




# Characteristics of Antibiotic-Resistant Bacteria in Libya Based on Different Source of Infections

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## Abstract

In recent years and for decades, antimicrobial resistance (AMR) has expanded into a major clinical issue. Infections were no longer a life-threatening issue for clinicians after the discovery of antibiotics. The misuse or overuse of antibiotics, however, contributes to global AMR, and numerous mobile genetic elements and relevant resistant genes worsen the spread of resistance. As antibiotics lose their effectiveness, a growing number of infections such as pneumonia, tuberculosis, and gonorrhoea are getting harder and sometimes impossible to treat. Infections that are resistant to antibiotics are correlated with antibiotic misuse. The majority of the antibiotic resistance in microbes is caused by improper use of antibiotics. Because there are a few antibiotics available to treat multidrug-resistant bacterial infections, there is a high rate of morbidity and mortality. Libya has a high burden of antibiotic resistance, and antimicrobial malpractice has frequently been reported. Providing information on the current state of antimicrobial resistance in Libya may assist the health authorities in addressing the problem more effectively in the future. Therefore, this review highlights the current situation of bacterial profile and their antimicrobial resistance in Libya based on the source of infection. Articles related to the topic were searched using databases and search engines such as PubMed, Google Scholar, and ResearchGate websites. These articles were selected if they were conducted in Libya and provided information on bacterial pathogens and AMR. Required data were extracted for the purpose of this review report, and then further verified for identifying the prevalence and number of susceptible and resistant pathogens in each source of infection.

## Keywords

- ▶ bacteria
- ▶ antibiotic
- ▶ microbial resistance
- ▶ infection
- ▶ Libya

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## ملخص المقال باللغة العربية

## خصائص البكتيريا المقاومة للمضادات الحيوية في ليبيا بناءً على مصادر العدوى المختلفة

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في السنوات الأخيرة وعلى مدى عقود، توسعت مقاومة مضادات الميكروبات إلى معضلة إكلينيكية كبرى. في البداية يعد اكتشاف المضادات الحيوية لم تعد العدوى تشكل خطراً على حياة المرضى ومع ذلك، فإن إساءة استخدام المضادات الحيوية أو الإفراط في استخدامها ساهم في ظهور ظاهرة مقاومة المضادات الحيوية على الصعيد العالمي، كما أن العديد من العناصر الوراثية المتنقلة بين أنواع مختلفة من البكتيريا والجينات المقاومة ذات الصلة تزيد من انتشار المقاومة سواً. وعندما تقف المضادات الحيوية فعاليتها، يصبح علاج عدداً متزايداً من العدوى مثل الالتهاب الرئوي والسل والسيلان أكثر صعوبة وأحياناً مستحيلًا. ولذلك أتفق الجميع ارتباط العدوى المقاومة للمضادات الحيوية بسوء استخدامها، وأن غالبية مقاومة الميكروبات للمضادات الحيوية ناتجة عن الاستخدام غير السليم للمضادات الحيوية. وتظن أن وجود عدد قليل من المضادات الحيوية المتاحة الآن لعلاج العدوى البكتيرية المقاومة للأدوية المتعددة، فأنه هناك معدل مرتفع من المراضة والوفيات. ليبيا لديها مشكلة كبيرة نتيجة مقاومة المضادات الحيوية، وكثيراً ما تم الإبلاغ عن سوء استعمالها. قد يساعد توفير المعلومات عن الوضع الحالي لمقاومة المضادات الحيوية السلطات الصحية في ليبيا لمعالجة المشكلة بشكل أكثر فعالية في المستقبل. لذلك، تسلط هذه المراجعة الضوء على الوضع الحالي للملف البكتيري ومقاومتها للمضادات الحيوية في ليبيا بناءً على مصدر العدوى. تم البحث في المقالات المتعلقة بالموضوع باستخدام قواعد البيانات ومحركات البحث مثل PubMed و Google scholar وموقع ResearchGate. تم اختيار المقالات التي أجريت في ليبيا وقدمت معلومات عن مسببات الأمراض البكتيرية ومقاومتها للمضادات الحيوية. تم استخلاص المعطيات المطلوبة لغرض هذه المراجعة، كما تم التحقق منها بشكل إضافي لتحديد انتشار وعدد مسببات الأمراض الحساسة والمقاومة في كل مصدر من مصادر العدوى.

الكلمات المفتاحية: - البكتيريا، المضادات الحيوية، مقاومة الميكروبات، العدوى، ليبيا.

## Introduction

Antimicrobial resistance (AMR), is the potency of microbes to become resistant to famous antibiotics.<sup>1</sup> AMR is an emerging global threat; it increases mortality and morbidity and strains healthcare systems.<sup>2</sup> The current antimicrobial profile studies have proved that bacteria can cause infections to become resistant to different groups of antibiotics, world health leaders have described antibiotic-resistant microorganisms as “nightmare bacteria” that “pose a catastrophic threat” to people.<sup>3</sup>

In the United States, according to the Center for Disease Control (CDC) in 2013, there are about 23000 deaths a year as a result of infection with bacteria that are resistant to known antibiotics, while about 2 million others develop an infection that is resistant to antibiotics.<sup>3</sup> While, the CDC newly report in 2022 found that infections and deaths from drug-resistant, hospital-acquired bacteria rose by 15% from 2019 to 2020, with alarming increases in some of the most highly resistant bacterial pathogens.<sup>4</sup> The costs of introducing a new pharmaceutical product into clinical use are very high, estimated at 1.7 billion \$, according to the US

department of health, which is the highest estimate based on the 2020 data.<sup>5</sup>

In 2017, the World Health Organization (WHO) released a list of bacteria for which new studies and medications were urgently required. High priority pathogens included methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), while critical priority pathogens included *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, carbapenem-resistant Enterobacteriaceae, and Enterobacteriaceae that produce extended spectrum beta-lactamases (ESBL).<sup>6</sup>

Gram-negative bacteria are more resistant than gram-positive bacteria because of their unique structure, which also contributes to their widespread global burden of morbidity and mortality.<sup>7</sup> The development of antimicrobial auxiliary agents, structural modification of existing antibiotics, and research into and study of chemical structures with new mechanisms of action and novel targets that resistant bacteria are sensitive to a few methods that have been reported to combat and control resistant gram-negative bacteria.<sup>7</sup>

The antimicrobial resistance crisis in Libya has reached a point where the authorities should work with other stakeholders to address it. The present review is highlighting the situation of antimicrobial resistance and bacterial pathogenic profile in Libya. Free-text web searches using PubMed, Google Scholar, and ResearchGate were searched for articles on AMR published in English using 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. Articles were retrieved if they were conducted in Libya and reported the proportion of bacterial pathogens and AMR. Required data were extracted for the purpose of this review report, and then further verified for identifying the prevalence and number of susceptible and resistant pathogens in each source of infection.

### **Bacteria Resistance Pattern in Urinary Tract Infections.**

Urinary tract infection (UTI) is one of the most common infections in routine clinical practice, resulting in high rates of morbidity and high economic costs associated with its treatment. It is the most common UTI and is responsible for 95% of all symptomatic urinary tract infection. The risk of UTI in the female population is higher than that in the male population although bacteria isolated from females were less resistant than those isolated from males.<sup>8</sup>

Ghenghesh et al, 2003, reported that *Escherichia coli* was detected in 538 (24%) urine samples. Other bacteria detected were *Staphylococcus* in 8%, *Proteus* in 4%, *Klebsiella* spp., in 2%, *Pseudomonas* in 1%, and beta-hemolytic streptococci in 0.3%.<sup>9</sup> In the same study, antimicrobial susceptibility testing of 538 *E. coli* strains found 74% were resistant to ampicillin, 49% to cephaloridine, 25% to nitrofurantoin, 49% to tetracycline, and 45% to trimethoprim-sulphamethoxazole.<sup>9</sup>

When comparing these findings to the results of a study carried out in Tripoli, Libya in 2017, shown that Staphylococci (64.5%), *E. coli* (29.0%), and *Klebsiella pneumonia* (6.5%) were the most often isolated bacteria from urine samples that had positive culture results. Staphylococci spp. (26.29%), *K. pneumonia* and *E. coli* were much more resistant (38.11% and 34.13%, respectively) and showed resistance to a wide variety of tested antibiotics. Gentamycin (17.6% resistance), erythromycin (19.0% resistance), and ciprofloxacin were the three most potent antibiotics tested that affected 87.7%, 82.4%, and 81.0% of the bacteria that cause urinary tract infections, respectively.<sup>10</sup> Similarly, a study conducted in Sabha, Libya in 2007 reported that 178 (68.5%) of urine samples were contaminated by *E. coli* with other microorganisms. About 170 (65.4%) strains of *E. coli* were susceptible to nitrofurantoin, 157 (60.4%) to gentamicin, and 116 (44.6%) to cephalexin. In contrast, only 6 (2.3%) of *E. coli* strains were sensitive to erythromycin and 14 (5.4%) to tetracycline.<sup>11</sup>

Another study investigated the resistance patterns of *E. coli*, *Klebsiella* spp., and *S. aureus* isolated from diabetic (DM) and non-diabetic patients to antimicrobial agents, revealed that *Klebsiella* species from the non-DM group were significantly more resistant than isolates from the DM group to co-amoxiclav acid [ $p = 0.002$ ].<sup>12</sup> Moreover, *S. aureus* isolates from the non-DM group were resistant to methicillin. Additionally, *E. coli*, *Klebsiella* spp., and *S. aureus* exhibited 40%, 65%, and 29% multiple drug resistance profiles, respectively.<sup>12</sup>

Wareg et al, in 2014, revealed that vancomycin resistance was not found in in-patient-MRSA strains while 5% of out-patient-MRSA strains were resistant by disc-diffusion assay. This result suggests that vancomycin can be used to treat MRSA infections.<sup>13</sup> Another study on the detection of inducible clindamycin resistance to MRSA from Libya reported 128 (24.2%) MRSA isolates collected were resistant to clindamycin, 63.2% of isolates were resistant to erythromycin.<sup>14</sup> The authors also emphasized that clindamycin could still be used to treat MRSA infection in Libyan hospitals.<sup>14</sup>

In 2011, a study by Buzaid et al reported that of 200 *S. aureus* examined, 62 (31%) were MRSA. MRSA was found in 31.8% (28/88) and 30.4% (34/112) of *S. aureus* in female and male patients. Based on the disc diffusion results, the pattern of antibiotic resistance in 62 MRSA patients was as follows: 11 (17.7%) to vancomycin, 21 (33.9%) to ciprofloxacin, 24 (38.7%) to chloramphenicol, 26 (41.9%) to fusidic acid, and 29 (46.8%) to erythromycin.<sup>15</sup>

Overall, *E. coli* accounted for most of UTI, and exhibited resistance to the common first-line regimes such as nitrofurantoin and cotrimoxazole.

### **Bacterial Resistance Pattern in Respiratory Tract Infection.**

Respiratory infections are one of the most common infectious diseases of various groups that continue to emerge as major causes of clinical morbidity and mortality.<sup>16</sup> Upper respiratory tract infections (URTIs) involve the common cold, tonsillitis, laryngitis, pharyngitis, rhinitis, and otitis media.

Lower respiratory tract infections (LRTIs) include acute bronchitis, and pneumonia.<sup>17</sup>

Previous study conducted by Elkammoshi in 2020 in Tripoli, Libya, in which 100 specimens divided equally between ventilator circuits and lower respiratory tract patients were analyzed. They found that the most common organism isolated was gram-negative from the ventilators (26, 68.4%) and mechanically ventilated patients' LRT was 14 (70%). Other isolates were gram-positive from patient's LRT were 6 (30%) and from ventilator circuits were 12 (31.6%), and most of the isolates were resistant to the known antibiotics.<sup>18</sup> In the same study, *A. baumannii* showed a full resistance to amoxicillin, gentamycin, and the first generation of cephalosporins, and it was intermediated to the third-generation cephalosporins. In contrast, *K. pneumoniae* was also a fully resistant to gentamycin and most other types of antibiotics. *Pseudomonas aeruginosa* was also resistant to all types of antibiotics except gentamycin, to which it was slightly sensitive. *E. coli* and *Serratia marcescens* were sensitive to most antibiotic disks except co-amoxiclav.<sup>18</sup>

Another study conducted by Atia in 2020 in Tripoli, showed the dominant bacterial pathogens in respiratory infection being *S. pneumonia* 43.3%, followed by *P. aeruginosa* 22.8%, *S. aureus* 13.8%, *E. coli* 6.9%, *Enterobacter* spp. 6.2%, *Citrobacter* 4.5%, and *Klebsiella* 2.2%.<sup>19</sup>

It was observed that *S. pneumonia* was highly resistant to gentamycin and ciprofloxacin, whereas it was least resistant to cefotaxime and doxycycline. *Pseudomonas aeruginosa* was resistant to  $\beta$ -lactam antibiotics such as co-amoxiclav, amoxicillin, ceftriaxone as well as macrolide antibiotics such as clarithromycin with percent resistance of 71%, 44%, 29%, and 37%, respectively. *P. aeruginosa* was also resistant to ciprofloxacin, gentamycin, and amikacin with percentages of 24%, 24%, and 23%, respectively.<sup>19</sup>

Another study done by El-Deeb in 2006 in Libya showed that *S. aureus* was the most common organism, followed by *Streptococcus pyogenes* and *K. pneumonia*. *Pseudomonas aeruginosa* were represented, with *S. marcescens* and *Morganella morganii* being the least isolated organisms.<sup>18</sup> Levofloxacin and gatifloxacin, in the same study, showed the highest activity (100%), followed by ofloxacin and ciprofloxacin (96.44% and 93.39%, respectively). Amoxicillin and tetracycline were the least active (36.64% and 32.06%, respectively).<sup>20</sup>

The spectrum of pathogenic bacterium causing upper respiratory infection in Libya is considerably wide, with *S. pneumoniae* and *P. aeruginosa* being the major causative bacteria.

### Bacterial Resistance Pattern in Skin infections

Skin infections are a worldwide significant clinical concern characterized by microbial attack of the skin layers and underlying soft tissues. Earlier study conducted in Tripoli, Libya, showed that the dominated species of pathogenic bacteria were identified as gram-positive bacteria *S. aureus* ( $n=272$ , 97.14%) and *Proteus* ( $n=8$ , 2.85%). Meanwhile, gram-negative bacteria were *E. coli* ( $n=164$ , 93.71%), *Pseudomonas* ( $n=8$ , 4.57%), *Klebsiella* ( $n=2$ , 1.14%), and

*Shigella* ( $n=1$ , 0.57%). Of the gram-positive bacteria, *S. aureus* and *Proteus* were highly resistant to penicillin (34.3%, 75% respectively) and ampicillin (28.6%, 62.5%, respectively). Moreover, *Proteus* had lower resistance rate to sulfamethoxazole and nalidixic acid (12.5%). Concerning gram-negative bacteria, *E. coli* was highly resistant to ampicillin (45.12%) and penicillin (35.96%), whereas the lowest resistant was against imipenem (3.05%).<sup>21</sup>

Similarly, a study conducted in 2015 in Sabha showed that 90.5% of *S. aureus* strains were resistant to vancomycin, 61.9% to tetracycline, 57.1% to amoxicillin, 52.4% to methicillin, 42.9% to erythromycin, and 23.8% streptomycin. In addition, 87.5% of *Staphylococcus epidermidis* isolated was resistant to vancomycin, 75% to methicillin, 62.5% to tetracycline, 50% to streptomycin 37.5% to amoxicillin, and erythromycin.<sup>22</sup>

In another study conducted by Dou in a different area in Libya in 2011 showed that *Acinetobacter* spp. was the most resistant pathogen. Most isolated gram-negative bacteria showed great resistance to third-generation cephalosporins and aminoglycosides. However, *P. aeruginosa* was quite susceptible to commonly used antipseudomonal therapy particularly carbapenems. Coagulase-negative staphylococci were found to be sensitive to all the antibiotics tested particularly gentamicin and vancomycin.<sup>23</sup>

Overall, *S. aureus* is stated to be among the most causative agent for skin infection, and shows high resistance to penicillin groups of antibiotics.

### Bacterial Resistance Pattern in Gynecological Infections

Bacterial vaginosis is a worldwide issue due to the raised risk of acquisition of sexually transmitted infections. Bacterial vaginosis is a state that occurs when the overgrowth of anaerobic bacteria. In some studies, however, other bacteria (*E. coli*, *Klebsiella* spp., *Acinetobacter* spp., *Staphylococcus* spp., enterococci, and *S. agalactiae* (group B streptococci) have been named "intermediate flora" or have been included in other studies of bacterial vaginosis.<sup>24</sup> Previous study conducted in Tripoli, showed that *E. coli* was the most frequently isolated bacterium from vaginal swab, and showed resistance to penicillin (62.5%), while the *S. aureus* and *Streptococcus agalactiae* were the dominant gram-positive bacteria showed high resistance to co-amoxiclav (40%).<sup>24</sup>

### Bacterial Resistance Pattern in Other Infections

Methicillin-resistant staph (MRSA) and methicillin-susceptible staph (MSSA) are important causes of infections in burn patients. A study conducted by Zorgani in Tripoli in 2012 showed that Tigecycline exhibited an excellent *in vitro* activity against MSSA and MRSA isolates (96.8% and 95.8%, respectively).<sup>25</sup>

Another study conducted by Al-awkally et al, in Tripoli 2020, aimed to assess the antibiotic susceptibility of *Pseudomonas aeruginosa* recovered from infected swabs, abscess, burn, medical tips and blood, reported that *P. aeruginosa* was highly susceptible to Colistin and ciprofloxacin with some of



the isolates shown resistance to septrin, tetracycline, and levofloxacin.<sup>26</sup>

In a study conducted by Musa et al, in Misurata, Libya, found that the most common bacteria isolated from anterior blepharitis were *S. aureus* 14 (25%) and *S. epidermidis* 14 (25%), and were resistant to vancomycin, gentamycin, ciprofloxacin, and amikacin. In contrast, they were highly resistant to ampicillin and moderately resistant to chloramphenicol, erythromycin, and cephalixin.<sup>27</sup>

Ermalli in 2017, collected 94 gram-negative bacteria isolates from different sources at a single hospital in Tripoli, and reported different antimicrobial resistance phenotypes including to the carbapenem classes. About 48% of the collection was identified as *A. baumannii*, 50% *K. pneumoniae*, and 2% *E. coli*. Resistance to the carbapenem classes was reported in 96% of the *A. baumannii* strains and 94% of the *K. pneumoniae* strains. Approximately 78% of the isolates showed different multidrug-resistant (MDR) phenotypes, of which *K. pneumoniae* expressing the highest rates of MDRs (i.e., 91%).<sup>28</sup>

## Conclusion

This review reported the current state of antimicrobial resistance in Libya. Drug resistance to frequently administered antibiotics is very widespread in Libya. Microbiological identification and susceptibility testing methods must be improved for national and international organizations to assess the scope of the AMR problem.

### Note

The article has not been previously presented or published, and is not part of a thesis project.

### Conflict of Interest

None declared.

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