Epidemiology of Microorganisms in intraabdominal infection/complicated intraabdominal infections in six centers of surgical care in Indonesia: A preliminary study

Yefta Moenadjat,1 Toar JM. Lalisang,1 Rofy S. Saunar,2 Nurhayat Usman,3 Adeodatus Y. Handaya,4 J. Iswanto,5 Safruddin Nasution,6 Anis Karuniawati,7 Tony Loho,8 Indah Suci Widyahening.9

1) Department of Surgery, Faculty of Medicine, Universitas Indonesia, dr Cipto Mangunkusumo General Hospital, Jakarta, 2) Fatmawati General Hospital, Jakarta, 3) Department of Surgery, Faculty of Medicine, Universitas Padjadjaran, dr Hasan Sadikin General Hospital, Bandung, 4) Department of Surgery, Faculty of Medicine, Universitas Gadjah Mada, dr Sardjito General Hospital, Yogyakarta, 5) Laboratory of Surgery, Faculty of Medicine, Universitas Airlangga, dr Sutomo Hospital, Surabaya, 6) Department of Surgery, Faculty of Medicine, Universitas Sumatera Utara, Adam Malik General Hospital, Medan, 7) Department of Microbiology, Faculty of Medicine, Universitas Indonesia, 8) Department of Clinical Pathology, Faculty of Medicine, Universitas Indonesia, dr Cipto Mangunkusumo General Hospital, Jakarta, 9) Department of Community Medicine, Faculty of Medicine, Universitas Indonesia

Abstract

Introduction. Data of complicated intraabdominal infections (cIAIs) and the epidemiology of causative microorganisms which is Indonesian characteristics is required to develop a guideline. Thus, a preliminary study run to find out such characteristics.

Method. Data of subjects with cIAIs managed in six centers of teaching hospital in Indonesia in period of 2015–2016 were collected. Those data of source of infection, the epidemiology of microorganism and susceptibility of antibiotics were descriptively provided.

Results. Source of infection were perforated appendicitis (26.64%), perforated gastric and duodenal ulcer (22.70%), small bowel perforation (11.84%), large bowel perforation (13.16%), postoperative (9.54%), and others (16.2%). Eschericia coli and Klebsiella pneumonia were the most microorganisms found in the pus specimen. The sensitivity of Escheria coli and Klebsiella pneumonia to cephalosporins were in range of 14.1–42% and 28.7–35.6%, respectively.

Conclusion. Perforated appendicitis, perforated gastric and duodenal ulcer, small bowel perforation, large bowel perforation, and postoperative in sequent are the main causal of cIAIs in Indonesia. The epidemiology predominated by Gram negative, particularly Eschericia coli and Klebsiella pneumonia (New Ropanasuri J Surg.2017;2(2):e149).

Keywords: cIAIs, source of infection, Eschericia coli, Klebsiella pneumonia

Introduction

Complicated intraabdominal infection, cIAIs, to date known as sepsis abdominal sepsis remains a serious problem to surgeons, intensivists, and other related disciplines worldwide. In Indonesia, this problem remains although there were improvement in all sectors such as universal precaution in accordance to Joint Commission International accreditation,1 sepsis management in accordance with the concept of surviving sepsis campaign,2,3 and rational use of antibiotic (antibiotic stewardship) in accordance with Gyssens.4,5

CIAIs emerged as a focus of surgeons worldwide since the entity revealed and
followed by the first clinical practice guidelines (CPGs) in 1992\(^\text{6,7}\) which were updated periodically until 2017; and we found two updates published recently.\(^\text{8,9}\) Problems were focused on this concept was high mortality rate,\(^\text{6}\) which is found in vary worldwide; in ranged of 3–42\(^\%\)\(^\text{10}\) and inseparable to sepsis syndrome. Though sepsis campaign were periodically updated\(^\text{11}\) and well implemented, the management of cIAIs is absolutely required as a strategy to decrease sepsis–related mortality. Thus, CPGs on cIAIs is the way to reduce mortality (and morbidity) in accordance to the highest evidence.

Although there were CPGs on cIAIs and were updated,\(^\text{3,12}\) Indonesian characteristics were different to population of where the CPGs developed; let updated CPGs were not feasible to Indonesian to be implemented. In other words, an Indonesian specific CPGs is required. Unfortunately, again, problems were encountered to develop an Indonesian guideline. Such problems were the characteristics found in well–developing countries, particularly in evidence based practice,\(^\text{13}\) i.e. 1) lack of local (regional) evidences generated by high-quality research (meta–analysis, systematic reviews), 2) implementation barrier to evidence based policy, 3) lack of human resources with the capability in knowledge translation, 4) conflict of interest in research, and 5) the fact that health–research often consider as the last component in the development of strategy process. In addition, the characteristic in the field of surgery. It was realized, that in evidence based medicine, (EBM) the highest evidence (level of evidence I, LOE 1) with recommendation A that develops a standard of procedure were only found based on meta–analysis and systematic review as well as randomized control trial studies, which is almost impossible to be found in surgery. Up to 2009 there were no study of LOE 1–2 in accordance with EBM since impossible to randomize subjects and surgical techniques due to ethical issues.\(^\text{14}\) Thus, guideline of the highest quality referred to evidence based surgery (EBS);\(^\text{15}\) which is clinical practice guidelines (CPGs) that in common dominated by studies of LOE 2–3 in the perspective of EBM.\(^\text{15}\)

Positively, a CPGs of Indonesian characteristic should be developed. But the first step is to find out the objective data regarding epidemiology of microorganisms found in cIAIs in Indonesia. In this perspective, a preliminary study was carried out.

Method

A descriptive study run enrolling data of the epidemiology of microorganisms found in cIAIs from six centers of surgical care in Indonesia: RS dr Cipto Mangunkusumo General Hospital, Jakarta (RSCM), RSUP Fatmawati, Jakarta (RSF), RSUP dr Hasan Sadikin, Bandung (RSHS), RSUP dr Sardjito, Yogyakarta (RSS), RSUP Adam Malik, Medan (RSAM), and RSUD dr Sutomo, Surabaya. Data taken from medical records includes those with diagnosis categorized as cIAIs in adults treated between 2015–2016.

Results

Collected data showed that source of infection in six centers were perforated appendicitis (26.64%), perforated gastric and duodenal ulcer (22.70%), small bowel perforation (11.84%), large bowel perforation (13.16%), postoperative (9.54%), and others (16.12%) as shown in figure 1. Such a grouping carried out based on the population of normal flora of a region. The pattern of microorganism grew in the media culture of pus taken from abdominal cavity intraoperatively was as follows. Data in dr Soetomo hospital showed that out of 114 subjects, bacteriology exams preceded on 65 subjects (57%) only for unknown reason, and data in dr Cipto Mangunkusumo showed that out of 74 isolates taken from
58 subjects (41.34%) there were no growth.\textsuperscript{16}

The 5 mostly found organisms in the culture was \textit{Eschericia coli} (35.41%), \textit{Klebsiella pneumonia} (13.44%), others (9.84%) \textit{Enterobacter cloaca} (9.34%), \textit{Proteus mirabilis} (8.69%). \textit{Enterococcus faecalis} (7.87%), \textit{Acinetobacter baumannii} (5.74%), \textit{Staphylococcus epidermidis} (3.44%), \textit{Pseudomonas aeruginosa} (3.44%), \textit{Staphylococcus haemolyticus} (1.31%), \textit{Klebsiella oxyca} (0.66%), and \textit{Staphylococcus aureus} (0.66%) were also reported (table 1).

Data obtained from RS Hasan Sadikin were not solely from pus, but in combination with sputum and blood samples. However, the data was reported in a published study of Asian population.\textsuperscript{17}

![Source of infection categorized in accordance to group of specific flora of a region.](image)

**Table 1. Organisms found in culture from pus taken from abdominal cavity**

|                     | Adam Malik | Fatmawati | Hasan Sadikin | RSCM | Sardjito | Surono | Total   |
|---------------------|------------|-----------|---------------|------|----------|--------|---------|
| \textit{Eschericia coli} | 40         | 33        | 30            | 46   | 17       | 50     | 216     (35.41%) |
| \textit{Klebsiella pneumonia} | 20         | 10        | 2             | 31   | 11       | 8      | 82      (13.44%)  |
| Others              | 10         | 3         | 3             | 8    | 30       | 6      | 60      (9.84%)   |
| \textit{Enterobacter cloaca} | 2          | 17        | 13            | 15   | 4        | 6      | 57      (9.34%)   |
| \textit{Proteus mirabilis} | NA        | 15        | 15            | 5    | NA       | 18     | 53      (8.69%)   |
| \textit{Enterococcus faecalis} | NA        | 16        | 5             | 19   | NA       | 8      | 48      (7.87%)   |
| \textit{Acinetobacter baumannii} | 18         | NA        | NA            | 0    | 17       | NA     | 35      (5.74%)   |
| \textit{Staphylococcus epidermidis} | NA        | 6         | 5             | 6    | NA       | 4      | 21      (3.44%)   |
| \textit{Pseudomonas aeruginosa} | 4          | NA        | NA            | 0    | 17       | NA     | 21      (3.44%)   |
| \textit{Staphylococcus haemolyticus} | 4          | NA        | NA            | 0    | 4        | NA     | 8       (1.31%)    |
| \textit{Klebsiella oxyca} | NA         | NA        | NA            | 4    | NA       | NA     | 4       (0.66%)    |
| \textit{Staphylococcus aureus} | NA         | NA        | NA            | 3    | NA       | NA     | 3       (0.49%)    |

Source: Secondary data from 6 centers.
Table 2 Bacterial susceptibility profile to non cephalosporin beta lactam antibiotics

| Organism                  | (n) | PEN (n) | PEN %S | AMP (n) | AMP %S | AMC (n) | AMC %S | TZP (n) | TZP %S | MEM (n) | MEM %S | IPM (n) | IPM %S | FOX (n) | FOX %S | OXA (n) | OXA %S | ATM (n) | ATM %S |
|---------------------------|-----|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|
| **Gram Positive**         |     |         |        |         |        |         |        |         |        |         |        |         |        |         |        |         |        |         |
| 1 Enterococcus faecalis   | 872 | 565     | 42.1   | 566     | 48.8   | 568     | 61.8   | 568     | 29.6   | 559     | 7      | 565     | 23     | 8       | 12.5   | 554     | 2      |
| 2 Staphylococcus epidermidis | 866 | 531     | 4      | 531     | 4      | 526     | 59.3   | 532     | 60.5   | 225     | 54.7   |         |        |         |        |         |        |
| **Gram Negative**         |     |         |        |         |        |         |        |         |        |         |        |         |        |         |        |         |        |
| 1 Klebsiella pneumonia    | 2619|         |        | 1843    | 37.8   | 1838    | 40.3   | 1843    | 66.8   | 1841    | 59.5   | 1838    | 37.1   |         |        |         |        |
| 2 Eschericia coli         | 1783|         |        | 1047    | 49.6   | 1046    | 65     | 1046    | 92.1   | 1045    | 81.9   | 1044    | 42.1   |         |        |         |        |
| 3 Acinetobacter baumannii| 1326|         |        | 912     | 10.1   | 912     | 25.3   | 911     | 31.1   | 909     | 27.5   | 908     | 5.9    |         |        |         |        |
| 4 Pseudomonas aeruginosa | 1141|         |        | 829     | 67.2   | 830     | 70.8   | 828     | 70.3   | 828     | 40.7   |         |        |         |        |         |        |
| 5 Enterobacter cloaca     | 408 |         |        | 277     | 8.7    | 277     | 58.5   | 276     | 83.3   | 277     | 35     | 276     | 53.6   |         |        |         |        |
| 6 Proteus mirabilis       | 228 |         |        | 156     | 57.7   | 156     | 80.8   | 155     | 71     | 156     | 26.9   | 156     | 78.2   |         |        |         |        |

PEN= Penicillin G, AMP= Ampicillin, AMC= Amoxicillin/Clavulanic acid, TZP= Piperacillin/Tazobactam, MEM= Meropenem, IPM= Imipenem, FOX= Cefoxitin, OXA= Oxacillin, ATM= Aztreonam

Source: Bacterial and Antibiotics Susceptibility Profile at Cipto Mangunkusumo Hospital July–December 2016 (reference no 16)
Table 3. Bacterial susceptibility profile to cephalosporin

| Organism                        | (n)  | CEP (n) | CEP %S | CFP (n) | CFP %S | CTX (n) | CTX %S | CAZ (n) | CAZ %S | CRO (n) | CRO %S | FEP (n) | FEP %S |
|---------------------------------|------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|
| **Gram Positive**               |      |         |        |         |        |         |        |         |        |         |        |         |        |
| 1. *Enterococcus faecalis*      | 872  | 568     | 10.2   | 557     | 6.3    | 553     | 3.4    | 559     | 2.7    | 568     | 4.4    | 217     | 4.6    |
| 2. *Staphylococcus epidermidis* | 866  | 532     | 57     |         |        |         |        |         |        |         |        | 232     | 46.1   |
| 3. *Staphylococcus haemolyticus*|      |         |        |         |        |         |        |         |        |         |        |         |        |
| **Gram Negative**               |      |         |        |         |        |         |        |         |        |         |        |         |        |
| 1. *Klebsiella pneumonia*       | 2619 | 1843    | 29.2   | 1842    | 31.9   | 1841    | 28.7   | 1843    | 35.6   | 1842    | 33.8   | 797     | 36     |
| 2. *Eschericia coli*            | 1783 | 1047    | 14.1   | 1047    | 30     | 1046    | 31     | 1047    | 42.8   | 1047    | 37.9   | 448     | 44.2   |
| 3. *Acinetobacter baumannii*    | 1326 | 912     | 0.8    | 912     | 7.8    | 911     | 5.3    | 912     | 29.7   | 912     | 5.3    | 382     | 30.9   |
| 4. *Pseudomonas aeruginosa*     | 1141 | 829     | 0      | 828     | 56.3   | 828     | 0.8    | 830     | 76.6   |         |        | 344     | 76.2   |
| 5. *Enterobacter cloaca*        | 408  | 276     | 5.1    | 277     | 50.2   | 277     | 37.9   | 279     | 52.2   | 277     | 45.8   | 118     | 64.4   |
| 6. *Proteus mirabilis*          | 228  | 156     | 50     | 156     | 51.3   | 156     | 48.7   | 156     | 69.9   | 156     | 63.5   | 72      | 69.4   |

CEP= Cephalothin, CFP= Cefoperazone, CTX= Cefotaxime, CAZ= Ceftazidime, CRG= Ceftriaxone, FEP= Cefepime

Source: Bacterial and Antibiotics Susceptibility Profile at Cipto Mangunkusumo Hospital July–December 2016 (reference no 16)
| Organism (n) | NAL (n) | NAL %S | PPA (n) | PPA %S | CIP (n) | CIP %S | LVX (n) | LVX %S | NEO (n) | NEO %S | GEN (n) | GEN %S | AMK (n) | AMK %S | KAN (n) | KAN %S |
|-------------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|
| **Gram Positive** |
| 1 Enterococcus faecalis | 872 | 320 | 2.5 | 320 | 0.6 | 568 | 4.8 | 205 | 36.1 | 53 | 1.9 | 565 | 12.2 | 549 | 3.6 | 456 | 2.9 |
| 2 Staphylococcus epidermidis | 866 | 78 | 5.1 | 77 | 3.9 | 528 | 33.9 | 224 | 41.5 | 20 | 75 | 3 | 33.3 | 2 | 50 | 1 | 0 |
| 3 Staphylococcus haemolyticus |
| **Gram Negative** |
| 1 Klebsiella pneumonia | 261 | 9 | 303 | 55 | 300 | 35.3 | 1838 | 41.3 | 725 | 56.7 | 216 | 68.5 | 1839 | 50.8 | 1839 | 73.1 | 1552 | 39.4 |
| 2 Eschericia coli | 178 | 3 | 627 | 33.3 | 621 | 34.1 | 1042 | 42.9 | 400 | 47.8 | 61 | 68.9 | 1047 | 72.2 | 1046 | 89.4 | 848 | 55.7 |
| 3 Acinetobacter baumannii | 132 | 6 | 86 | 23.3 | 84 | 11.9 | 907 | 29.9 | 386 | 29.8 | 24 | 45.8 | 912 | 30 | 909 | 32.6 | 772 | 23.3 |
| 4 Pseudomonas aeruginosa | 114 | 1 | 139 | 1.4 | 140 | 17.9 | 825 | 69.1 | 319 | 68 | 52 | 13.5 | 830 | 73.1 | 829 | 81.4 |
| 5 Enterobacter cloaca | 408 | 24 | 50 | 24 | 58.3 | 277 | 66.8 | 114 | 91.2 | 34 | 79.4 | 277 | 68.2 | 277 | 92.4 | 226 | 61.1 |
| 6 Proteus mirabilis | 228 | 46 | 52.2 | 46 | 60.9 | 156 | 64.1 | 68 | 76.5 | 36 | 75 | 156 | 64.7 | 156 | 95.5 | 140 | 54.3 |

NAL= Nalidixic acid, PPA= Pipemidic acid, CIP= Ciprofloxacin, LVX= Levofloxacin, NEO= Neomycin, GEN= Gentamicin, AMK= Amikacin, KAN= Kanamycin
Source: Bacterial and Antibiotics Susceptibility Profile at Cipto Mangunkusumo Hospital July–December 2016 (reference no 16)
| Organism                          | (n) | FOS (%) | FOS %S | VAN (%) | VAN %S | TEC (%) | TEC %S | TCY (%) | TCY %S | SXT (%) | SXT %S | CHL (%) | CHL %S | NIT (%) | NIT %S | LNZ (%) | LNZ %S | TGC (%) | TGC %S |
|----------------------------------|-----|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|--------|--------|--------|--------|--------|--------|--------|
| **Gram Positive**                |     |         |        |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 1 **Enterococcus faecalis**      | 872 | 320     | 76.2   | 554     | 48.2   | 552     | 77.9   | 19      | 567    | 34      | 562    | 48      | 322    | 54.3   | 4      | 50     |        |        |        |
| 2 **Staphilococcus epidermidis** | 866 | 76      | 75     | 529     | 0      | 522     | 91.8   | 62      | 532    | 43.2    | 532    | 58      | 77     | 79.2   | 528    | 99.8   |        |        |        |
| **Gram Negative**                |     |         |        |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 1 **Klebsiella pneumonia**       | 2619| 295     | 77.3   |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 2 **Eschericia coli**            | 1783| 615     | 86.8   |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 3 **Acinetobacter baumannii**    | 1326| 82      | 18.3   |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 4 **Pseudomonas aeruginosa**     | 1141| 137     | 38.7   |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 5 **Enterobacter cloacae**       | 408 | 24      | 83.3   |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |
| 6 **Proteus mirabilis**          | 228 | 45      | 60     |         |        |         |        |         |        |         |        |         |        |        |        |        |        |        |        |

FOS = Fosfomycin, VAN = Vancomycin, TEC = Teicoplanin, TCY = Tetracycline, SXT = Trimethoprim-sulfamethoxazole, CHL = Chloramphenicol, NIT = Nitrofurantoin, LNZ = Linezolid, TGC = Tigecycline.

Source: Bacterial and Antibiotics Susceptibility Profile at Cipto Mangunkusumo Hospital July–December 2016 (reference no 16)
Discussion

A study was found as the first multicenter one carried out in the region, addressed to find out the data showing that the most source of intraabdominal infection was perforated appendicitis, perforated gastric and duodenal ulcers, and intestinal perforation. In the study, the data collected through the selection of the diagnosis met the criteria of cIAIs, which is not on the list of international classification of diseases (ICD) ver.10. This finding showed similarity to those reported in developing countries, particularly in South East Asia.

The microorganisms found as the pattern in the epidemiology predominated by *Eschericia coli* and *Klebsiella pneumonia*. *Eschericia coli* which microorganism in the ecosystem of gastrointestinal tract particularly ileum; a little bit higher than reported by Garcia-Sanchez, et al in 2013 but lower than reported by de Ruiter et al in 2009. As perforated appendicitis is the major finding in cIAIs, it might be explaining why *Eschericia coli* is the microorganism found. However, this commensal microorganism reveals different manifestation as it comprising three main sub-sets, namely commensal strains innocuously colonize the colon of healthy hosts, causing extraintestinal disease when a large inoculum and/or significant host compromise found such as in cIAIs, diarrhoeagenic strains, and extraintestinal pathogenic *Eschericia coli* (ExPEC), often innocuously colonize the human gut which have a unique ability to enter and survive within normally sterile extraintestinal body sites, and to cause disease when they do so. However, to this knowledge, it is now reported that ExPEC strains are the main cause of human extraintestinal *Eschericia coli* infections. It might be the answer of why *Eschericia coli* were found in sputum of those with pneumonia in cIAIs (data is excluded in the analysis).

*Klebsiella* known as the second microorganism frequently found to be responsible in cIAIs and somehow, together with *Eschericia coli* found to be related to community acquired intraabdominal infections.

Antibiotic susceptibility is a matter of a worldwide concern regarding these microorganisms as the etiology of cIAIs. In the study, though the accurate data available from RSCM and Sardjito only. In RSCM, the sensitivity of *Eschericia coli* to cephalosporins were in range of 14.1–42%, whereas for non-cephalosporin was found in vary (Amoxicillin/Clavulanic acid 49.5%, Piperacillin/Tazobactam 40.3%; while as Meropenem and Imipenem were 92.1% and 81.9%, respectively). Sensitivity to quinolones and aminoglycosides were under 50%, except for Neomycin (68.9%), Gentamycin (72.2%) and Amikacin (89%). For other antibiotics, it showed the sensitivity to Fosfomycin (86.8%) and Tigecycline (90.5%). Data from Sardjito showed that sensitivity to Cefoperazone+Sulbactam (94.1%), Meropenem (100%), and Tigecycline (100%), while as others found less than 50%.

In RSCM *Klebsiella pneumonia* showed the sensitivity cephalosporins were in range of 28.7–35.6%, whereas for non-cephalosporin was found in vary (Amoxicillin/Clavulanic acid 37.8%, Piperacillin/Tazobactam 40.3%; while as Meropenem and Imipenem were 66.8% and 59.5%, respectively). Sensitivity to quinolones and aminoglycosides were under 50%, except for Neomycin (68.5%), and Amikacin (73.1%). For other antibiotics, it showed the sensitivity to Tigecycline (77.3%) and Tigecycline (48.4%). Data from Sardjito showed that sensitivity to Cefoperazone+Sulbactam (85.7%), Meropenem (89.5%), and Tigecycline (98.4%), while as others found less than 50%.

In the study, it found that the etiology of cIAIs predominated by microorganisms of Gram negative, particularly *Eschericia coli* and *Klebsiella pneumonia* replacing *Pseudomonas aeruginosa* that
predominate for last decades. Other microorganisms of Gram negative and Gram positive is of the minor. This finding, however showed epidemiology of the most frequent microorganisms found as the etiology of cIAIs in the region and somehow representing the Indonesian characteristics. It was the strength of a study. Otherwise, inadequacy of data, which is incomplete information of the clinical setting such as peritonitis, anaerobic organisms and fungus was not the big issues in clinical setting referred to the limitation of a study. The other limitation realized in this retrospective study was that samples were obtained from pus, but not from the tissues; and inability to find out the information regarding hospital/community acquired kind of infection accurately.

Conclusion

Perforated appendicitis, perforated gastric and duodenal ulcer, small bowel perforation, large bowel perforation, and postoperative in sequent are the main causal of cIAIs in Indonesia. The epidemiology predominated by Gram negative, particularly Eschericia coli and Klebsiella pneumonia.

Acknowledgment

A great appreciation to those assists the data collection.

Disclosure

Authors disclosed no conflict of interests

Reference

1. Joint Commission International. Joint Commission International Accreditation Standards for Hospitals [Internet]. 5th ed. Joint Commission International Accreditation Standards for Hospitals. Joint Commission International; 2013. 72 p. Available from: http://www.jointcommissioninternational.org/assets/3/7/Hospital-5E-Standards-Only-Mar2014.pdf
2. Lalisanj TJM. Klinik Praktis Pengendalian Sumber Infeksi pada Tatalaksana Sepsis. Lalisanj TJ, editor. Jakarta: Sagung Seto; 2015.
3. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165–228.
4. Gyssens IC. Antibiotic policy. Int J Antimicrob Agents [Internet]. 2011;38(SUPPL.):11–20. Available from: http://dx.doi.org/10.1016/j.ijantimicag.2011.09.002
5. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Heal Pharm. 2013;70(3):195–283.
6. Bohnen J, Solomkin J, Dellinger P, Bjornson S, Page C. Guidelines for Clinical Care: Anti-infective Intra-abdominal Infection Agents for Intra-abdominal Infection. Arch Surg. 1992;127:83–9.
7. Solomkin JS, Hemsell DL, Sweet R, Tally F, Bartlett J. Evaluation of new anti-infective drugs for the treatment of intraabdominal infections. Infectious Diseases Society of America and the Food and Drug Administration. Clin Infect Dis. 1992;15 Suppl 1:S33-42. Pubmed 1477248.
8. Mazuski JE, Tessier JM, May AK, Sawyer RG, Nadler EP, Rosengart MR, et al. The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection. Surg Infect (Larchmt). 2017;18(1):1–76. doi.10.1089/sur.2016.261
9. Sartelli M, Catena F, Abu-Zidan FM, Ansaloni L, Biffi WL, Boermeester MA, et al. Management of intra-abdominal infections: recommendations by the WSES 2016 consensus conference. World J Emerg Surg. 2017;1–31.
10. Sartelli M, Catena F, Ansaloni L, Moore E, Malangoni M, Velmahos G, et al. Complicated intra-abdominal infections in a worldwide context: an observational prospective study (CIAOW Study). World J Emerg Surg. 2013;8(1):1.
11. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017;43:304-77.

12. Mazuski JE, Sawyer RG, Nathens AB, DiPiro JT, Schein M, Kudsk KA, et al. The Surgical Infection Society Guidelines on Antimicrobial Therapy for Intra-Abdominal Infections: An Executive Summary. Surg Infect (Larchmt). 2002;3(3):161–73. doi.10.1089/109629602761624171

13. Research TCC for GH. Knowledge Translation in Low and Middle Income Countries. Canadian Coalition for Global Health Research; 2010.

14. McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC, et al. No surgical innovation without evaluation: the IDEAL recommendations. Lancet. 2009;373(9695):1105–12. doi.10.1016/S0140-6736(09)61116-8

15. Shearman AD, Shearman CP. How to practise evidence-based surgery. Surg (United Kingdom). 2012;30(9):481–5.

16. Loho T, Astrawinata DAW. Bacterial and Antibiotics Susceptibility Profile at Cipto Mangunkusumo Hospital July–December 2016. Department of Clinical Pathology Cipto Mangunkusumo General Hospital, Jakarta; 2016. 1-272 p.

17. Kurup A, Liu K-H, Ren J, Lu M-C, Navarro NS, Farooka MW, et al. Antibiotic management of complicated intra-abdominal infections in adults: The Asian perspective. Ann Med Surg. 2014;3(3):85–91.

18. De Ruiter J, Weel J, Manusama E, Kingma WP, Van Der Voort PHJ. The epidemiology of intra-abdominal flora in critically Ill patients with secondary and tertiary abdominal sepsis. Infection. 2009;37(6):522–7.

19. Boueil A, Guégan H, Colot J, D’Ortenzio E, Guerrier G. Peritoneal fluid culture and antibiotic treatment in patients with perforated appendicitis in a Pacific Island. Asian J Surg. 2015;38(4):242–6.

20. van der Plas H. Microbiological evaluation and antimicrobial treatment of complicated intra-abdominal infections. South Afr J Epidemiol Infect. 2012;27(2):53–7.

21. Guirao X, García MS, Bassetti M, Bodmann KF, Dupont H, Montravers P, et al. Safety and tolerability of tigecycline for the treatment of complicated skin and soft-tissue and intra-abdominal infections: An analysis based on five European observational studies. J Antimicrob Chemother. 2013;68(SUPPL.2):37–44.

22. García-Sánchez JE, García-García MI, García-Garrote F, Sánchez-Romero e I. Diagnóstico microbiológico de las infecciones gastrointestinales. Enferm Infecce Microbiol Clin. 2013;31(4):230–9.

23. Johnson JR, Russo TA. Extraintestinal pathogenic Escherichia coli: “The other bad E coli.” J Lab Clin Med. 2002;139(3):155–62.

24. Vila J, Sáez-López E, Johnson JR, Römling U, Dobrindt U, Cantón R, et al. Escherichia coli: An old friend with new tidings. FEMS Microbiol Rev. 2016;40(4):437–63.

25. Riley LW. Pandemic lineages of extraintestinal pathogenic Escherichia coli. Clin Microbiol Infect. 2014;20(5):380–90. doi.10.1111/1469-0691.12646

26. Köhler CD, Dobrindt U. What defines extraintestinal pathogenic Escherichia coli? Int J Med Microbiol. 2011;301(8):642–7.

27. Debray TPA, Damen JAAG, Snell KIE, Ensor J, Hooft L, Reitsma JB, et al. A guide to systematic review and meta-analysis of prediction model performance. BMJ. 2017;6460.

28. Montravers P, Dufour G, Guglielminiotti J, Desmad M, Muller C, Houissa H, et al. Dynamic changes of microbial flora and therapeutic consequences in persistent peritonitis. 2015;1–13.

29. Montravers P, Lepape A, Dubreuil L, Gauzit R, Pean Y, Benchimol D, et al. Clinical and microbiological profiles of community-acquired and nosocomial intra-abdominal infections: Results of the French prospective, observational EBIIA study. J Antimicrob Chemother. 2009;63(4):785–94.