Campylobacter and Emerging Antimicrobial Resistance

A. Zafar (Department of Pathology and Microbiology, Aga Khan University,)

Various species of Campylobacter have been recognized since the late 1970s as important agents of gastrointestinal infections. It is interesting to know that in the last few decades, this zoonotic disease has become the leading cause of enteric infections in developed as well as developing countries. Campylobacter jejuni and coli are the most common species causing illness and among these two, C. jejuni accounts for a vast majority of infections.

Campylobacter species is a Gram-negative slender, curved, motile (due to polar flagella) rod. The unique shape of the cell and flagella are extremely useful in identification. Infections due to these organisms lead to acute gastroenteritis, which typically resolves in a period of few days to few weeks. Furthermore, it is a common cause of traveler's diarrhea and is the single most identifiable antecedent infection associated with the development of Guillain-Barre syndrome.

Most cases of Campylobacteriosis do not require antimicrobial treatment since they are clinically mild and self-limiting in nature, although antimicrobial therapy is required for serious enteritis and systemic infections. Macrolides and fluoroquinolones are considered as drugs of choice for the treatment of enteric infections, and intravenous aminoglycoside for those cases present with systemic manifestations. In many cases, fluoroquinolones are preferred if the differential diagnosis includes Salmonella, Shigella or other enteric bacterial pathogens. Unfortunately, antimicrobial resistance to various drugs is on the rise and repeatedly has been reported from several countries during previous years. 1-4

Antimicrobials have been used in animal feed (farm animals and poultry) for nearly half a century. Most commonly used drugs are either identical to or are related to those administered to humans, including penicillins, tetracyclines, cephalosporins (even third generation) and fluoroquinolones. These antimicrobial agents are given to animals as therapy for an infection, or in the absence of illness for sub therapeutic purposes with the goals of growth promotion and enhanced feed efficiency (the ability to grow animals faster on less feed, is improved by adding small amount of antibiotics to animal feed).

Food producing animals, especially poultry, are considered as one of the most important sources of Campylobacter infection amongst human beings. Many studies have shown that poultry meat available at super markets have been found contaminated by C. jejuni.2,3,5 Moreover, various studies suggest that the incidence of antimicrobial resistant strains have increased with the introduction of the sub-therapeutic and therapeutic use of these drugs in animals.6-10 The use of antimicrobials in animal feed selects resistant strain and enhances their persistence in the environment. Drug resistance in Campylobacter and other organisms can increase the frequency and severity of infections, limit treatment options and raise health care costs. Therefore, development of antimicrobial resistance in Campylobacter and other zoonotic enteric pathogens such as Salmonella typhimurium, Enteroinvasive and Enterohemorhagic E. coli is a matter of concern.

An 11 year study by Ibrahim et al.11 conducted in Karachi consisted of a large number of clinical isolates. Though it was a single center study, specimens were submitted from all over the country; hence, it can be recognized as dependable data for this region. But the authors did not analyze the data further on to a district, city or provincial level, which would have been more informative for the understanding of epidemiology of this disease locally. The limitation, which has already been commented upon by the authors, is that it was retrospective and simply laboratory based. Thus, it is hard to know how many of the isolates were from clinically symptomatic patients or were merely from a carrier. The overall isolation rate was 14-18%, which is superior to various studies previously published

w

from Asia.10,12 Vibrio cholera was the most common pathogen, with an isolation rate of 31% followed by Salmonella 26%, Campylobacter 24.8% and Shigella 12%.

It is important to note that the rate of isolation of Campylobacter is less than that of Salmonella, though it has superceded in the developed world. This can be explained if the fastidious nature of Campylobacter is taken under consideration. It is known that the isolation rate of fastidious organisms reduces during transportation of clinical specimens due to various reasons such as a prolonged period between the collection of a specimen and it's inoculation in the laboratory, along with poorly controlled environmental conditions. As specimens were included from all over the country, it can be speculated that the isolation rate of Campylobacter would have been much higher if only those specimens were to be included in the study that were submitted directly to the central laboratory or were immediately transported for the processing. For future studies, interesting epidemiological information can be gathered if a prospective study is designed and data is analyzed on the basis of geographic location, after which the variation in isolation is compared.

Recently, a dramatic rise in the number of resistant Campylobacter to quinolone, ampicillin, erythromycin and tetracycline was reported from various centers of the developed world.1-4 Similarly, Ibrahim et al reported a consistent rise in antimicrobial resistance to quinolones, ampicillin and tetracycline.11 However, it is not as rampant12-15, which can be explained by taking into account the difference in the practices of western countries and in this region. In Pakistan, the use of antimicrobials in animal feed at subtherapeutic dosage is not in practice (personal communication), though an indiscriminate use of antibiotics among human beings is a pertinent issue. Perhaps the widespread use of antimicrobials in animals and agriculture is causing more harm to the environment, bacterial ecosystem and is facilitating the development of antimicrobial resistance at large scale.

It is interesting to note that erythromycin resistance in Campylobacter has been declined throughout the reported study period. This is an important finding, which can help clinicians, in the management of severe enteric and systemic Campylobacteriosis (sporadic or outbreak) where empirical use of erythromycin would be the most appropriate choice, particularly for children with 45% isolation rate. 11

The findings of Ibrahim et al are informative and clearly indicate that Campylobacter is one of the leading enteric pathogens with a rising trend in antimicrobial resistance for most antimicrobials. This information reinforces the fact that indiscriminate use of antimicrobials should be controlled in the region and future studies are required to estimate the burden of this disease and trends of antimicrobial resistance.

transabdominal route. A transvaginal scan was performed in cases where the quality of ultrasound was unacceptable.

For maintaining the quality of the scan, the outcome of each pregnancy was monitored. The variables noted were weight of the baby, apgar scores and any additional abnormality at the time of birth.

All the above-mentioned variables along with the ultrasound details and demographic variables including gestational age were entered in a database file and analysed by SPSS version 10.

References

1. Gaudreau C, Giblert H. Antimicrobial resistance of Campylobacter jejuni subsp. Jejuni strains isolated from humans in 1998 to 2001 in Montreal, Canada. Antimicrob. Agents Chemother. 2003; 47: 2027-9.
2. Luber P, Wagner J, Hahn H, et al Antimicrobial resistance in Campylobacter jejuni and Campylobacter coli strains isolated in 1991 and 2001-2002 from poultry and humans in Berlin, Germany. Antimicrob. Agents Chemother. 2003; 47: 3825-30.
3. Chuma T, Maeda T, Niwa H, et al. Acquisition of quinolone resistance and point mutation of the gyr A gene in Campylobacter jejuni isolated from broilers and in vitro-induced resistant strains. J Vet Med Sci. 2004; 66: 155-160.
4. Gaudreau C, Michaud S. Cluster of erythromycin and ciprofloxacin-resistant Campylobacter jejuni subsp. from 1999 to 2001 in men who have sex with men, Quebec, Canada. Clin. Infect. Dis. 2003; 37: 131-6.
5. Benason GS, Khakhria R, Bollegraaf E. Nosocomial outbreak caused by antibiotic-resistant strain of Salmonella typhimurium acquired from dairy cattle. Can. Med. Assoc. J. 1983; 128: 426-7.
6. Animal Health Institute. Backgrounder: Antibiotic Use in farm animals. Available at: www.ahi.org/features/antibiotic%20backgrounder.htm. Accessed April 17, 2001.
7. Levy SB, FitzGerald GB, Macone AB. Changes in intestinal flora of farm personnel after introduction of a tetracycline-supplemented feed on

a farm. N. Engl J Med. 1976; 295: 583-8.
8. Molbak K, Baggesen DL, Aarestrup FM, et al. An outbreak of multidrug-resistant, quinolone-resistant Salmonella entericaserotype typhimurium DT104. N. Engl. J. Med 1999; 341: 1420-25.
9. Engberg J, Aarestrup FM, Taylor D, et al. Quinolone and macrolide resistance in Camplobacter jejuni and coli: Resistance mechanism and trends in human isolates. Emerg. Infect. Dis. 2001; 7: 24-34.
10. Haq JA, Rahman KM. Campylobacter jejuni as a cause of acute diarrhea in children: a study in an urban hospital in Bangladesh. J Trop Med Hyg 1991; 94:50-4.
11. Ibrahim NG, Zafar A, Hasan R. Evaluation of frequency of isolation and trends in antibiotic resistance among Campylobacter isolates over 11-year period. J Pak Med Assoc 2004;54:291-4.
12. Hoge CW, Gambel JM, Srijan A, Pitarangsi C, Echeverria P. Trends in antibiotic resistance among diarrheal pathogens isolated in Thailand over 15 years. Clin Infect Dis 1998;26:341-5.
13. Rautelin H, Renkonen OV, Kosunen TU. Emergence of fluoroquinolone resistance in Campylobacter jejuni and Campylobacter coli in subjects from Finland. Antimicrob Agents Chemother 1991;35:2065-9.
14. Smith KE, Besser JM, Hedberg CW, Leano FT, Bender JB, Wicklund JH, et al. Quinolone-resistant Campylobacter jejuni infections in Minnesota, 1992-1998. N Engl J Med 1999;340:1525-32.
15. Saenz Y, Zarazaga M, Lantero M, Gastanares MJ, Baquero F, Torres C. Antibiotic resistance in Campylobacter strains isolated from animals: Foods, and humans in Spain in 1997-1998. Antimicrob Agents Chemother 2000;44:267-71.