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

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Abstract

Introduction. Data of complicated intraabdominal infections (cIAI) 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 cIAI 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%). *Escherichia coli* and *Klebsiella pneumonia* were the most microorganisms found in the pus specimen. The sensitivity of *Escherichia 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 cIAI in Indonesia. The epidemiology predominated by Gram negative, particularly *Escherichia coli* and *Klebsiella pneumonia*.

Keywords: *cIAI, source of infection, Escherichia coli, Klebsiella pneumonia*

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Introduction

Complicated intraabdominal infection, cIAI, 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}

cIAI emerged as a focus of surgeons worldwide since the entity revealed and followed by the first clinical practice guidelines (CPGs) in 1992,⁷ which were updated periodically until 2017; and we found two updates published recently.^{8,9} Problems were focused on this concept was high mortality rate,⁶ which is found in vary worldwide; in ranged of 3–42%¹⁰ and inseparable to sepsis syndrome. Though sepsis campaign were periodically updated¹¹ and well implemented, the management of cIAI is absolutely required as a strategy to decrease sepsis-related mortality. Thus, CPGs on cIAI is the way to reduce mortality (and morbidity) in accordance to the highest evidence.

Although there were CPGs on cIAI and were updated,^{8,12} 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,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.¹⁴ Thus, guideline of the highest quality referred to evidence based surgery (EBS);¹⁵ which is clinical practice guidelines (CPGs) that in common dominated by studies of LOE 2–3 in the perspective of EBM.¹⁵

Positively, a CPG of Indonesian characteristic should be developed. But the first step is to find out the objective data regarding

epidemiology of microorganisms found in cIAI 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 cIAI from six centers of surgical care in Indonesia: RS dr. Cipto Mangunkusumo General Hospital, Jakarta (RSCM), RSUP Fatmawati General Hospital, Jakarta (RSF), dr. Hasan Sadikin General Hospital, Bandung (RSHS), dr. Sardjito General Hospital, Yogyakarta (RSS), Adam Malik General Hospital, Medan (RSAM), and RSUD dr. Sutomo, Surabaya. Data taken from

medical records includes those with diagnosis categorized as cIAI 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.

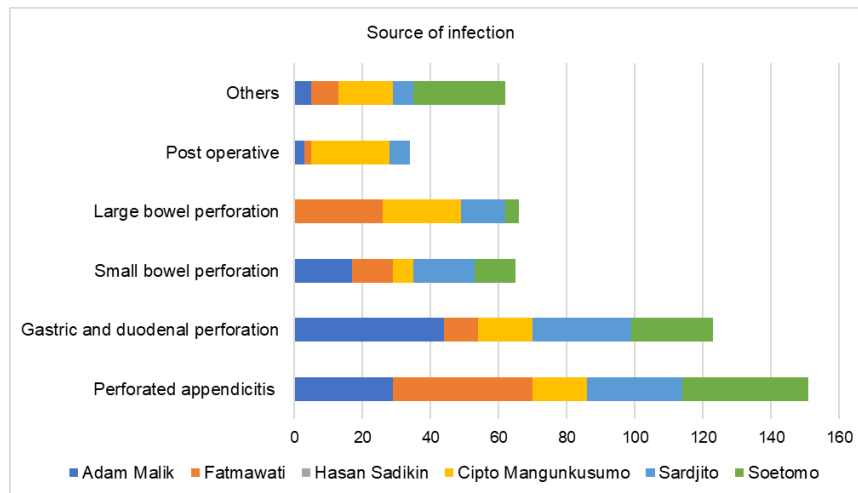


Figure 1. Source of infection categorized in accordance to group of specific flora of a region.

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

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

Source: Secondary data from 6 centers.

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.¹⁶

The five mostly found organisms in the culture was *Escherichia coli* (35.41%), *Klebsiella pneumonia* (13.44%), others (9.84%) *Enterobacter cloaca* (9.34%), *Proteus mirabilis* (8.69%), *Enterococcus faecalis* (7.87%), *Acinetobacter baumannii* (5.74%), *Staphylococcus epidermidis* (3.44%), *Pseudomonas aeruginosa* (3.44%), *Staphylococcus haemolyticus* (1.31%), *Klebsiella oxycata*

(0.66%), and *Staphylococcus aureus* (0.66%) were also reported (table 1).

Data obtained from Hasan Sadikin General Hospital 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.¹⁷

Data of bacterial susceptibility to antibiotic were obtained from three centers, i.e. RSCM, Soetomo and Sardjito, and were found not different; whereas data from other four were insufficient and unable to be analyzed further. In the collection, the focused were on the most organisms found from pus specimen of intraabdominal (see table 2 to 5).

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	<i>Enterococcus faecalis</i>	872	565	42.1	566	48.8	568	61.8	568	29.6	559	7	565	23	8	12.5	554	2	
2	<i>Staphylococcus epidermidis</i>	866	531	4	531	4	526	59.3						532	60.5	225	54.7		
3	<i>Staphylococcus haemolyticus</i>																		
Gram Negative																			
1	<i>Klebsiella pneumonia</i>	2619				1843	37.8	1838	40.3	1843	66.8	1841	59.5					1838	37.1
2	<i>Escherichia coli</i>	1783				1047	49.6	1046	65	1046	92.1	1045	81.9					1044	42.1
3	<i>Acinetobacter baumannii</i>	1326				912	10.1	912	25.3	911	31.1	909	27.5					908	5.9
4	<i>Pseudomonas aeruginosa</i>	1141						829	67.2	830	70.8	828	70.3					828	40.7
5	<i>Enterobacter cloaca</i>	408				277	8.7	277	58.5	276	83.3	277	35					276	53.6
6	<i>Proteus mirabilis</i>	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 <i>Enterococcus faecalis</i>	872	568	10.2	557	6.3	553	3.4	559	2.7	568	4.4	217	4.6
2 <i>Staphylococcus epidermidis</i>	866	532	57									232	46.1
3 <i>Staphylococcus haemolyticus</i>													
Gram Negative													
1 <i>Klebsiella pneumonia</i>	2619	1843	29.2	1842	31.9	1841	28.7	1843	35.6	1842	33.8	797	36
2 <i>Escherichia coli</i>	1783	1047	14.1	1047	30	1046	31	1047	42.8	1047	37.9	448	44.2
3 <i>Acinetobacter baumannii</i>	1326	912	0.8	912	7.8	911	5.3	912	29.7	912	5.3	382	30.9
4 <i>Pseudomonas aeruginosa</i>	1141	829	0	828	56.3	828	0.8	830	76.6			344	76.2
5 <i>Enterobacter cloaca</i>	408	276	5.1	277	50.2	277	37.9	276	52.2	277	45.8	118	64.4
6 <i>Proteus mirabilis</i>	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)

Table 4 Bacterial susceptibility profile to quinolones and aminoglycosides

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	
<i>Gram Positive</i>																		
1	<i>Enterococcus faecalis</i>	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	<i>Staphylococcus epidermidis</i>	866	78	5.1	77	3.9	528	33.9	224	41.5	20	75	3	33.3	2	50	1	0
3	<i>Staphylococcus haemolyticus</i>																	
<i>Gram Negative</i>																		
1	<i>Klebsiella pneumonia</i>	2619	303	35	300	35.3	1838	41.3	725	56.7	216	68.5	1839	50.8	1839	73.1	1552	39.4
2	<i>Escherichia coli</i>	1783	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	<i>Acinetobacter baumannii</i>	1326	86	23.3	84	11.9	907	29.9	386	29.8	24	45.8	912	30	909	32.6	772	23.3
4	<i>Pseudomonas aeruginosa</i>	1141	139	1.4	140	17.9	825	69.1	319	68	52	13.5	830	73.1	829	81.4		
5	<i>Enterobacter cloaca</i>	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	<i>Proteus mirabilis</i>	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)

Table 5 Bacterial susceptibility profile to other antibiotics

Organism	(n)	FOS (n)	FOS %S	VAN (n)	VAN %S	TEC (n)	TEC %S	TCY (n)	TCY %S	SXT (n)	SXT %S	CHL (n)	CHL %S	NIT (n)	NIT %S	LNZ (n)	LNZ %S	TGC (n)	TGC %S
Gram Positive																			
1	<i>Enterococcus faecalis</i>	872	320	76.2	554	48.2	552	77.9		19	567	34	562	48	322	54.3	4	50	
2	<i>Staphylococcus epidermidis</i>	866	76	75	529	0	522	91.8		62	532	43.2	532	58	77	79.2	528	99.8	
3	<i>Staphylococcus haemolyticus</i>																		
Gram Negative																			
1	<i>Klebsiella pneumonia</i>	2619	295	77.3				1788	42.1	1842	49.1	1842	54.2	304	32.2			1837	48.4
2	<i>Escherichia coli</i>	1783	615	86.8				1022	32.7	1047	37.9	1047	64.4	627	80.2			1043	90.5
3	<i>Acinetobacter baumannii</i>	1326	82	18.3				894	29	912	36.5	912	5.3	86	5.8			912	32.8
4	<i>Pseudomonas aeruginosa</i>	1141	137	38.7										139	0.7				
5	<i>Enterobacter cloaca</i>	408	24	83.3				271	52.8	276	60.9	277	62.8	24	45.8			276	70.7
6	<i>Proteus mirabilis</i>	228	45	60				152	16.4	156	42.3	156	28.8	46	6.5			156	64.1

FOS= Fosfomicin, 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 cIAI, which is not on the list of international classification of diseases (ICD) ver.10. This finding showed similarity to those reported in developing countries,^{18,19} particularly in South East Asia.

The microorganisms found as the pattern in the epidemiology predominated by *Escherichia coli* and *Klebsiella pneumoniae*. *Escherichia coli* which microorganism in the ecosystem of gastrointestinal tract particularly ileum,²⁰ a little bit higher than reported by Garcia-Sanchez, et al in 2013^{21,22} but lower than reported by de Ruiter et al in 2009¹⁸ As perforated appendicitis is the major finding in cIAI, it might be explaining why *Escherichia coli* is the microorganism found. However, this commensal microorganism reveals different manifestation as it comprising three main subsets,^{23,24} 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 cIAI, diarrhoeagenic strains, and extraintestinal pathogenic *Escherichia coli* (ExPEC)²⁵⁻²⁷ 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 *Escherichia coli* infections.^{24,27} It might be the answer of why *Escherichia coli* were found in sputum of those with pneumonia in cIAI (data is excluded in the analysis).

Klebsiella known as the second microorganism frequently found to be responsible in cIAI^{17,20,28} and somehow, together with *Escherichia coli* found to be related to community acquired intraabdominal infections.²⁹

Antibiotic susceptibility is a matter of a worldwide concern regarding these microorganisms as the etiology of cIAI. In the study, though the accurate data available from RSCM and Sardjito only. In RSCM, the sensitivity of *Escherichia 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%), Amikacin (89.5%), Chloramphenicol (89.5%) and Tigecycline (100%), while as others found less than 50%.

In RSCM *Klebsiella pneumoniae* 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 Fosfomycin (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 cIAI predominated by microorganisms of Gram negative, particularly *Escherichia coli* and *Klebsiella pneumoniae* 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 cIAI 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

Product of ischemic reperfusion injury in the lower extremities approached and leading to damage in gastric mucosa. The antrum injured severely than the corpus. Ischemia preconditioning has a protective effect on the destructive effects produced by ischemic reperfusion injury of lower extremities to the gastric mucosa. Hypothermia also has a protective effect on the destructive effects produced by ischemic reperfusion injury of lower extremities to the gastric mucosa, but not as good as ischemia preconditioning.

Disclosure

This study has no conflict of interest.

Acknowledgment

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

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