

Campylobacter Infection Antimicrobial Resistance Trends

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Abstract

Aim: To determine the trends of campylobacter sensitivity and resistance to antibiotics, at the Bahrain Defence Force Hospital (BDF), in 13 months period.

Methodology: Resistance of campylobacter to erythromycin, clindamycin, ciprofloxacin, tetracycline and levofloxacin on human isolates of campylobacter taken within a period from October 2009 – October 2010 was assessed. Statistical analysis was done by entering the data Microsoft excel and analyzing using the SPSS version 12 statistical package.

Results: Ciprofloxacin and levofloxacin antibiotics were resistant in most of the cases, whereas clindamycin and erythromycin antibiotics were never resistant; this implies that the former two are safer to use with their high sensitivity rates.

Conclusion: The principal purpose of monitoring antimicrobial resistance trends is to provide clinicians with data that can be used to select appropriate treatment regimens.

Keywords: Campylobacter sensitivity, Campylobacter testing, Campylobacteriosis

Introduction:

Campylobacter is one of the most commonly reported bacterial causes of human food borne infections, and increasing proportions of these pathogens become resistant to medically important antimicrobial agents, imposing a burden on public health¹. Both Campylobacter and Salmonella are primarily intestinal organisms in a wide range of animals and are commonly present in the environment of food-producing animals²⁻³

Campylobacter is a bacteria, that is a major cause of diarrheal illness in humans and generally considered the most common bacterial cause of gastroenteritis worldwide. In developed and developing countries, they cause more cases of diarrhea than food borne Salmonella bacteria. Campylobacter infections in children under the age of two years are frequent and can result in death.³

Campylobacter is mainly spiral-shaped, S-shaped or curved rod-shaped bacteria. There are 16 species and six subspecies assigned to the genus Campylobacter, of which the most frequently reported in human

disease are *C. jejuni*, *C. coli*, *C. lari* and *C. upsaliensis* which are considered as primary pathogens, but are generally reported far less frequent in cases of human disease. Most species prefer a micro-aerobic (containing 3-10% oxygen) atmosphere for growth.³

Campylobacter is widely distributed and occur in most warm-blooded domestic and wild animals. They are prevalent in food animals such as poultry, cattle, pigs, sheep, ostriches and shellfish; and in pets, including cats and dogs⁴. The source of infection can be from GIT of poultry, farm animals (cattle swine), household pets (puppies and kittens), contaminated food (undercooked or poorly handled poultry), birds pecking the tops of doorstep milk, wombats and Kangaroo feces (bushwalker's diarrhea), unpasteurized milk and public water supplies associated with some defect in purification.³ Campylobacteriosis is the disease caused by the presence of campylobacter. The incubation period is usually three to four days, but can range from eight to nine days. Typically there is a 24 hours prodromal

illness – fever, headache, followed by onset of the clinical symptoms. The most common clinical symptoms include diarrhea associated frequently with blood in the stool, abdominal pain, fever, headache, nausea, and/or vomiting, which last five to seven days. A fatal outcome is rare and is usually confined to immunocompromised patients, very young or elderly patients. Complications such as bacteremia, hepatitis, pancreatitis, toxic mega colon and abortion have all been reported with various degrees of frequency. Post-infection complications may include reactive arthritis and Guillain-Barré syndrome (<than 1 in 1000 cases).⁴

The main route of transmission is generally believed to be food borne, via undercooked meats and meat products, as well as raw or contaminated milk. The ingestion of contaminated water or ice is also a recognized source of infection. Campylobacteriosis is considered to be a zoonotic disease transmitted to humans from animals or animal products. In animals, campylobacter seldom cause disease⁴. 500 organisms are needed for infection to occur. They Adhere to jejunum and ileum, were there is mucosal invasion leading to cytotoxin release that causes local damage associated with enlarged mesenteric lymph nodes, occasionally severe hemorrhagic necrosis of the small intestine, or large bowel involvement with crypt abscess formation in severe cases (DDX Ulcerative colitis). Occasionally bacteremia may occur with focal manifestations and organism may be invasive. Enterotoxin may also play a role.⁵

Diagnosis of campylobacter is mainly through history and clinical diagnosis, Stool stained with methylene blue (reveals PMNs and RBCs), Culture (Feces, blood), Curved Gram Negative bacteria (flagella). Grown on especially selected agar plates with microaerophilic atmosphere and 42°C, it illustrates oxidase positive.

Incidence of Campylobacter food poisoning is 2.5 million cases per year in USA as estimated by the Centers for Disease Control and Prevention (CDC) and the National Institute of Allergy and Infectious Diseases Fact sheet (NIAID)⁶; 2 million cases to 8 million cases a year. Incidence Rate of

Campylobacter food poisoning is approximately 1 in 108 or 0.92%. Incidence of Campylobacter food poisoning is 40.12 per 100,000 in Canada 2000⁷. Also, 112.2 new cases of campylobacteriosis per 100,000 populations were notified in Australia in 2002.⁶ Incidence usually peaks in summer. The incidence of human campylobacter infections has been steadily increasing for several years. The reason for this is unknown.

Prevalence of Campylobacter food poisoning is over 10,000 cases reported to the CDC each year, equaling approximately six cases per 100,000 population. Many more cases went undiagnosed or unreported, and campylobacteriosis is estimated to affect over 2 million persons every year, or 1% of the population. Incidence is about 20 cases per 100,000 population diagnosed in the United States. An estimated 2.4 million persons are affected each year.⁷ Campylobacter organisms cause between 5 and 14 percent of all diarrhea illnesses worldwide. In industrialized countries, illness is more common in children younger than 2 years of age. In developing countries, older children and young adults have the highest incidence of infection. Most frequently, cattle and poultry are the sources of human infection, but puppies, kittens, pigs, sheep, rodents, and birds may also serve as reservoirs⁸.

Although Campylobacter doesn't commonly cause death, the death rate extrapolation for USA has been estimated to be 500 per year. This extrapolation calculation uses the deaths statistic estimated 500 deaths annually by the Division of Bacterial and Mycotic Diseases (DBMD). An estimated 124 fatal cases each year can cause life-threatening sepsis in persons with compromised immune systems⁹.

The objective of this study is to determine the trends in Campylobacter antibiotic resistance occurring in Bahrain Defence Force hospital (BDF) and assessing the differences in the isolates. Since antimicrobial resistance of campylobacter species to erythromycin is already being done since years in BDF microbiology laboratory, we are going to assess the resistance of campylobacter to ciprofloxacin, tetracycline and quinolones on human isolates of

campylobacter taken within a period from October 2009 – October 2010.

Materials and Methods:

Stool samples are generally processed at the microbiology laboratory at BDF according to guidelines set out in the Bahrain National Quality Control Manual. (20) Since antimicrobial resistance of campylobacter species to erythromycin and clindamycin is already being done since years in BDF microbiology laboratory, we are going to assess the resistance of campylobacter to erythromycin, clindamycin, ciprofloxacin, tetracycline and levofloxacin on human sample isolates of campylobacter taken within a period from October 2009 – October 2010 was assessed. Campylobacter cultures were carried out using blood-free selective agar containing modified charcoal cefoperazone deoxycholate selective supplement (Oxoid). Plates called Campylo plates were incubated at 42°C for 48h under microaerobic condition (CampyGen; Oxoid). Suspected colonies were subcultured on chocolate agar plates and incubated microaerobically at 37°C for 24 h (CampyGen; Oxoid). Negative cultures were reincubated for an additional 24 h. Campylobacter isolates were identified to species level using routine biochemical tests (production of catalase, hippurate and indoxyl acetate). Statistical analysis of the data gathered was done by entering the data Microsoft Excel and analyzing using the SPSS version 12 statistical package. Statistical significance was calculated using chi square test.

Results and Discussion:

Over 10,000 cases of campylobacter is reported to the Centers for Disease Control and Prevention (CDC) each year, equaling approximately six cases per 100,000 population. The rapid emergence of antibiotic resistance for Campylobacter species were noted in Europe in 1980's, from 0% in 1982 to 11% in 1989, in the United States it rose from 0% in 1989 to 19% in 2001. Campylobacteriosis is a disease caused by the presence of campylobacter. Treatment is not generally indicated unless symptomatic, except

electrolyte replacement and rehydration. Antimicrobial treatment with erythromycin, Ciprofloxacin, tetracycline or quinolones is indicated in invasive cases or to eliminate the carrier states. In Bahrain Defense Force Hospital, only erythromycin resistance is done as a routine test when campylobacter is found. In this analysis results showed that Ciprofloxacin and levofloxacin antibiotics were resistant in most of the cases, whereas clindamycin and erythromycin antibiotics were never resistant; this implies that the former two are safer to use with their high sensitivity rates. (Figure 1 and 2)

The prevention of infection requires control measures at all stages of the food chain, from agricultural production on the farm, to processing, manufacturing and preparation of food in both commercial establishments and the domestic environment. Education in hygienic handling of food for abattoir workers and those involved in the production of raw meat is essential to keep microbiological contamination to a minimum. The only effective method of eliminating campylobacter from contaminated foods is to introduce a bactericidal treatment, such as heating (cooking or pasteurization) or irradiation. Preventive measures for campylobacter infection in the household kitchen are similar to those used against other food borne bacterial diseases¹⁰.

Distinguishing infections caused by different enteric pathogens is seldom possible, antimicrobial drug use in the clinical setting is not confined to the treatment of Campylobacter species but rather to empiric treatment of community-acquired diarrhoea in general. Systematic surveillance data and timely reporting of antibiotic resistance patterns in pathogens from different regions should become a high priority since the principal purpose of monitoring antimicrobial resistance trends is to provide clinicians with data that can be used to select appropriate treatment regimens, it can be of great help in drawing the attention to the most effective antibiotics that could be used worldwide in addition to the fact that it will give physicians an idea about the trend of resistant percentages for each antibiotic,

by emphasizing the antibiotics that are being used routinely to treat diarrhoea, as well as any alternatives, such as fluoroquinolones, macrolides, and gentamicin.¹¹

A meta-analysis demonstrated that antibiotic treatment was beneficial when begun early, decreasing diarrhea duration by a mean of 1.32 days as well as shortening the microbiologic carriage duration.¹²

In our study, we studied the range of antibiotic sensitivity that could be used in the treatment of campylobacter. Ciprofloxacin and levofloxacin were resistant in most of the times, whereas clindamycin and erythromycin were never resistant; this implies that the former two are safer to use with their high sensitivity rates. (Figure 3) Resistance in *Campylobacter* species is of paramount importance when antibiotics are used to treat human infections. Erythromycin has been the cornerstone of therapy,

demonstrating consistent bacteriologic cure of sensitive strains when compared with placebo but with an inconsistent benefit for clinical cure.¹³⁻¹⁴

With the introduction of fluoroquinolones, ciprofloxacin became the mainstay of empiric treatment for acute community acquired bacterial diarrhea and even for traveler's diarrhea.¹⁵⁻¹⁶

However rapid emergence of resistant strains were noted in Europe in 1980's from 0% in 1982 to 11% in 1989, in the United States it rose from 0% in 1989 to 19% in 2001.¹⁷⁻¹⁸

Additional resistance to other relevant therapeutic agents poses a risk when there is no effective antimicrobial regimen for *Campylobacter* infections. Recently, Hoge et al. found 100% co-resistance between Thai isolates resistant to azithromycin and ciprofloxacin in the last 2 years of surveillance.¹⁹

Figure 1:

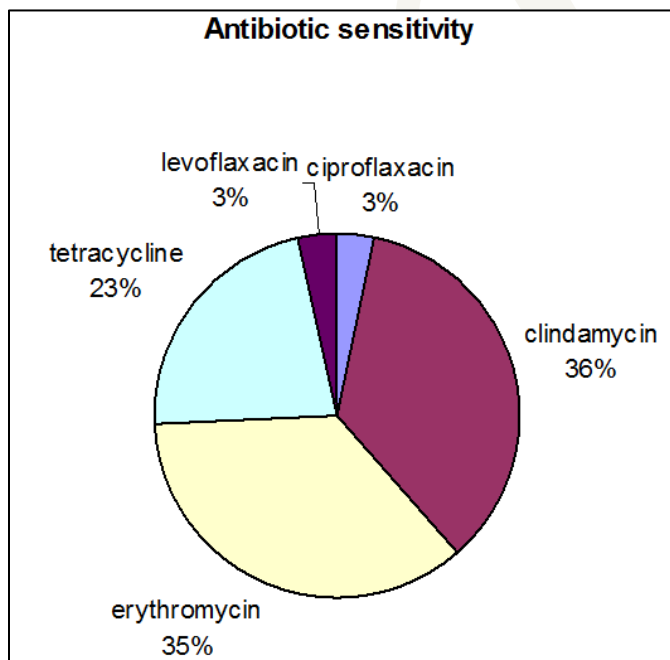


Figure 2:

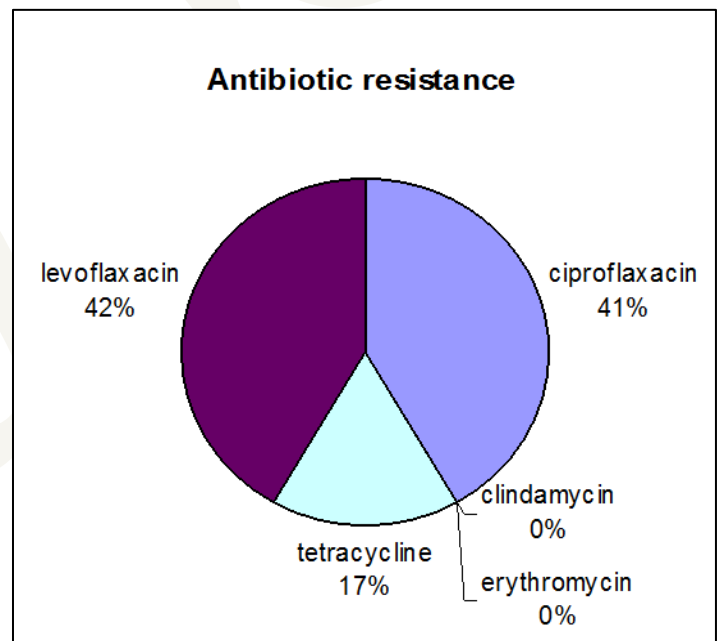
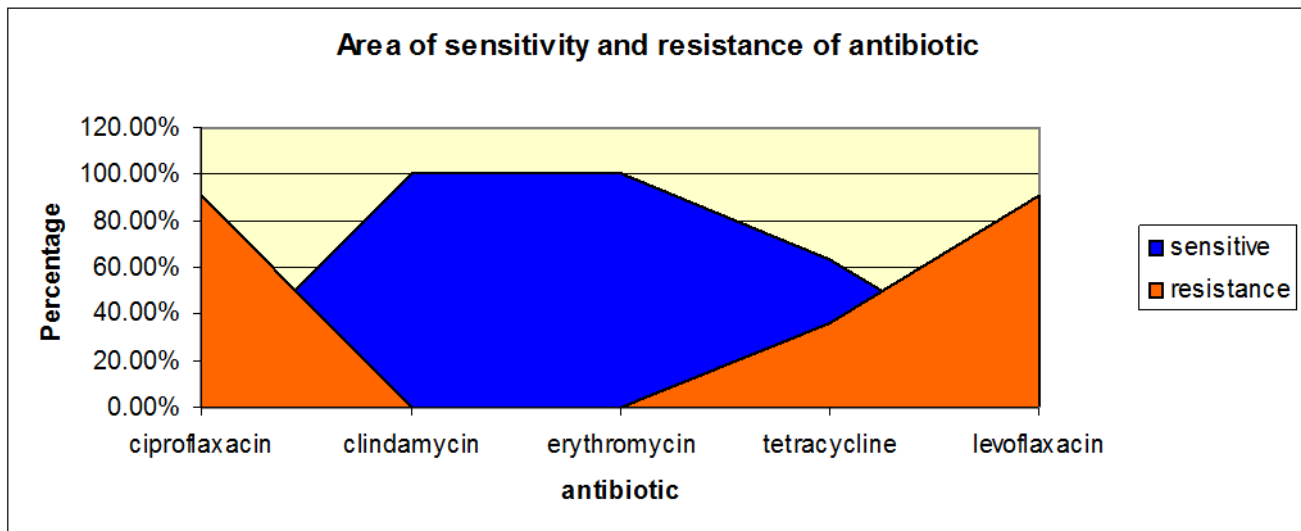


Figure 3:



Conclusion:

Campylobacteriosis is a common cause of diarrhoea and enterocolitis worldwide. Although commonly self limiting, infections can be associated with systemic and recurrent disease in immunocompromised, and severe complications (reactive arthritis, Guillain-Barré syndrome) in healthy individuals, hence treatment options have to be clearly demarcated and sensitivity to the pathogen performed. The rapid emergence of antibiotic resistance has limited the antibiotic options but more antibiotics are emerging and continuous sensitivity testing is going to provide a range of the most effective drugs to consider in the treatment options.

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