Antimicrobial resistance in Libya: 1970–2011

Khalifa Sifaw Ghenghesh1*, Amal Rahouma1, Khaled Tawil1, Abdulaziz Zorgani1 and Ezzedin Franka2

1Department of Microbiology and Immunology, Faculty of Medicine, University of Tripoli, Tripoli, Libya; 2Department of Family and Community Medicine, Faculty of Medicine, University of Tripoli, Tripoli, Libya

Resistance to antimicrobial agents is a major health problem that affects the whole world. Providing information on the past state of antimicrobial resistance in Libya may assist the health authorities in addressing the problem more effectively in the future. Information was obtained mainly from Highwire Press (including PubMed) search for the period 1970–2011 using the terms ‘antibiotic resistance in Libya’, ‘antimicrobial resistance in Libya’, ‘tuberculosis in Libya’, and ‘primary and acquired resistance in Libya’ in title and abstract. From 1970 to 2011 little data was available on antimicrobial resistance in Libya due to lack of surveillance and few published studies. Available data shows high resistance rates for Salmonella species in the late 1970s and has remained high to the present day. High prevalence rates (54–68%) of methicillin-resistant Staphylococcus aureus (MRSA) were reported in the last decade among S. aureus from patients with burns and surgical wound infections. No reports were found of vancomycin-resistant S. aureus (VRSA) or vancomycin-intermediate-resistant S. aureus (VISA) using standard methods from Libya up to the end of 2011. Reported rates of primary (i.e. new cases) and acquired (i.e. retreatment cases) multidrug-resistant tuberculosis (MDR-TB) from the eastern region of Libya in 1971 were 16.6 and 33.3% and in 1976 were 8.6 and 14.7%, in western regions in 1984–1986 were 11 and 21.5% and in the whole country in 2011 were estimated at 3.4 and 29%, respectively. The problem of antibiotic resistance is very serious in Libya. The health authorities in particular and society in general should address this problem urgently. Establishing monitoring systems based on the routine testing of antimicrobial sensitivity and education of healthcare workers, pharmacists, and the community on the health risks associated with the problem and benefits of prudent use of antimicrobials are some steps that can be taken to tackle the problem in the future.

Keywords: antibiotic resistance; enteric bacteria; methicillin-resistant Staphylococcus aureus; multidrug-resistant tuberculosis; Libya

*Correspondence to: Khalifa Sifaw Ghenghesh, Department of Microbiology and Immunology, Faculty of Medicine, University of Tripoli, Tripoli, Libya, Email: ghenghesh_micro@yahoo.com

To access the supplementary material to this article please see Supplementary files under Article Tools online

Received: 4 February 2013; Accepted in revised form: 4 March 2013; Published: 27 March 2013

Resistance to antimicrobial drugs is a major health problem that affects the whole world. The problem is still worse in developing countries where lack of antimicrobial-resistance surveys and control policies are the norm. In Libya, misuse of antimicrobial agents by the public is widespread. As in many developing countries antimicrobials can be purchased from pharmacies without prescription in Libya. A study carried out on self-medication with antibiotics in the ambulatory care setting within eight countries of the Euro-Mediterranean region between 2004–2005 found 19.1% (range ≤0.1% in Cyprus to 37% in Lebanon) of total interviewed healthy individuals admitting self-medication and in Libya the percentage was 24% (1). The study also found that nearly 50% of interviewed Libyans indicated that they would take antibiotics for their own use without a prescription if they believe that they needed to. Furthermore, antibiotics can easily be obtained in Libya on demand from, usually but not always, relatives, friends, and others employed in government medical stores and hospitals (KS Ghenghesh, unpublished data).

In the past, the state of health in Libya was not good particularly in the few years prior to the 17 February 2011 uprising. The reasons for this include, among
others, lack of good administration, resources, maintenance of hospitals, well-trained healthcare workers, and surveillance of different diseases and support of biomedical research. The poor state of health undoubtedly aggravated the problem of antimicrobial resistance in the country. However, providing information on the past state of antimicrobial resistance in Libya may assist the health authorities in addressing the problem more effectively in the future.

The objective of the present work was to review the published data and available reports on antimicrobial resistance in Libya, covering mainly three important topics of antimicrobial resistance in enteric bacteria, methicillin-resistant Staphylococcus aureus (MRSA), and multidrug-resistant tuberculosis (MDR-TB) from 1970 to 2011. The information presented in this review was obtained from Highwire Press (including PubMed) search for the period 1970-2011 using the terms ‘antibiotic resistance in Libya’, ‘antimicrobial resistance in Libya’, ‘tuberculosis in Libya’, and ‘primary and acquired resistance in Libya’ in title and abstract. Additional data were also obtained from a Google search using the aforementioned terms. Furthermore, papers published in local biomedical journals, and when available, abstracts presented in local and international meetings on the subject were included.

**Enteric bacteria**

These include members of the family Enterobacteriaceae mainly *Salmonella* and *Shigella* species from stool samples of diarrheic patients and *Escherichia coli* from cases of urinary tract infections (UTI). Other enteric bacteria isolated less frequently from UTI include *Klebsiella*, *Enterobacter*, and *Proteus* species.

### Salmonella and Shigella

Resistance rates for *Salmonella* varied tremendously among the different commonly used antibiotics. High resistance rates for ampicillin were reported in 1979–2008 from Tripoli (Table 1).

In the mid-1980s, Sood et al. in Benghazi reported on 38 children with acute gastroenteritis due to *Salmonella* treated with gentamicin, to which the organisms were sensitive in-vitro (7). Most (30 out 38) of the stool cultures from the children remained positive after treatment. The authors concluded that antibiotics have no role to play in the treatment of pediatric *Salmonella*-associated acute gastroenteritis.

During the period 1990–1999, more than 40% of *Salmonella* and *Shigella* from children with diarrhea were resistant to ampicillin and trimethoprim-sulfamethoxazole (3, 8). Similar findings were reported for *Salmonella* from Benghazi (4). A study carried out in Zliten city between 2001 and 2002 reported multidrug resistance (MDR, resistance to three or more antibiotics) of more than 75% among *Salmonella* species isolated from diarrheic children (9). Recently, Rahouma et al. reported that 63% (12/19) of *Salmonella* species isolated from diarrheic children in Tripoli were resistant to ciprofloxacin (6). Their finding is a serious health problem as fluoroquinolones are indicated for the treatment of severe salmonellosis in adults (10).

### Escherichia coli

*Escherichia coli* is the predominant causative agent of acute UTI worldwide. A study from Benghazi in the early 1980s reported 22% resistance to ampicillin among *E. coli* from UTI (11). The rate of resistance to ampicillin increased nearly three-fold from 1990 to 1999. High rates of resistance to trimethoprim-sulfamethoxazole were also observed during the same period for *E. coli* from the

### Table 1. Antimicrobial resistance of *Salmonella* isolated from diarrheic fecal specimens from 1979 to 2008 in different Libyan cities

| Year/city          | No. tested | Amp | AMC | CEF | C | Gen | NA | Cip/Nor | TMX | References |
|--------------------|------------|-----|-----|-----|---|-----|----|---------|-----|------------|
| 1979/Tripoli       | 244        | 89  | NT  | NT  | 79| 17  | 12 | NT      | NT  | (2)        |
| 1979/Tripoli       | 238        | 29  | NT  | NT  | 89| 14  | 17 | NT      | NT  | (2)        |
| 1992–1993/Tripoli  | 21         | 52  | NT  | 43  | 52| 43  | 0.0| 0.0     | 48  | (3)        |
| 1993/Benghazi      | 157        | 70  | 58.5| NT  | 66.2| 64.3| NT | NT      | 67.5| (4)        |
| 2000–2001/Zliten   | 23         | 100 | 96  | 96  | 84| 63  | 21 | (6)     |      |            |

Amp, ampicillin; AMC, amoxicillin-clavulanic acid; CEF, cephaloridine; C, chloramphenicol; Gen, gentamicin; NA, nalidixic acid; Cip/Nor, ciprofloxacin/norfloxacin; TMX, trimethoprim-sulfamethoxazole; NT, not tested.

*S. wein* isolates.

*S. muenchen* isolates.

Citation: Libyan J Med 2013, 8: 20567 - http://dx.doi.org/10.3402/ljm.v8i0.20567
UTI in Tripoli and Benghazi. However, studies carried out between 2002 and 2008 reported lower resistance rates to ampicillin and trimethoprim-sulfamethoxazole and an increase in resistance rates to fluoroquinolones.

Ciprofloxacin and other fluoroquinolones are drugs of choice in the treatment of UTI in adults, particularly in areas where resistance to ampicillin and trimethoprim-sulfamethoxazole among uropathogens are high (12). These drugs became available in pharmacies in Libya (mainly in Tripoli and Benghazi) in the late 1990s (KS Ghenghesh, personal observation). The use of ciprofloxacin in recent years may lead to a reduction in the use of ampicillin and trimethoprim-sulfamethoxazole for the treatment of UTI in Libya. This may in turn have resulted in the increased resistance to the former antibiotic and reduced resistance to the latter drugs. Table 2 shows the antimicrobial-resistance profile of E. coli isolated in the period 1981–2008 from acute UTI in different Libyan cities.

**Escherichia coli** strains are part of the normal gut flora. However, some types known as diarrheagenic *E. coli* (DEC) are important intestinal pathogens that cause a variety of gastrointestinal diseases particularly among children in developing countries (19). A study examined 155 *E. coli* strains isolated from diarrheic children in Tripoli between September 1992 and August 1993 for their susceptibility to antibiotics. Of the strains examined, 79% were resistant to ampicillin, 23% to cephalaxin, 12% to chloramphenicol, 26.5% to kanamycin, 2% to NA, 65% to tetracycline, and 50% to trimethoprim-sulfamethoxazole (20).

Recently, a study tested 21 strains of DEC (10 enter-aggregative *E. coli*, 3 enteropathogenic *E. coli*, and 8 enterotoxigenic *E. coli*) isolated from Libyan children with diarrhea in Zliten and Alkhoums cities identified by PCR for their susceptibility to antibiotics (21). Of the DEC strains tested, 81% were resistant to ampicillin, 57.1% to amoxicillin-clavulanic acid, 42.9% to chloramphenicol, 9.5% to Nalidixic acid, and 61.9% to trimethoprim-sulfamethoxazole. All strains were susceptible to ceftriaxone, ciprofloxacin, and imipenem.

**Other enteric bacteria**

Ghenghesh et al. examined 215 strains of enterobacteria isolated from human feces, urine, foods and waters during 1991–1993 in Tripoli and represent the following genera: *Escherichia*, *Citrobacter*, *Serratia*, *Kluyvera*, *Klebsiella*, *Enterobacter*, *Morganella*, *Proteus*, *Providencia*, as well as *Salmonella* and *Shigella* (22). Of the organisms examined, 57.7% were resistant to ampicillin, 25.6% to chloramphenicol, 6% to gentamicin, 29.3% to kanamycin, 28.4% to trimethoprim-sulfamethoxazole, and 65.6% to tetracycline.

**Extended-spectrum β-lactamases in Escherichia coli and Klebsiella pneumoniae**

Extended-spectrum β-lactamases (ESBLs) are enzymes produced by bacteria, mostly *E. coli* and *Klebsiella* species, rendering them resistant to cephalosporins including cefotaxime, cefuroxime, and ceftazidime. These enzymes were first reported in the mid-1980s mainly in hospitals. A study carried out in 2002 reported ESBL in 8.6% of 383 *E. coli* and in 15.3% of 209 *K. pneumoniae* isolated from different clinical specimens submitted by Trauma and Surgery Departments in Tripoli Central Hospital (23). The study also found that production of ESBL is significantly associated with *E. coli* and *K. pneumoniae* in inpatients compared with outpatients (*P <0.000001*). Production of ESBL in *E. coli* and *Klebsiella* species from Tripoli and Benghazi cities is shown Table 3.

**Methicillin-resistant Staphylococcus aureus** (MRSA), vancomycin-resistant *S. aureus* (VRSA), vancomycin-intermediate *S. aureus* (VISA), and heterogeneous VISA (hVISA) *Staphylococcus aureus* is well established as an important cause of hospital- and community-acquired infections.

### Table 2. Escherichia coli isolated during 1981–2008 from urinary tract infections in different Libyan cities

| Year/city          | No. tested | Amp  | C     | Gen  | NA  | Cip | NF  | TMX | References |
|--------------------|------------|------|-------|------|-----|-----|-----|-----|------------|
| 1981/Benghazi      | 38         | 22   | NT    | 0.0  | 0.0 | NT  | 0.0 | NT  | (11)       |
| 1993–1995/Tripoli  | 31         | 97   | 29    | 6    | 0.0 | NT  | 13  | 55  | (13)       |
| 1994–1995/Tripoli  | 534        | 74   | 29    | 7    | 11  | NT  | 25  | 45  | (14)       |
| 1996/Benghazi      | 148        | 75   | 45    | 18   | 10  | NT  | 7   | 81  | (15)       |
| 2002–2005/Sirte    | 1265       | 49   | 23    | 9    | 28  | 2   | 7   | 36  | (16)       |
| 2005–2006/Tripoli  | 29         | 59   | 21    | 10   | 28  | 14  | NT  | 24  | (17)       |
| 2006–2008/Benghazi | 105        | 57   | 14    | 7    | 23  | 17  | 0.0 | 31  | (18)       |

Amp, ampicillin; C, chloramphenicol; Gen, gentamicin; NA, nalidixic acid; Cip, ciprofloxacin; NF, nitrofurantoin; TMX, trimethoprim-sulfamethoxazole; NT, not tested.

Citation: Libyan J Med 2013, 8: 20567 - http://dx.doi.org/10.3402/ljm.v8i0.20567
In addition, *S. aureus* isolates that are resistant to methicillin (MRSA) are resistant to all β-lactam drugs, and often to aminoglycosides, which makes them difficult to treat, particularly in hospitals (25, 26).

The first report of MRSA from Libya was by Goda in 1976 (27). He examined 16 *S. aureus* strains isolated from mastitis in cows in Benghazi during 1971/1972 for their susceptibility to six antibiotics including methicillin and oxacillin. Goda found that 25% (4/16) and 19% (3/16) were resistant to oxacillin and methicillin, respectively. Of the 16 *S. aureus* strains examined, 11 gave conflicting results between methicillin and oxacillin. However, Goda did not use control organisms nor did he compare the zones of inhibition obtained to the criteria set by the Food and Drug Administration at the time of the study as required by the standard method of Bauer and Kirby (28) used to determine the susceptibility of bacteria to antibiotics. This may explain the conflicting results obtained by the author and in turn render his results questionable.

Until the early 1990s, data regarding *S. aureus* and MRSA infections in Libya were lacking. However, an outbreak of MRSA occurred in 1981 in the Zurich-area University Hospital, Switzerland was related to a patient with multiple injuries from Libya (29). This indicates that MRSA was present in Libya since that time but not reported. In recent years, the highest prevalence rate (54–68%) of MRSA from Libya was found among *S. aureus* from patients with burns and surgical wound infections (30, 31). Isolation of MRSA from different sources in Libyan cities in the period 1995–2008 is shown in Table 4.

From this table, it can be noticed that the reported rates of MRSA from clinical sources were on the rise as years go by. The rise can be due to several factors that include an increase in the β-lactam drugs consumption in the country and better detection and reporting of MRSA. The lack of surveying studies in the country makes it difficult to pinpoint the causes associated with the increase in MRSA. However, in the last decade of this study, the prevalence of MRSA from clinical specimens in Libya was within the range reported for the Mediterranean region, which constitutes a high prevalence area for MRSA (39).

Conversely, there are no reports of MRSA from food sources in Libya. Of 60 *S. aureus* strains isolated from ice

### Table 3. Extended spectrum β-lactamases in *Escherichia coli* and *Klebsiella* species from Libya

| Year/city       | Source        | E. coli | No. tested | % ESBL | Klebsiella species | No. tested | % ESBL | References |
|-----------------|---------------|---------|------------|--------|--------------------|------------|--------|------------|
| 2002/Tripoli    | Clinical specimens | 383     | 8.6        | 209    | 15.3               | (23)       |
| 2005–2006/Tripoli | Urine        | 48      | 4          | NT     | NT                 | (17)       |
| 2000–2007/Tripoli | BICU<sup>a</sup> | NT      | NT         | 32     | 47                 | (24)       |
| 2006–2008/Benghazi | Urine        | 105     | 1.9        | 42     | 2.4                | (18)       |

NT, not tested.

<sup>a</sup>Blood specimens from patients with microbiological evidence of septicemia admitted to the burn intensive care unit.

### Table 4. Isolation of methicillin-resistant *Staphylococcus aureus* (MRSA) from different sources in Libyan cities in the period 1995–2009

| Year/city       | Source                        | No. tested | % MRSA | References |
|-----------------|-------------------------------|------------|--------|------------|
| 1995–1996/Tripoli | Different food samples       | 23         | <1     | (32)       |
| 1995–1996/Tripoli | Different clinical specimens | 40         | <1     | (32)       |
| 1998/Tripoli     | Used banknotes                | 50         | 4      | (33)       |
| 1998–2001/Tripoli | Neonatal SCU<sup>a</sup>     | 25         | 12     | (34)       |
| 2001–2002/Tripoli | Ice cream                     | 60         | <1     | (35)       |
| 2004/Tripoli     | DVDs                          | 35         | 11     | (36)       |
| 2005–2006/Tripoli | UTI                          | 24         | 21     | (17)       |
| 2007/Benghazi    | Different clinical specimens | 200        | 31     | (30)       |
| 2007/Tripoli     | Burn patients                 | 120        | 54     | (31)       |
| 2000–2007/Tripoli | Burn ICU<sup>b</sup>         | 174        | 55     | (24)       |
| 2008/Tripoli     | Healthcare workers            | 643        | 37     | (37)       |
| 2009/Sabrata     | Healthcare workers            | 43         | 11     | (38)       |

<sup>a</sup>Blood specimens from babies attended special care unit with a clinical diagnosis of neonatal sepsis.

<sup>b</sup>Blood specimens from patients with microbiological evidence of septicemia admitted to the burn intensive care unit.
Tuberculosis (TB) caused by the bacterium *Mycobacterium tuberculosis* is a serious health problem in Libya. The WHO estimated TB incidence rate in Libya for the period 1990–2010 at 40 per 100,000 (45). The recommendation of the National Institute for Health and Clinical Excellence (NICE) for vaccination and screening in England and Wales considers countries with the above-mentioned incidence rate or greater to have a high incidence of TB (46).

Anti-tuberculosis agents are classified mainly into first- and second-line drugs. First-line agents are the most effective anti-TB drugs that include isoniazid, rifampicin, ethambutol, and pyrazinamide. In the past, streptomycin was considered a first-line drug; however, a worldwide increase in the frequency of resistance to this agent has made it less useful (47). Second-line anti-TB drugs have limited bactericidal capacity and are less effective and much more expensive compared with first-line agents (48, 49). These agents include injectable aminoglycosides (kanamycin, amikacin, capreomycin), ethionamide, cycloserine, para-aminosalicylic acid, and fluoroquinolones (levofloxacin, moxifloxacin, ofloxacin, ciprofloxacin).

Multidrug-resistant tuberculosis (MDR-TB) is defined as tuberculosis caused by *M. tuberculosis* strains resistant to at least isoniazid and rifampicin. MDR-TB can be either a ‘new case’ (primary resistance) defined as a newly registered episode of TB in a patient with no prior anti-tuberculosis treatment, or a ‘previously treated case or retreatment case’ (acquired resistance) defined as a newly registered episode of TB in patient treated for TB for 1 month or more (50). Extensively drug-resistant TB (XDR-TB) is resistant to the same drugs as MDR-TB, plus any fluoroquinolone and at least one second-line aminoglycoside. MDR-TB and XDR-TB cannot be treated with the standard 6 months course of first-line agents and can take up to 2 years or more to treat with second-line drugs (49).

In the past, Libya never reported data on MDR-TB to the WHO. Also, there is no information on the effect of HIV on the prevalence of MDR-TB in the country. Data reported by the WHO on MDR-TB in Libya from 2002 to 2011 are estimates (49, 51, 52). However, few studies on the rate of MDR-TB in Libya have been reported in the biomedical literature. Khalil and Sathianathan examined the records of 771 Libyans with culture-positive cases of newly diagnosed pulmonary tuberculosis and 789 cases of both Libyans and non-Libyans with positive cultures during treatment on the Regional Tuberculosis and Chest Diseases Centre in Benghazi over a period of approximately 5 years (June 1971-August 1976) (53). They reported that the primary (new cases) and acquired resistance (retreatment cases) to streptomycin, isoniazid, and para-aminosalicylic acid in 1971 were 16.6 and 33.3%, and in 1976 were 8.6 and 14.7%, respectively. The authors indicated that the decline in both new and retreatment cases was mainly due to the introduction of anti-tuberculosis legislation in Libya in 1973. Another study from the western region of Libya examined a total of 598 and 246 strains of *M. tuberculosis* isolated during 1984–1986 for new and retreatment MDR-TB, respectively. MDR-TB was found to be 11% among new cases and 21.5% in retreatment cases (54).

In general, it can be observed from available data that new MDR-TB cases decreased significantly in the first decade of 21st century compared with the early 1970s. On the other hand, retreatment MDR-TB cases remained high (21–39%) during 1971–2011. Improvement in the standard of living and health services compared with that in 20th century pre-1970s era may represent some of the reasons for the decline in cases of new MDR-TB. However, rates of previously treated MDR-TB remaining high for several years have been reported from many countries worldwide (51). This is due to several factors that include duration of treatment that lasts for months which results in high rates of new case MDR-TB patients defaulting treatment. Rates of new and retreatment cases of MDR-TB in Libya from 1971 to 2011 are shown in Table 5.
Antimicrobial resistance is a threat to health associated with a heavy financial burden (56). The Libyan health authorities urgently need to allocate resources for surveillance of antimicrobial resistance using WHO guidelines and starting with hospital-acquired infections caused by MRSA, Gram-negative bacilli, and MDR-TB. Also, surveillance of antimicrobial use is needed. Information from both surveillance programs will provide data required to direct policy on the prudent use of antimicrobials and to appraise and evaluate resistance containment interventions at local and national levels (56).

In addition, reducing the impact of hospital-acquired (nosocomial) infection in our hospitals is urgently required. Such action will most likely reduce antimicrobial use in the hospital setting and may lead to a reduction in high rates of antimicrobial resistance reported from hospitals in Libya. Programs dealing with control of nosocomial infections in the country should be strengthened and updated regularly.

A major component of future policies for prevention and control of antimicrobial resistance in Libya should be education of healthcare workers, pharmacists, students, and the general public. Examples of classroom approaches for teaching the dynamics of antibiotic resistance that can be adopted and used and articles that may encourage teachers to understand that antibiotic resistance is a serious health problem and should be discussed with students in biology classes in our high schools and universities are available (57, 58). There are many international agencies (particularly the WHO), scientific societies, and other institutions that provide excellent and accurate educational resources on the subject for free (see supplemental box). Such agencies can be consulted and their educational resources should be used as guidelines. In addition, local scientific and culture societies, sport clubs, mosques, schools, universities, welfare and correctional centers, and the media should be involved in such programs. The crisis of antimicrobial resistance in Libya has reached a stage that requires the Ministries of Health, Education, and Higher Education and Scientific research to join forces in addressing this issue.

Conflict of interest and funding

The authors declare no conflict of interest and not receiving funding or benefits from any source.

References

1. Scicluna EA, Borga MA, Gürb D, Rasslan O, Taher I, Redjeb SB, et al. Self-medication with antibiotics in the ambulatory care setting within the Euro-Mediterranean region; results from the ARMed project. J Infect Public Health. 2009; 2: 189-97.
2. el Nageh MM. Salmonella isolations from human faeces in Tripoli, Libya. Trans R Soc Trop Med Hyg. 1988; 82: 324-6.
3. El-Ghodban A, Ghenghesh KS, Marialigeti K, Abed S. Serotypes, virulence factors, antibiotic sensitivity, beta-lactamase activity and plasmid analysis of Salmonella from children with diarrhea in Tripoli (Libya). Acta Microbiol Immunol Hung. 2002; 49: 433-44.
4. Salih BA, Kashbur I, Mismari A, Al-Jehani S. Salmonellosis: a common cause of diarrhea among children in Benghaz. Jamahiriya’s Second Conf. on Medical Sciences, Benghaz, Libya, 8-11 May 1994.

5. Ghenghesh KS, Ali MB, Abuhelafia A, Dufani MA. High rates of resistance to antibiotics by salmonella from diarrheic children in Zliten-Libya. 4th European Congress of Chemotherapy and Infection, Paris, France, 4-7 May 2002.

6. Rahouma A, Klena JD, Krema Z, Abokker AA, Treesh K, Franka E, et al. Enteric pathogens associated with childhood diarrhea in Tripoli-Libya. Am J Trop Med Hyg. 2011; 84: 886-91.

7. Sood SC, Bilaziz M, Basbas N. Salmonella enteritis in children in Libya: role of antibiotic therapy. Ann Trop Paediatr. 1986; 6: 93-4.

8. Ghenghesh KS, Bara F, Bukris B, Aissa RB, Abuhelfaia A, Dufani MA. High rates of resistance to antibiotics by salmonella from diarrheic children in Tripoli-Libya. Saudi Med J. 1997; 18: 557-9.

9. Ali M, Ghenghesh KS, Aissa RB, Abuhelafia A, Dufani MA. Etiology of childhood diarrhea in Zliten-Libya. Saudi Med J. 2005; 26: 1759-65.

10. Molbak K, Gerner-Smidt P, Wegener HC. Increasing quinolone resistance in Salmonella enterica serotype enteritidis. Emerg Infect Dis. 2002; 8: 514-5.

11. Karoumi RM, Hanna A. An epidemiological study of urinary tract infections in Benghaz, Libya. J Hyg Epidemiol Microbiol Immunol. 1981; 25: 277-85.

12. Gupta K. Emerging antibiotic resistance in urinary tract pathogens. Infect Dis Clin North Am. 2003; 17: 243-59.

13. Alotmi AS, Abeer SS, Tloba SE, Rhouma AA, Daw MA, Ghenghesh KS. Urinary tract infections in Tripoli and drug sensitivity of the causative agents. The First Conference on Postgraduate Studies in Medical Sciences, Benghaz, Libya, 31 March-2 April 1997.

14. Ghenghesh KS, Alotmi AS, Gashout S, Abouhagar B. High antimicrobial-resistance rates of Escherichia coli from urine specimens in Tripoli-Libya. Garyounis Med J. 2003; 20: 89-93.

15. Tobgi RS, Taher IAA, Ali MB. Antibiotic susceptibility of uropathogens in Benghaz, Libya. Jamahiriya Med J. 2001; 1: 46-9.

16. Bagar SR, Hussein AA, Elahamel AM, Alani SMH. Antibiotic resistance pattern of urinary tract isolates. Jamahiriya Med J. 2007; 7: 116-21.

17. Ghenghesh KS, Elkatbe E, Berbash N, Nada RA, Ahmed SF, Rahouma A, et al. Uropathogens from diabetic patients in Libya: virulence factors and phylogenetic groups of isolated Escherichia coli. J Med Microbiol. 2009; 58: 1006-14.

18. Buzayan MM, Tobgi RS, Taher I. Detection of extended spectrum β-lactamases among urinary Escherichia coli and Klebsiella pneumoniae from two centres. Jamahiriya Med J. 2010; 10: 10-6.

19. Nataro JP, Kaper JB. Diarrheagenic Escherichia coli. Clin Microbiol Rev. 1998; 11: 142-201.

20. Abosak NY, El-Bosil KM, Hermas RA, Abeer SS, Ghenghesh KS. Antibiotic susceptibility of Escherichia coli isolated from Libyan children with diarrhea. Jamahiriya’s Second Conf. on Medical Sciences, Benghaz, Libya, 8-11 May 1994.

21. Ali MM. Molecular characterization of virulence factors of Escherichia coli isolated from Egypt and Libya. PhD Thesis, Faculty of Science, Cairo University, Cairo, Egypt, 2011.

22. Ghenghesh KS, Alotmi AS, Said MTA. Antibiotic susceptibility of enterobacteria isolated from different sources. Jamahiriya’s Second Conference on Medical Sciences, Benghaz, Libya, 8-11 May 1994.
41. Clinical Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing, 18th Informational Supplement (M100-S18). Wayne, PA: CLSI; 2008.
42. Ahmed MO, Abuzweda A, Alghazali MH, Elramalli AK, Amri SG, Aghila ESH, et al. Misidentification of methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals in Tripoli, Libya. Libyan J Med. 2010; 5: 5230. doi:10.3402/ljm.v5i0.5230.
43. Howden BP, Davies JK, Johnson PD, Stinear TP, Grayson ML. Reduced vancomycin susceptibility in *Staphylococcus aureus*, including vancomycin-intermediate and heterogeneous vancomycin-intermediate strains: resistance mechanisms, laboratory detection, and clinical implications. Clin Microbiol Rev. 2010; 23: 99–139.
44. Dhand A, Sakoulas G. Reduced vancomycin susceptibility among clinical *Staphylococcus aureus* isolates (‘the MIC Creep’): implications for therapy. F1000 Med Reports. 2012; 4: 4. doi:10.3410/M4-4.
45. WHO (2011). Global tuberculosis control. WHO/HTM/TB/2011.16. Geneva: World Health Organization.
46. Health Protection Agency (HPA). World Health Organization (WHO) estimates of tuberculosis incidence by country. 2010 (sorted by rate). Available from: http://www.hpa.org.uk/web/HPAweb&HPAweb_C/1195733837507 [cited 5 April 2012].
47. Centers for Disease Control and Prevention (CDC). Treatment of tuberculosis. MMWR. 2003; 53: 2.
48. Sharma SK, Mohan A. Multidrug-resistant tuberculosis: a menace that threatens to destabilize tuberculosis control. Chest. 2006; 130: 261–72.
49. WHO (2010). Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. WHO/HTM/TB/2010.3. Geneva: World Health Organization.
50. WHO (2009). Guidelines for surveillance of drug resistance in tuberculosis. 4th ed. WHO/HTM/TB/2009.422. Geneva: World Health Organization.
51. WHO (2008). Anti-tuberculosis drug resistance in the world: fourth global report. WHO/HTM/TB/2008.394. Geneva: World Health Organization.
52. WHO (2013). Tuberculosis profile: Libyan Arab Jamahiriya. Available from: www.who.int/tb/data [cited 15 January 2013].
53. Khalil A, Sathianathan S. Impact of anti-tuberculosis legislation in Libya on the prevalence of primary and acquired resistance to the three main drugs at a major tuberculosis centre. Tubercle. 1978; 59: 1–12.
54. Elghoul MT, Joshi RM, Rizghalla T. Primary and acquired drug resistance in *Mycobacterium tuberculosis* in western region of Libyan Arab Jamahiriya. Trop Geogr Med. 1989; 41: 304–8.
55. Rao BN, Kashbur IM, Shembesh NM, el Bargathy SM. In vitro antibiotic sensitivity pattern of common bacterial isolates from cases of acute bacterial meningitis with special reference to ceftriaxone. Indian J Pediatr. 1997; 64: 849–54.
56. WHO (2012). The evolving threat of antimicrobial resistance: options for action. Available from: http://whqlibdoc.who.int/publications/2012/9789241503181 [cited 12 November 2012].
57. Lawson MA. The antibiotic resistance problem revisited. Am Biol Teacher. 2008; 70: 405–10.
58. Wassmer GT, Kipe-Nolt JA, Chayko CA. Why finish your antibiotics? A novel, hands-on, classroom approach for teaching the dynamics of antibiotic resistance. Am Biol Teach. 2006; 68: 476, 478–80.