ORIGINAL ARTICLE

Antimicrobial Resistance Profile in Complicated Intra-abdominal Infections

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Abstract

Background
Early administration of appropriate empirical antibiotics is integral part of early management of complicated intra-abdominal infections. Selection of empiric antibiotics relies upon microbiologic profile and resistance patterns of commonly encountered organisms in hospital and community. In developing countries, limited microbiological susceptibility information can result in either under treatment or unnecessarily broad coverage.

Objectives
To find out frequency of various micro-organisms and their resistance profiles to help decide empiric antibiotics to be used in complicated intra-abdominal infections.

Methods
We conducted review of medical records of adult patients admitted from Jan 2012 to Dec 2015 with complicated intra-abdominal infections.

Results
Mean age of 317 patients included in the study was 51+/-18 years. Healthcare associated infections were present in 57% of patients. Most common source of infection was large bowel and appendix accounting for 22% of cases, followed by pancreatic infection (20%). Common organisms reported were *E. Coli* (56%), *Enterococci* (28%) and *Klebsiella Pneumoniae* (15%). Extended Spectrum Beta Lactamase (ESBL) producers were 75% of *E Coli* and 55% of *Klebsiella Pneumoniae* isolates. Cabapenem resistance was present in 8% of Klebsiella Pneumoniae isolates.

Conclusion
High prevalence of ESBL producing gram negative rods and resistance to other broad spectrum antibiotics especially in healthcare associated infection needs to be kept in mind while planning empiric antibiotics therapy in complicated intra-abdominal infections. Antibiotic stewardship program is proposed to avoid emergence of multi-drug resistant organisms.

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Key Words
Intra-abdominal Infections, Antibiotics, Microbiology, Bacteria

Introduction
Intra-abdominal infections (IAIs) include a wide variety of pathological conditions, ranging from cholecystitis to fecal peritonitis. In complicated IAIs, the infectious process proceeds beyond a single organ, causing either localized or generalized peritonitis.[1] Examples of complicated intra-abdominal infections are perforation of large or small intestine with abscess formation or fecal contamination and appendicitis complicated by perforation or abscess formation. Complicated IAIs are further classified into community-acquired intra-abdominal infections (CAIAIs) which are acquired in community, and healthcare associated intra-abdominal infections (HA-IAIs) which are acquired in hospitalized patients or residents of long-term care facilities. HA-IAIs are common and are usually associated with Increased mortality, multi drugs resistant organisms and fungal Infections.[2,3]

Complicated IAIs can cause frequent hospital readmissions, reoperation or radiological interventions, increased length of hospital stay and increased cost of care.[4] Mortality rates associated with complicated intra-abdominal infections range from 7% to up to 30% in different studies.[5,6] Management of complicated IAIs include hemodynamic support, source control and early appropriate empirical antibiotics administration.[2] Surviving Sepsis Campaign Guidelines recommend administration of effective empirical intravenous antimicrobials having activity against all likely pathogens, with in first hour of recognition of sepsis.[7] Knowledge of prevalence of pathogens and local resistance patterns play key role in selection of empirical antibiotics.[8]

There is no data available from our country regarding prevalence and resistance patterns of organisms involved in complicated intra-abdominal infections. Hospital infection control surveillance reports and antibiograms report overall prevalence of organisms and their resistance patterns without clinical correlation. So objective of present study was to determine frequency of various organisms involved in complicated intra-abdominal infections and to find out their resistance patterns to guide selection of empirical antibiotics.

Material and Methods:

We reviewed files of all adult patients who were admitted in the Aga Khan University Hospital (AKUH) Karachi Pakistan with diagnosis of complicated intra-abdominal infection from July 2012 to Jun 2015. Patients who did not have abdominal fluid culture or those who did not grow any organisms in cultures were excluded from analysis. Data was collected on a preformed questionnaire regarding demographics, source of infection, community acquired vs. healthcare associated infection, organisms reported and their resistance profiles. Infections were labeled as healthcare associated if acquired after at least 48 hours of hospitalization. Data was analyzed using SPSS version 19.[9] Qualitative data was reported in percentages while quantitative data was reported as mean +/- SD. Chi Square test was used to test association between qualitative variables. P value of less than 0.05 was considered significant.

Results

Of the 317 patients included in the study, 211 (66%) were males and 116 (34%) were females. Mean age of patients was 50 +/- 18 years. Healthcare associated infections were present in 181 (57%) patients and community acquired infection was present in 127 (40%) patients. State of health care vs. community acquired could not be determined for 9 patients. Generalized peritonitis was present in 58 (18%) patients at the time of presentation. Post laparotomy cases accounted for 25% (79) of cases, while pancreas was source of infection in 20% of cases. Contribution by other sources of infection is given in table 1. Most common organisms involved were *E. Coli* and Enterococci infecting 56% and 28% of the patients respectively. Fungal growth was seen in 13% of cases. Pseudomonas infection and fungal infection were significantly more common in hospital acquired settings. Other organisms and their frequencies are given in table 2. Extended Spectrum Beta Lactamase (ESBL) producing *E. Coli* were 75% and ESBL producing Klebsiella Pneumoniae (*KPneumoniae*) were 54%. Carbapenem resistance in K. Pneumoniae was reported in 8% of isolates. Frequency of Vancomycin Resistant Enterococci was 13%. Detailed antibiotic sensitivity of various gram negative rods is reported in table 3. Analyzing antibiotic coverage of commonly used antibiotics, we found that more than 90% of gram negative rods and anaerobes were covered by carbapenems alone as compared to less than 90% for piperacillin/tazobactam (pip/tazo) or amikacin if used alone. Coverage of combination of amikacin with pip/tazo or combination of amikacin with carbapenems was more than 90% against prevalent gram negative rods and anaerobes. Activity of pip/tazo against Pseudomonas (85%)

Table 1. Source of Infection in Complicated Intra-abdominal Infections

Source of Infection	Number of Patients (317)	Percentage (100%)
Post Laparotomy	79	25%
Pancreas	64	20%
Large Bowel and Appendix	69	22%
Biliary Ducts	59	19%
Liver	35	11%
Gastro-duodenal and Small Bowel	18	6 %

Table 2. Organisms involved in complicated intra-abdominal infections

Organisms Involved	Number of Patients (317)	Percentage (%)
Gram Negative Bacteria		
E. Coli	178	56%
KlebsiellaPneumoniae	48	15%
Pseudomonas	45	14%
Enterobacter	21	07%
Acinetobacter	15	05%
Proteus	16	05%
Other Gram Negatives	29	09%
Gram Positive Bacteria		
Enterococci	90	28%
Staph Aureous	23	07%
Streptococcus Milleri	17	05%
Other Streptococci	40	13%
Anaerobes		
Bacteroids	17	05%
Clostridium	1	0.3%
Fungal Infection		
Fungal Infection	32	13%
Candida Albicans	15	47%
Candida Non-Albicans	16	50%
Aspergillus	1	03%

Table 3. Percentage Sensitivity of Gram Negative Rods

Organisms	CTX	CTZ	CBP	PTZ	AKN	CIP	PMX
E. Coli	25.3	-	96.1	74.7	95.5	28.3	100
K. Pneumoniae	45.8	-	91.7	83.3	87.5	62.2	66.7
Pseudomonas	-	72.1	57.1	84.6	85.4	75.0	100
Acinetobacter	13.3	-	20.0	33.3	26.7	20.0	100

CTX: Ceftriaxone, CTZ: Ceftazidime, CBP: Carbapenems, PTZ: PiperacillinTazobactam, AKN: Amikacin, CIP: Ciprofloxacin, PMX: Polymyxin

was better than carbapenems (57%), while in community acquired complicated IAIs combination of Carbapenems with amikacin had better coverage.

Discussion

Knowledge of common organisms encountered in various clinical situations and their resistance profile is necessary prerequisite to select appropriate empirical antibiotics. Lack of this information on one hand can result in inadequate antimicrobial coverage and resulting unsuccessful outcomes.[10,11] While on the other hand, unnecessary broad antimicrobial coverage can result in antibiotics associated toxicities, acquisition of more resistant organisms and higher costs of treatment.[12] Extended spectrum beta lactamase (ESBL) producing enterobacteriaceae are becoming increasingly common in both community-acquired and hospital acquired infections worldwide.[13] Reports also show that resistant to fluoroquinolones has increased over time in both E. coli and K. Pneumoniae.[14] Our results also show increased prevalence of ESBL producing E. Coli and K. Pneumoniae but as compared to western data which reports prevalence to be 15-35% in E. Coli and 34 – 52% in K. Pneumoniae[5,14], it was 75% and 54% respectively in our study. Reported from India also showed comparable prevalence of ESBL producing E.Coli and K. Pneumoniae viz. 61 – 80% and 63 – 74% respectively.[15,16] This shows regional trends of high prevalence of ESBL producing organisms. This is the reason that cephalosporins as empirical antibiotics in complicated intra-abdominal infections have gone out of favor worldwide.[17]

There is evidence of recent and rapid spread of serine carbapenemases especially in Klebsiella Pneumoniae Carbapenemase (KPC) and it has become an important concern when administering antimicrobial therapy in hospitals worldwide.[14] Prevalence of carbapenem resistant K. Pneumoniae in western countries is 0.5-1%[14] which in our study population turned out to be 8%. Studies from India report it to be from 20-30%.[15,16] Thus though there is regional trend of high resistance of K Pneumoniae to carbapenems, our study population profile is still better than neighboring country. Irrational use of antibiotics could be the underlying cause of higher resistance profiles in resource constrained countries.

Antibiotic coverage against Enterococci in intra-abdominal infections is not routinely recommended. But in specific clinical conditions like critically ill patients and healthcare associated infections, coverage against Enterococci may be required. Antibiotic coverage against Enterococci infections pose challenge due to both intrinsic and acquired resistance to many antibiotics. Our study showed prevalence of Vancomycin Resistant Enterococci (VRE) to be 11% which is similar to those reported from Europe and India i.e. 10% and 12% respectively.[5,15] Our study showed fungal infection in up to 13% of patients which is almost double as compared to reported frequencies (7%) in complicated intra-abdominal infections.[18]

Literature guidelines for management of complicated intra-abdominal infection, including those from Surgical Infection Society (SIS) and the Infectious Diseases Society of America (IDSA)[19] and 2013 WSES guidelines[20] have made evidence based recommendations for empirical antimicrobial coverage in intra-abdominal infections. These guidelines recommend administration of either single agent (Carbapenems or Pip/Tazo) or combination of antibiotics (metronidazole with ciprofloxacin or co-amoxiclav) as empirical coverage in intra-abdominal infections. While analyzing these recommendations for our study population, we found inadequate coverage by Pip/Tazo alone. Though Carbapenems alone had adequate coverage for community acquired IAIs, combination of Amikacin with Carbapenems had even better coverage. For HA-IAIs pip/tazo in combination with amikacin can be 1st line empirical therapy in patients high risk for Pseudomonas infection. There is no recommendation of empirical antifungal therapy. In view of higher prevalence of fungal infections in our study population, further research is needed to evaluate need of empirical antifungal therapy in critically ill patients in our region. Fluconazole covers 98% of candidal species and can be used as empiric antifungal agent in critically ill patients.[21]

Conclusion

This study identifies higher resistance profile of microorganisms in complicated intra-abdominal infections in our country. These results can be employed for appropriate selection of empirical antibiotics in complicated IAIs. Presuming irrational use of antibiotics as the underlying factor for relatively higher prevalences, antibiotic stewardship program needs to be applied in hospitals.

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