobacterium tuberculosis* were also reported in one study showing high resistance to streptomycin (100%), and linezolid, while rifampin showed 100% susceptibility against 28 tested isolates.

Discussion

Antibiotic resistance is a worldwide concern but developing and underdeveloped countries are particularly vulnerable due to gross abuse of antimicrobials. AMR poses a threat to the effective control and treatment of a variety of bacterial diseases all over the world.[7] The gains made in reducing mortality and morbidity through the early use of antibiotics based on empiric guidelines are threatened if appropriate measures to control AMR are not taken.[56] Repetitive research data on pathogen vulnerabilities is essential for developing targeted strategies to combat the global AMR crisis. The current review describes data that have been extracted and analyzed from a total of 43 articles published between 2002 and 2021 on antibiotic drug susceptibility from Libya.

Findings in this study revealed that UTI was one of the most commonly reported clinical diagnoses. In terms of bacterial pathogens, *S. aureus* was found in most studies to have high resistance to first-line antibiotics. The pattern of bacterial resistance in the current study was similar to other Africa's scenarios due to the same trend of inappropriate antibiotic use in developing and undeveloped countries. However, resistance to oxacillin and amoxicillin is higher in this study, which could be attributed to differences in AMR testing methodologies.[57] In addition, MRSA is considering for high mortality rates.[58] In the current study, among 3458 tested *S. aureus* against methicillin, 916 (26.5%) were MRSA. The actual value may differ due to differences in the source of infection.[59]

VRSA is mainly involved in hospital-acquired infections.[60] In the current research, VRSA was account for 1%, which is lower than the results reported from Nigeria 4.1%[61] and Ethiopia 14.1%.[62] Moreover, the pooled prevalence of VRSA in Africa was estimated to be 2.5%.[63]

A notable result of this review was the high resistance rate of *E. coli*, that account for most of UTI, to common first-line regimes such as nitrofurantoin and cotrimoxazole. Patients with UTIs are more likely to develop renal damage and future risks of renal failure or hypertension if their treatment fails.[64] Similarly, the high levels of resistance to amoxicillin and oxacillin in *S. aureus* are also concerning given that pneumonia is a leading cause of death.[65,66]

Our findings support the growing trend of quinolone-resistant *Salmonella* spp. in the African region,[67] with a resistance rate of 26% for nalidixic acid and 22.2% for ciprofloxacin, respectively, in 54 tested isolates. In this study, *Shigella* spp. were reported in two studies with 51.8% to levofloxacin. *Shigella* spp. was identified by the WHO as the primary bacteria causing community-acquired infection,[68] implying that more research is needed to gain a thorough understanding.

Pseudomonas spp. and *Acinetobacter* spp. which are inherently resistant to many antibiotics, also have a high rate of resistance to other CLSI (Clinical and Laboratory Standards Institute)-recommended antibiotics. For example, *Pseudomonas* spp. show 10.4% resistance to piperacillin and *Acinetobacter* spp. show 15.5% resistance to cephazolin and ceftazidime. The evolving trend is due to acquired resistance.[69] The outcomes of the current study support the 2017 WHO report in which they considered *Pseudomonas* spp. and *Acinetobacter* spp. as important bacteria.[70]

The current study focuses on antibiotic resistance in Libya; however, its consequences are global. Libya has a strategically important geographical location as an important bridge linking Africa and Europe, and has its featured on the southern coast of the Mediterranean and the Sahara Desert, and it is the fourth-largest country in Africa and the Arab world.[71] It is well understood that resistant species from its reservoir can spread to other parts of the world via humans, water, and

animals.[72] The consequences in Libya appear to be the most serious threat.

Limitations of study

The data presented in the current review was not allocated from all Libyan cities, which could be considered a limitation of the study. In addition, the majority of studies were from the western districts, which may not be an accurate representation of the entire country. In some studies, the infection sources were not identified as thoroughly as they should have been. In addition, various types of patient data, demographics, and methodologies are combined. Our research, on the other hand, provides an exclusive aspect of antibiotic resistance in Libya, that researchers must keep track of all the gaps in future studies.

Conclusion

This report provides an in-depth examination of the current state of AMR in Libya. These AMR cases pose a significant and continuing public health concern, and they are emphasized on the WHO list of critical-priority AMR bacteria, for which new research, exploration, and development of new antibiotics is urgently required. According to our findings, there is a high level of drug resistance to commonly prescribed antibiotics in Libya. Standardization and quality of microbiological identification and susceptibility testing methods must be improved to allow national and international organizations to screen the scope of the AMR problem.

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Conflicts of interest

There are no conflicts of interest.

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