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# Multidrug resistance organisms (MDRO) infection and multidimensional approaches as predictors of mortality in complicated intra-abdominal infection

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## ABSTRACT

Complicated intra-abdominal infection (cIAI) is a frequently encountered emergency surgery case with a high mortality rate. While the mortality scoring system in cIAI has been widely adopted, its accuracy has not been fully optimized, yet. The study aimed to analyze the prognostic value of APACHE II, MPI, CCI, MODS, and MDRO infections in the mortality of patients with cIAI. A prospective cohort observational study was conducted on cIAI patients who underwent laparotomy procedures in November 2023 to July 2024 at Dr. Sardjito Hospital, Yogyakarta. Microbiological examinations in the form of identification and antibiotic sensitivity tests were carried out on intra-abdominal specimens using Vitek II. Information on demographic characteristics, clinical presentation, laboratory characteristics, and mortality outcomes was collected by following patients for 30 d of post-laparotomy care until the patient died or was discharged from the hospital. Statistical analysis was carried out using a t test, X2, and ROC curve, determining the cut-off point of the score, sensitivity, specificity, PPV, NPV, and accuracy of each prognostic variable. Out of the 91 cIAI patients who underwent laparotomy, mortality was observed in 28.6% of them. MDRO infection was identified in 52.7% of the subjects. Significant factors affecting mortality were APACHE II scores (p=0.00), MPI scores (p=0.00), MODS scores (p=0.00), and MDRO infection (p=0.03). The prognostic performance of mortality based on the AUC, sensitivity, and specificity scores were as follows: APACHE II (AUC=0.938; sensitivity=88.5%; specificity=86.2%), MPI (AUC=0.920; sensitivity=92.3%; specificity=81.5%), MODS (AUC=0.916; sensitivity=76.9%; specificity=93.8%), CCI (AUC= 0.582; sensitivity=61.5%; specificity=56.9%), and MDRO infection (AUC= 0.623; sensitivity=61.5%; specificity=63.1%). In conclusion, the APACHE II, MPI, MODS scores showed strong performance in predicting the mortality of cIAI patients. MDRO infection is significant determinant for mortality but has weak diagnostic value. Developing new algorithms that consider comprehensive factors including agents, hosts, and environments will enhance the accuracy of assessing mortality in these patients.

## ABSTRAK

Infeksi intra-abdominal komplikata (IIK) merupakan salah satu kasus bedah emergency terbanyak dengan mortalitas yang tinggi. Sistem klasifikasi/skoring mortalitas pada IIK telah banyak digunakan namun nilai akurasinya belum maksimal. Penelitian ini bertujuan menganalisis nilai prognostik skor APACHE II, MPI, CCI, MODS, dan infeksi MDRO pada mortalitas pasien IIK. Penelitian dengan desain observasional kohort prospektif dilakukan pada pasien IIK yang menjalani tindakan laparatomi pada bulan November 2023 sampai Juli 2024 di RSUP Dr. Sardjito Yogyakarta. Pemeriksaan mikrobiologi berupa identifikasi dan uji kepekaan antibiotik dilakukan pada spesimen intra-abdominal menggunakan Vitek II. Informasi mengenai karakteristik demografis, presentasi klinis, karakteristik laboratorik, dan mortalitas dikumpulkan dengan mengamati pasien selama 30 hari perawatan paska laparatomi sampai dengan pasien meninggal atau pulang atau keluar rumah sakit. Analisis statistik dilakukan dengan menggunakan uji t, X2, kurva ROC, menentukan titik potong skor, menentukan nilai sensitivitas, spesifisitas, PPV, NPV, dan akurasi dari masing-masing variabel

***Keywords***:
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prognostic score;
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MPI

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prognostik. Dari 91 pasien IIK dengan laparatomi yang dilibatkan dalam penelitian, mortalitas terjadi 28,6% subyek. Infeksi MDRO terjadi pada 52,7% subyek. Skor APACHE II (p=0,00), MPI (p=0,00), MODS (p=0,00), dan infeksi MDRO (p=0,03) berpengaruh secara signifikan terhadap mortalitas. Nilai prognostik mortalitas (AUC, sensitivitas, spesifisitas) skor APACHE 3II (AUC=0,938; sensitivitas=88,5%; spesifitas=86,2%), MPI (AUC=0,920; sensitivitas=92,3%; spesivitas=81,5%), MODS (AUC=0,916; sensitivitas=76,9%; spesifitas=93,8%), CCI (AUC=0,582; sensitivitas=61;5%; spesivitas=56,9%), dan infeksi MDRO (AUC=0,623; sensitivitas=61,5%; spesifitas=63,1%). Skor APACHE II, MPI, MODS, memiliki performa yang baik dalam menentukan mortalitas pada pasien IIK. Simpulan, infeksi MDRO merupakan determinan yang signifikan terhadap mortalitas namun memiliki nilai diagnostik yang rendah. Algoritma baru yang melibatkan faktor holistik agen, host, dan lingkungan perlu dibuat untuk menilai mortalitas pasien IIK dengan lebih akurat.

## INTRODUCTION

Complicated intra-abdominal infection (cIAI) is a life-threatening infection and is considered one of the most urgent surgical emergency conditions.[1,2] The mortality rate of cIAI can reach up to 50% in developing countries.[3] The high mortality rate among cIAI patients highlights the importance of identifying predictive factors that impact the severity and survival of patients[2] This is crucial for informing preventive measures and ensuring appropriate patient management so it can enhance patient outcomes and ensure the delivery of safe, effective, high-quality healthcare services, and control the cost burden.[4]

The triad concept in infectious epidemiology explains how the roles of agents, hosts, and environments are interconnected and contribute to the occurrence of infectious diseases.[5] Any changes within these factors can impact the frequency, severity, and fatality rates of infectious diseases.[5] Numerous algorithms have been developed to classify disease severity, provide treatment guidance, and forecast clinical outcomes or mortality rates in patients.[6-9] While some algorithms have displayed reliable predictive abilities for mortality in cIAI patients, the findings have not been uniform, yet.[10] The prevalent classification and scoring systems typically do not consider the infectious agent as a variable in their evaluations.[11.]

In general, the scoring system comprises two types: scores that do not depend on the type of disease and are commonly used for evaluating seriously ill patients requiring intensive care unit (ICU) treatment, such as the acute physiology and chronic health evaluation II (APACHE II), and specific scores like the Mannheim peritonitis index (MPI).[7.] The APACHE II score has proven to be a reliable predictor of mortality but does not account for evaluating interventions. Interventions often greatly impact various physiological variables.[12] The MPI is tailored for peritonitis cases, straightforward to calculate, and can be determined during surgical procedures.[6] Furthermore, there are other scoring systems positing that intrinsic factors play a more significant role as predictors of mortality compared to the source and type of infection. These alternative scoring systems include the Charlson comorbidity index (CCI) for assessing comorbid diseases and the multiple organ dysfunction score (MODS) to evaluate organ failure presence.[9,13-14] Several studies have been conducted to determine the effectiveness of various scoring systems in predicting death from cIAI in the European population. However, the results have not been consistent due to the different advantages and disadvantages of each scoring system.[1] Other commonly used scores include CPIRO (Calgary predisposition infection response and organ dysfunction), WSESSSS (world society of emergency surgery sepsis severity score), and SOFA (sequential organ failure assessment).[15]

Several previous studies have shown the specific role of pathogens as an independent variable that increases the mortality of patients with cIAI.[16.] Infections by multidrug resistance organisms (MDRO) have been identified associated with worse outcomes and increased mortality.[16,17] An increased prevalence of MDRO has been reported as a cause of cIAI.[18] In general, about 60% of infections are caused by Gram-negative bacteria, and less than 5% are caused by fungi[10,19] It is related to the pathogenesis mechanism of cIAI, which mainly involves the translocation of intestinal bacteria[19] The most common causative agent is *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Enterococcus faecalis*, and *E. faecium*.[10]

The high mortality rate, varied diagnostic value, and limitations of existing prognostic scores provide the foundation for identifying factors that significantly impact the mortality of patients with cIAI[1] This study aims to discover new predictors that are straightforward, easy to conduct, and highly accurate in predicting mortality outcomes in the treatment of cIAI patients. The factors under scrutiny are a combination of elements within the infection triangle of agents, hosts, and environments.[5] Given the aforementioned context, investigating a combination of intrinsic factors included in established prognostic scores (APACHE II, MPI, CCI, MODS) and the role of MDRO is crucial as a mortality prognostic factor that aligns more with the characteristics and conditions in Indonesia, especially at Dr. Sardjito General Hospital, Yogyakarta a national referral health facility that can represent the patient population in Indonesia[10,14]

## MATERIAL AND METHODS

### Design and subject

It was a prospective cohort study conducted at Dr. Sardjito General Hospital, Yogyakarta from November 2023 to July 2024. The study focused on patients with cIAI who underwent exploratory laparotomy at the hospital. The inclusion criteria included patients who were ≥18 y.o., had complete medical records, underwent culture examination and antibiotic susceptibility tests on intra-abdominal specimens, and provided informed consent before any study-related assessment is performed. Patients with primary peritonitis, traumatic perforated peritonitis, and those who dropped out at the time of surgery were excluded from the study.

### Procedure

Patients meeting the inclusion and exclusion criteria underwent laparotomy surgery to collect intra-abdominal specimens. Subsequently, antibiotic susceptibility tests were conducted on the intra-abdominal specimens using the VITEK II automatic machine. MDRO are characterized by resistance to one or more agents from at least three antimicrobial categories.[21]

Complicated intra-abdominal infection is an infection that affects intraperitoneal organs and may spread beyond a single organ, leading to either localized or diffuse peritonitis. A clinical diagnosis can be established by evaluating signs and symptoms of peritonitis, as well as through laboratory and radiological assessments, which are further confirmed through direct observation by the doctor during laparotomy. A definitive diagnosis is achieved through positive microbiological examination.[1,4]

Patients will be monitored for 30 d following cIAI-related laparotomy. A patient is classified as “mortality” if they pass away during treatment following a laparotomy. Patients falling under the “alive” category have completed the 30-d treatment period, been discharged from the hospital with improved health, or recovered and have ongoing monitoring through outpatient clinic visits or telephone follow-ups for up to 30 d.

Demographic variables, sources of cIAI, comorbidities, clinical characteristics, laboratory results, culture findings, and antibiotic susceptibility tests of cIAI patients were gathered during hospitalization, up to 30 d post-laparotomy. The APACHE II,[12] MPI,[6] CCI,[14] and 90-day all-cause mortality. 358 patients were analyzed. a-CCI score for each patient was calculated and then divided in two comorbid categories whether they were ≤ or > to percentile 75 (=4 and MODS[17] scores were calculated following the respective guidelines.

### Statistical analysis

Bivariate analysis was conducted to compare all independent variables with mortality. Significance is established if the p value is < 0.05. The cutoff value for each score and MDRO infection status as a predictor of mortality was determined by constructing an ROC curve using the Youden index. The prognostic value of each score alone and in conjunction with MDRO infection status was analyzed by creating a 2x2 TABLE. The TABLE was then manually processed to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy.

The research was approved by the Medical and Health Research Ethics Committee of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia (ref. no. KE/FK/2044/EC/2023).

## RESULTS

### Demographic characteristics of subjects

Ninety-one subjects diagnosed with cIAI participated in this study. The average age of the participants was 51.79 ± 17.09 y.o., with 53 (58.2%) males and 48 (41.8%) females. Among them, 26 subjects passed away, resulting in a mortality rate of 28.6%. TABLE 1 illustrates the demographic characteristics of the study cohort. The length of stay in the ICU emerged as a prognostic indicator for mortality among cIAI patients. The study identified appendix perforation (16%), ileal perforation (16%), and gastric perforation (11%) as the most prevalent cIAI etiologies. The highest mortalities were associated with ileum perforation (27%), gastric perforation (26%), and jejunal perforation (19%). The source of cIAI is depicted in FIGURE 1.

The history of comorbidities suffered by the study subjects is shown in TABLE 2. Peptic ulcers, chronic kidney disease, and malignancy without metastases are comorbidities that have a significant effect on the mortality of cIAI patients.

TABLE 1. Demographic characteristics of the study subjects (n=91)

| Characteristic | Mortality | | Total | OR | CI 95% | p |
|---|---|---|---|---|---|---|
| | Yes | No | | | | |
| Sex [n (%)] | | | | | | |
| • Male | 18 (69.2) | 35 (53.8) | 53 (100) | 1.929 | 0.735-5.063 | 0.179[a] |
| • Female | 8 (30.8) | 30 (46.2) | 38 (100) | | | |
| Age (mean ±SD) | 54.35±15.8 | 50.69±17.62 | 51.79±17.09 | | | 0.360[b] |
| BMI (mean ±SD) | 20.18±3.79 | 21.20±3.46 | 20.91±3.56 | | | 0.218[b] |
| Reoperation [n (%)] | | | | | | |
| • Yes | 10 (38.5) | 17 (26.2) | 27 (100) | 1.765 | 0.673-4.630 | 0.246[a] |
| • No | 16 (61.5) | 48 (73.8) | 64 (100) | | | |
| Hospital of LoS (mean ±SD) | 12.58±10.46 | 11.45±8.44 | 11.77±9.02 | | | 0.592[b] |
| ICU LoS (mean ±SD) | 5.88±7.97 | 1.27±3.60 | 2.59±5.59 | | | 0.000[b*] |

BMI: body mass index; LoS: length of stay; [a] $X^2$; [b]t test; *p<0.05

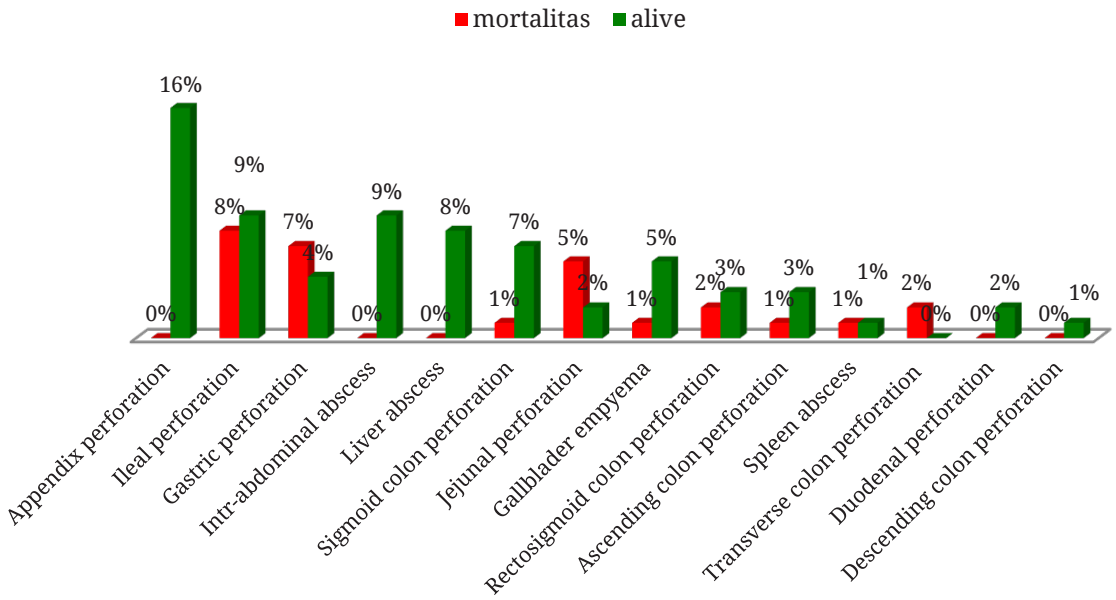


FIGURE 1. Source of cIAI

TABLE 2. Comorbid diseases in study subjects with cIAI

| Comorbid | Mortality | | OR | CI 95% | p |
|---|---|---|---|---|---|
| | Yes | No | | | |
| Myocardial infarction | 0 (0.0) | 2 (3.1) | - | - | 0.366 |
| Congestive heart failure | 2 (7.7) | 4 (6.2) | 1.271 | 0.218-7.400 | 0.789 |
| Cerebrovascular disease | 1 (3.8) | 3 (4.6) | 0.827 | 0.082-8.331 | 0.872 |
| Chronic pulmonary disease | 1 (3.8) | 9 (13.8) | 0.249 | 0.030-2.072 | 0.168 |
| Peptic ulcer | 7 (26.9) | 6 (9.2) | 3.623 | 1.084-12.110 | 0.029* |
| DM with chronic complication | 0 (0.0) | 2 (3.1) | - | - | 0.366 |
| DM without chronic complication | 1 (3.8) | 5 (7.7) | 0.480 | 0.053-4.320 | 0.504 |
| Hemi/paraplegia | 0 (0.0) | 2 (3.1) | - | - | 0.366 |
| CKD | 4 (15.4) | 1 (1.5) | 11.636 | 1.234-109.765 | 0.009* |
| Malignancy without metastasis | 6 (23.1) | 5 (7.7) | 3.600 | 0.991-13.081 | 0.042* |
| Leukemia | 1 (3.8) | 0 (0.0) | - | - | 0.112 |
| Moderate/severe liver disease | 0 (0.0) | 2 (3.1) | - | - | 0.366 |
| Metastatic solid tumour | 4 (15.4) | 10 (15.4) | 1.000 | 0.284 – 3.527 | 1.000 |
| AIDS | 0 (0.0) | 1 (1.0) | - | - | 0.525 |

DM: diabetes mellitus; CKD: chronic kidney disease; AIDS: acquired immunodeficiency syndrome; *p<0.05

**Clinical characteristics of subjects**

The clinical characteristics of the subjects regarding specific signs and symptoms related to cIAI are illustrated in TABLE 3. Factors such as respiratory rate, GCS, abdominal rigidity, sepsis, organ failure, preoperative duration exceeding 24 hours, general peritonitis, and exudate condition were significantly associated with the mortality of the study subjects.

**Laboratory characteristics and microorganisms responsible for cIAI**

The characteristics of the research subject's laboratory are detailed in TABLE 4. All research subjects underwent culture examination. Cultures were conducted on 67 peritoneal fluid samples (73.62%) and 24 intraabdominal abscess samples (26.37%) to identify the etiology of cIAI. Thirteen samples (14.3%) were cultured but yielded no growth. The profiles of the etiological microorganisms in cIAI are presented in TABLE 5. The most common microorganism causing cIAI is *E. coli* (42%), of which extended-spectrum beta-lactamase (ESBL) producing *E. coli* account for 60.52%. MDRO infection was detected in 40 study subjects (52.7%). The identified MDRO infections were ESBL producing *E. coli* infection (57%), methicillin-resistant coagulase-negative *Staphylococcus* sp (MRCoNS) (20%), ESBL producing *K. pneumonia* (7%), MDR *Enterococcus* sp.(5%), ESBL producing *Enterobacter* sp. (3%), carbapenem-resistant *Acinetobacter baumannii* (3%), XDR *A. baumannii* (3%) and MDR *P. aeruginosa* (2%), in the study subjects is depicted in FIGURE 2.

TABLE 3. Clinical characteristics of the cIAI

| Clinical characteristics | Mortality | | OR | CI 95% | p |
|---|---|---|---|---|---|
| | Yes | No | | | |
| | [n=26 (28.6%)] | [n=65 (71.4%)] | | | |
| Vital sign | | | | | |
| • Heart rate (bpm) | 99.92±16.32 | 93.64±15.96 | | | 0.096 |
| • Respiration rate (brpm) | 22.03±4.16 | 20.43±2.54 | | | 0.027* |
| • Temperature (°C) | 36.86±1.24 | 36.98±0.718 | | | 0.541 |
| GCS | 6.92±3.63 | 14.84±1.24 | | | 0.000* |
| Abdominal pain [n (%)] | 26 (100) | 64 (98.5) | | | 0.525 |
| Abdominal rigidity [n (%)] | 22 (84.6) | 28 (43.1) | 7.268 | 2249-23.488 | 0.000* |
| Temperature <36 or >38 [n (%)] | 5 (19.2) | 11 (16.9) | 1.169 | 0.362-3.770 | 0.794 |
| Leukosit <4000 or >12.000 [n (%)] | 17 (65.4) | 39 (60) | 1.259 | 0.488-3.250 | 0.633 |
| Sepsis [n (%)] | 25 (96.2) | 18 (27.7) | 65.278 | 8.226-517.985 | 0.000* |
| Organ failure [n (%)] | 26 (100) | 3 (4.6) | | | 0.000* |
| Preoperative duration >24 hr [n (%)] | 21 (80.8) | 28 (43.1) | 5.550 | 1.862-16.539 | 0.001* |
| Not colonic origin sepsis [n (%)] | 18 (69.2) | 33 (50.8) | 2.182 | 0.832-5.723 | 0.109 |
| Diffuse generalized [n (%)] | 24 (92.3) | 24 (36.9) | 20.500 | 4.448-94.476 | 0.000* |
| Exudate [n (%)] | | | | | |
| • Clear | 0 (0.0) | 20 (30.8) | | | |
| • Purulent | 3 (11.5) | 22 (33.8) | | | 0.000* |
| • Fecal | 23 (88.5) | 23 (35.4) | | | |

*p<0.05; GCS: Glasgow coma scale; bpm: beats per minute; brpm: breaths per minute

TABLE 4. Laboratory characteristics of cIAI (mean ± SD)

| Laboratory parameters | Mortality | | p |
|---|---|---|---|
| | Yes [n=26 (28.6%)] | No [n=65 (71.4%)] | |
| CVP (mmHg) | 4.30±1.67 | 6.78±0.94 | 0.000* |
| MAP (mmHg) | 81.41±22.52 | 95.11±13.55 | 0.001* |
| $AaDO_2$ (mmHg) | 196.51±166.24 | 86.01±124.44 | 0.001* |
| $PaCO_2$ (mmHg) | 43.96±16.96 | 37.27±7.64 | 0.011* |
| $PaO_2$ (mmHg) | 314.33±145.69 | 191.57±136.47 | 0.000* |
| $FiO_2$ (mmHg) | 0.53±0.23 | 0.36±0.18 | 0.000* |
| $PaO_2/FiO_2$ (%) | 595.44±102.49 | 499.87±118.16 | 0.000* |
| pH | 7.27±0.17 | 7.38±0.66 | 0.000* |
| $HCO_3^-$ (mEq/L) | 19.21±6.37 | 22.78±4.95 | 0.005* |
| $Na^+$ (mEq/L) | 138.19±7.67 | 137.03±6.54 | 0.469 |
| $K^+$ (mEq/L) | 4.70±1.12 | 3.99±0.92 | 0.002* |
| Hematocrit (%) | 30.99±7.71 | 33.61±6.69 | 0.109 |
| WBC (x 1000 cells/L) | 15.33±8.16 | 13.68±7.15 | 0.344 |
| Thrombocyte (x 1000 cells/L) | 288.73±263.66 | 350.26±197.61 | 0.227 |
| Albumin (g/dL) | 2.51±0.59 | 2.84±0.65 | 0.030* |
| Bilirubin (µmol/L) | 32.18±85.88 | 17.34±33.19 | 0.235 |
| Creatinine (µmol/L) | 141.69±87.02 | 92.30±79.79 | 0.011* |

*significant different (p<0.05)

TABLE 5. Microorganisms that cause cIAI

| Etiology | Non MDRO [n (%)] | MDRO [n (%)] | Infection [n (%)] |
|---|---|---|---|
| Microorganism | | | |
| • *Escherichia coli* | 15 (39.5) | 23 (60.5) | 38 (42.0) |
| • *Klebsiella pneumonia* | 6 (66.7) | 3 (33.3) | 9 (10.0) |
| • *Staphylococcus* CoN | 1 (11.1) | 8 (88.9) | 9 (10.0) |
| • *Enterococcus* sp. | 6 (75.0) | 2 (25.0) | 8 (9.0) |
| • *Pseudomonas aeruginosa* | 4 (80.0) | 1 (20.0) | 5 (5.0) |
| • *Streptococcus* sp. | 5 (100.0) | 0 (0.0) | 5 (5.0) |
| • *Enterobacter* sp. | 3 (75.0) | 1 (25.0) | 4 (4.0) |
| • *Acinetobacter baumannii* | 1 (33.3) | 2 (66.7) | 3 (3.0) |
| • *Serratia* sp. | 1 (100.0) | 0 (0.0) | 1 (1.0) |
| • *Stenotrophomonas* sp. | 1 (100.0) | 0 (0.0) | 1 (1.0) |
| • *Erysipelothrix* sp. | 1 (100.0) | 0 (0.0) | 1(1.0) |
| • *Bacteroides* sp. | 1 (100.0) | 0 (0.0) | 1 (1.0) |
| • *Micrococcus* sp. | 1 (100.0) | 0 (0.0) | 1 (1.0) |
| • *Zygosaccharomyces* sp. | 1 (100.0) | 0 (0.0) | 1 (1.0) |
| • No growth | - | - | 13 (14.0) |
| Infection type | | | |
| • Monomicrobial | | | 65 (83.3) |
| • Polymicrobial | | | 13(16.7) |

CoN: coagulase negative

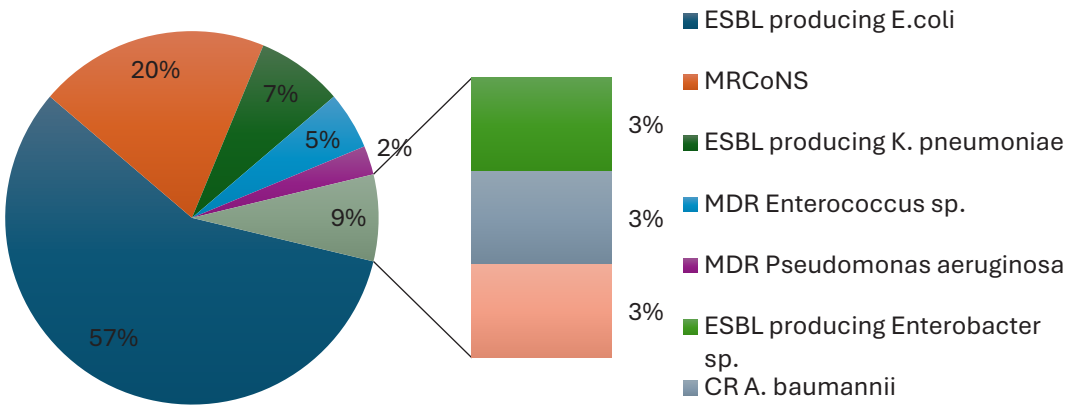


FIGURE 2. MDRO Infection in cIAI. ESBL: extended spectrum beta lactamase; MRCoNS: methicillin-resistant coagulase-negative *Staphylococcus* sp; MDR: multidrug resistant; CR: carbapenem resistant; XDR: extensively-drug resistant.

**Prognostic value of infection on the mortality of patients with cIAI**

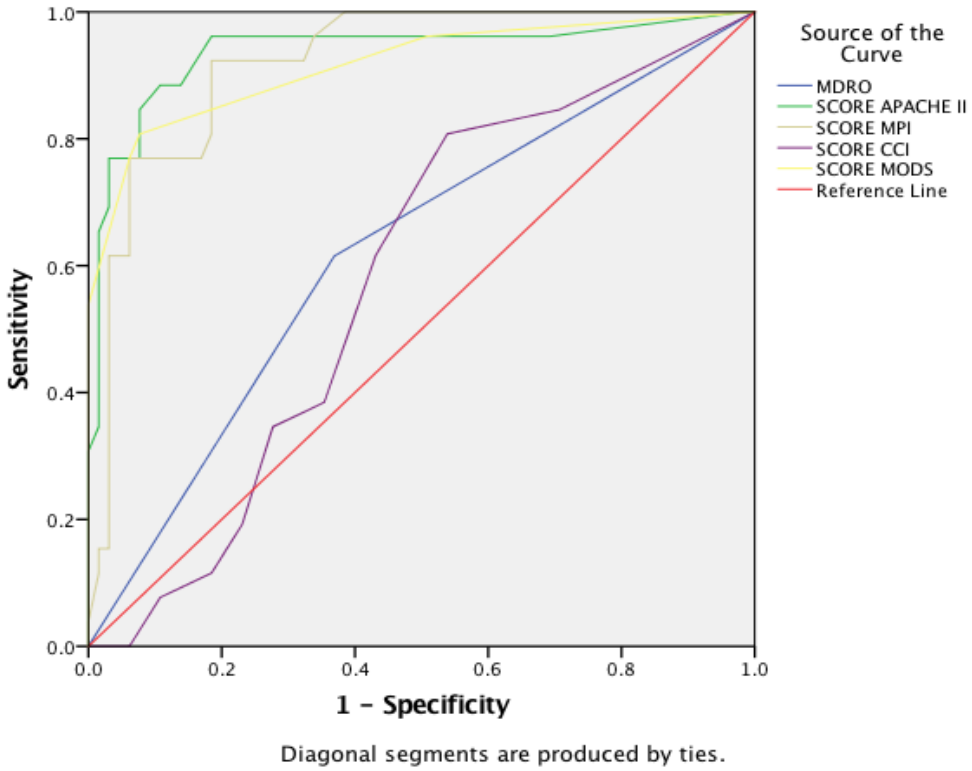


FIGURE 3. ROC curves for APACHE II, MPI, CCI, MODS and MDRO infection predicting mortality in cIAI. APACHE II: acute physiology and chronic health evaluation II;, MPI: Mannheim peritonitis index; CCI: Charlson comorbidity index; MODS: multiple organ dysfunction score; MDRO: multidrug resistant organisms.

TABLE 6. The prognostic value of APACHE II, MPI, CCI, MODS, and MDRO infection on the mortality of patients with cIAI

| Score | Mortality | | OR | CI 95% | p |
|---|---|---|---|---|---|
| | Yes [n (%)] | No [n (%)] | | | |
| APACHE II ≥ 10.5 | 23 (88.5) | 9 (13.8) | 47.704 | 11.836-192.270 | 0.000* |
| MPI ≥ 27.5 | 24 (92.3) | 12(18.5) | 53.000 | 10.997-255.442 | 0.000* |
| CCI ≥ 2.5 | 16 (61.5) | 28 (43.1) | 2.114 | 0.834-5.360 | 0.111 |
| MODS ≥ 3.5 | 20 (76.9) | 4 (6.2) | 50.833 | 13.018-198.498 | 0.000* |
| MDRO | 16 (61.5) | 24 (36.9) | 2.733 | 1.071-6.976 | 0.033* |

APACHE II: acute physiology and chronic health evaluation II; MPI: Mannheim peritonitis index; CCI: Charlson comorbidity index; MODS: multiple organ dysfunction score; MDRO: multidrug resistant organisms; *p<0.05.

TABLE 7. Prognostic significance of APACHE II, MPI, CCI, MODS, and MDRO infection on mortality in patients with cIAI

| Score | AUC | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|
| APACHE II ≥10.5 | 0.938 | 88.5 | 86.2 | 71.9 | 94.9 | 86.8 |
| MPI ≥ 27.5 | 0.920 | 92.3 | 81.5 | 66.7 | 96.4 | 84.6 |
| CCI ≥ 2.5 | 0.582 | 61.5 | 56.9 | 36.4 | 78.7 | 58.2 |
| MODS ≥ 3.5 | 0.916 | 76.9 | 93.8 | 83.3 | 91.0 | 89 |
| MDRO | 0.623 | 61.5 | 63.1 | 40.0 | 80.4 | 62.6 |

APACHE II: acute physiology and chronic health evaluation II; MPI: Mannheim peritonitis index; CCI: Charlson comorbidity index; MODS: multiple organ dysfunction score; MDRO: multidrug resistant organisms

The ROC curve as shown in FIGURE 3 illustrates a robust positive correlation between the enhancement of APACHE II (AUC=0.938), MPI (AUC=0.920), and MODS (AUC=0.916) scores and the mortality rate of cIAI patients. Conversely, the rise in CCI score (AUC=0.582) did not have a significant impact on the mortality of cIAI patients. MDRO infection was found to have a notable effect on the mortality of cIAI patients but the diagnostic value of MDRO was low (AUC=0.623). The impact of APACHE II, MPI, CCI, MODS, and MDRO infection on the mortality of cIAI patients can be observed in TABLE 6 and 7.

## DISCUSSION

The mortality rate of cIAI patients in this study was relatively high, at 28.6%. This figure aligns with previous studies conducted in Indonesia, particularly at the referral hospital Dr. Soetomo General Hospital, Surabaya, where the mortality rate of cIAI patients from 2020 to 2022 ranged from 32.2 to 34.7%.[8,22] The CIAOW (Complicated Intraabdominal Infection Worldwide Observational Study) involving 68 medical facilities worldwide from 2012 to 2013 reported a cIAI mortality rate of 10.5%.[1] Additionally, a multicentre study conducted in six tertiary hospitals in Indonesia in 2017 found a cIAI prevalence of 10% with a mortality rate of 16.6%.[4] The higher mortality rate observed in this study compared to others can be attributed to Dr. Sardjito General Hospital as a national referral center hospital. Therefore, the

cIAI patients included in the study had more severe cases, with sepsis occurring in 47.3% of subjects (43 out of 91) and organ failure in 31.9% of subjects (29 out of 91). Previous research indicated that the mortality rate for cIAI with sepsis ranged from 19 to 60%.[3,4,7]

The high mortality rate revealed in this study emphasizes the need to evaluate critical factors influencing mortality in patients. The study demonstrated the multifactorial impact of host, agent, and environmental components on the mortality of patients with cIAI.[5] Host predictor factors that significantly influenced the study included the presence of comorbidities (such as peptic ulcer, chronic kidney disease, non-metastatic malignancy), clinical presentation (respiratory rate, abdominal rigidity, sepsis, organ failure, prolonged preoperative duration ( ≥24 hr ), diffuse peritonitis, intra-abdominal fecal exudate), and laboratory characteristics (such as CVP, MAP, AaDO2, PaCO2, PaO2, FiO2, PaO2/FiO2, pH, $HCO3^-$, $K^+$, albumin, and creatinine). The impact of the agent causing cIAI on patient mortality was also significant. Patients with MDRO infections experienced a 2.7 times higher mortality rate in cIAI cases. These results align with previous studies that have demonstrated the role of MDRO as a significant prognostic factor in mortality.[10,17] Environmental factors also played a crucial role in increasing mortality, as evidenced by the significant influence of ICU treatment duration on cIAI patient mortality. Early detection of predictive mortality factors is essential as an initial step in identifying patients at increased risk of mortality.[23] This allows for early intervention, appropriate management (such as source control), or timely referral to more advanced healthcare facilities.[23]

The performance analysis of the algorithm widely employed in predicting mortality in cIAI patients indicates that the APACHE II, MPI, and MODS values exhibit good diagnostic accuracy. In this study, an APACHE II score of ≥ 10.5 was found to have a good diagnostic value (AUC 0.938, sensitivity 88.5%, specificity 86.2%). These findings align with the "Clinical Practice Guideline in Complicated Intra-Abdominal Infection 2018: Indonesian Perspective," which identifies an APACHE score of ≥ 10 as a risk factor for treatment failure.[4] A higher score indicates a more severe condition and a greater risk of in-hospital mortality[12] These study results reinforce this understanding, highlighting the APACHE II score as an independent prognostic factor for cIAI patients.[12] The APACHE II score is a scoring system utilized to evaluate disease severity and predict the likelihood of death. While widely used in clinical settings, it has its limitations.[24] Challenges in implementing the APACHE II scoring system include the extensive array of laboratory parameters required for evaluation, time-consuming analysis, and associated expenses. The necessity for sophisticated laboratory facilities restricts the feasibility of this scoring system in remote areas lacking access to such resources.[7]

The MPI score, with a cut-off value of ≥27.5, demonstrates good prognostic value in predicting the mortality of cIAI patients (AUC:0.920; sensitivity: 92.3%; specificity: 81.5%). This finding aligns with previous studies that have also shown the high prognostic value of MPI, using a cut-off value of ≥27, with sensitivity at 90.90% and specificity at 78.13%.[6] Several studies have investigated the accuracy of MPI scores in predicting mortality among cIAI patients. However, the accuracy values from these studies vary widely, and the results are inconsistent across different cut-off values. Some studies have utilized cut-offs ranging from 21 to 29, resulting in sensitivity values between 71% to 100% and specificities ranging from 58 to 91.7%.[7] The MPI score is a straightforward and easy-to-use tool

that considers the etiology of cIAI and the nature of peritoneal contamination, aspects not covered by the APACHE II score.[7] Nonetheless, the MPI score has limitations, such as requiring surgical findings to complete the score, rendering it unsuitable for preoperative assessment.[6]

The results indicated that a CCI score of ≥ 2.5 had a low prognostic value in predicting the mortality of patients with cIAI (AUC: 0.582; sensitivity: 61.5%; specificity 56.9%). These findings align with previous research on peritonitis patients, which also demonstrated a marginal significance of CCI scores ≥ 2 with mortality.[25] This contrasts with earlier studies that identified the CCI score as a robust and independent prognostic indicator for mortality in cIAI patients (AUC: 0.887).[14] This discrepancy may be due to variations in age adjustments made in previous studies, impacting patient comorbidities and resulting in different cut-off values, specifically ≥ 4. However, this study highlights that the presence of comorbidities such as peptic ulcer, CKD, and non-metastatic malignancy strongly influences mortality risk in patients. Identifying one or more existing comorbidities in a patient increases their mortality risk.[26] Preoperative risk assessment in cIAI settings is vital for enhancing postoperative outcomes and avoiding unnecessary interventions. The CCI score offers a straightforward method of calculating data upon admission, enabling the evaluation of death risk and significant postoperative morbidity beforehand. This aids healthcare professionals in making informed clinical decisions, optimizing treatment, and efficiently managing resources.[14] This study discovered that a MODS score of ≥ 3.5 had significant prognostic value in determining mortality (AUC: 0.916; sensitivity: 76.9%; specificity 93.8%). These findings are consistent with previous studies that have indicated the MODS score as an independent predictor of severity and mortality outcome in cIAI patients.[27,28] The MODS score is a straightforward physiological assessment of dysfunction in six organ systems, strongly linked to the risk of death in critical care units and hospitals.[20] Organ dysfunction is a dynamic process, and the level of dysfunction can fluctuate based on time and treatment. Continual assessments of organ dysfunction scores are more reliable in predicting outcomes compared to one-time measurements.[15] Certain studies suggest that utilizing maximum, average, or delta scores can better predict mortality than using only the initial score or the first 24 hours of dysfunction scores of each organ.[20]

Multidrug resistance organisms infection is a significant prognostic factor for the mortality of patients with cIAI but have limited diagnostic value. This study's findings support previous research that has shown a strong association between MDRO infection and mortality in patients.[16] The rate of MDRO infection among cIAI patients in this study was notably high at 52.7%, surpassing rates seen in previous studies. For example, a multicenter study in Italy reported an MDRO infection rate of 13.9%, while in Taiwan, a MDR Gram-negative bacteria infection rate of 32% was observed.[16] This alarming incidence emphasizes the critical issue of MDRO infection in cIAI cases. It is essential to recognize that the actual prevalence of MDRO infections may be even higher than reported in this study due to undiagnosed cases that were not subjected to routine microbiological examination during the diagnosis of cIAI. The predominant pathogens causing cIAI in this study align with the profile of pathogens that most commonly cause healthcare associated infections (HAIs), such as *E. coli* and pathogens deemed a high priority by the WHO, including those classified in the critical group (carbapenem-resistant *A. baumannii*, third-generation cephalosporin-resistant

Enterobacterales, and carbapenem-resistant Enterobacterales) and in the high group (vancomycin-resistant *E. faecium*, carbapeneme-resistant *P. aeruginosa*).[30] These pathogens are given priority due to their high resistance levels, which can lead to increased morbidity, mortality, and treatment costs. Understanding the local patterns of pathogens is crucial in developing guidelines for the appropriate use of antibiotics tailored to the specific domestic situation.[32]

Developing an algorithm with high accuracy for predicting mortality is crucial for early detection of elevated mortality risk in patients for prompt and effective management.[13] This research emphasizes the importance of considering various factors that contribute to infections comprehensively, encompassing agents, hosts, and the environment[5] Identifying factors with a higher risk of mortality could help in making the right interventions during admission and reduce unwanted outcomes. However, the study has limitations such as being limited to a single site and tertiary referral hospitals, which may not fully represent the broader population, quality, and healthcare standards of Indonesia. The absence of detection of atypical bacteria, anaerobic bacteria, or fungal infections in the culture could have influenced the negative growth findings. Additionally, the study lacked data on infection control practices, which can impact patient mortality outcomes.[33] It is recommended to conduct multicenter studies across hospitals with diverse populations and services, enhance microbiological testing for precise identification of causative pathogens, and focus on areas like infection control protocols for patients to address these limitations.

## CONCLUSION

The APACHE II, MPI, MODS scores show efficiency in predicting the mortality of cIAI patients. The MDRO infection is significant determinant for mortality but has weak diagnostic value. Yet, it is essential to develop new algorithms that consider comprehensive factors, including agents, hosts, and environments, to enhance the accuracy of mortality assessment for cIAI patients.

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## REFERENCES

1. Sartelli M, Catena F, Ansaloni L, Coccolini F, Corbella D, Moore EE, *et al*. Complicated intra-abdominal infections worldwide: the definitive data of the CIAOW Study. World J Emerg Surg 2014; 9:37. https://doi.org/10.1186/1749-7922-9-37
2. Pathak AA, Agrawal V, Sharma N, Kumar K, Bagla C, Fouzdar A. Prediction of mortality in secondary peritonitis: a prospective study comparing p-POSSUM, Mannheim peritonitis index, and Jabalpur peritonitis index. Perioper Med 2023; 12(1):65. https://doi.org/10.1186/s13741-023-00355-7
3. Abaziou T, Vardon-Bounes F, Conil JM, Rouget A, Ruiz S, Grare M, *et al*. Outcome of community- versus hospital-acquired intra-abdominal infections in intensive care unit: a retrospective study. BMC Anesthesiol 2020; 20(1):295. https://doi.org/10.1186/s12871-020-01209-1
4. Lalisang TJM, Usman N, Hendrawidjaya I, Handaya AY, Nasution S, Saunar RY, *et al*. Clinical practice guidelines in complicated intra-abdominal infection 2018: An Indonesian perspective. Surg Infect 2019; 20(1):83-90. https://doi.org/10.1089/sur.2018.120
5. Johnson-Walker YJ, Kaneene JB.

Epidemiology: Science as a tool to inform one health policy. In: Herrmann JA, Johnson-Walker YJ, editors. Beyond One Health. 1st ed. Wiley; 2018; p.1-30. https://doi.org/10.1002/9781119194521.ch1

6. Gueiros LDS, Fonseca CMD, Duarte NMDM, Antunes OS. Mannheim's peritonitis index in the prediction of postoperative outcome of peritonitis. Rev Col Bras Cir 2022; 49:e20222991. https://doi.org/10.1590/0100-6991e-20222991_en
7. Kumar P, Singh K, Kumar A. A comparative study between Mannheim peritonitis index and APACHE II in predicting the outcome in patients of peritonitis due to hollow viscous perforation. Int Surg J 2017; 4(2):690. https://doi.org/10.18203/2349-2902.isj20170215
8. Nugraha GL, Septarendra D, Lesmana T. Comparative study of SOFA, WSESSSS, and CPIRO scoring systems as mortality predictors in a patient with complicated intra-abdominal infection. Bali Med J 2022; 11(3):1397-403. https://doi.org/10.15562/bmj.v11i3.3523
9. Inui T, Haridas M, Claridge JA, Malangoni MA. Mortality for intra-abdominal infection is associated with intrinsic risk factors rather than the source of infection. Surgery. 2009; 146(4):654-61; discussion 661-2. https://doi.org/10.1016/j.surg.2009.06.051
10. Yoon YK, Moon C, Kim J, Heo ST, Lee MS, Lee S, *et al*. Korean guidelines for use of antibiotics for intra-abdominal infections in adults. Infect Chemother 2022; 54(4):812-53. https://doi.org/10.3947/ic.2022.0156
11. Sartelli M, Coccolini F, Kluger Y, Agastra E, Abu-Zidan FM, Abbas AES, *et al*. WSES/GAIS/SIS-E/WSIS/AAST global clinical pathways for patients with intra-abdominal infections. World J Emerg Surg 2021; 16(1):49. https://doi.org/10.1186/s13017-021-00387-8
12. Mumtaz H, Ejaz MK, Tayyab M, Vohra LI, Sapkota S, Hasan M, *et al*. APACHE scoring as an indicator of mortality rate in ICU patients: a cohort study. Ann Med Surg 2023; 85(3):416-21. https://doi.org/10.1097/MS9.0000000000000264
13. Sartelli M. A focus on intra-abdominal infections. World J Emerg Surg 2010; 5:9. https://doi.org/10.1186/1749-7922-5-9
14. Payá-Llorente C, Martínez-López E, Sebastián-Tomás JC, Santarrufina-Martínez S, de'Angelis N, Martínez-Pérez A. The impact of age and comorbidity on the postoperative outcomes after emergency surgical management of complicated intra-abdominal infections. Sci Rep 2020; 10(1):1631. https://doi.org/10.1038/s41598-020-58453-1
15. Tolonen M, Coccolini F, Ansaloni L, Sartelli M, Roberts DJ, McKee JL, *et al*. Getting the invite list right: a discussion of sepsis severity scoring systems in severe complicated intra-abdominal sepsis and randomized trial inclusion criteria. World J Emerg Surg 2018; 13:17. https://doi.org/10.1186/s13017-018-0177-2
16. Labricciosa FM, Sartelli M, Abbo LM, Barbadoro P, Ansaloni L, Coccolini F, *et al*. Epidemiology and risk factors for isolation of multi-drug–resistant organisms in patients with complicated intra-abdominal infections. Surg Infect 2018; 19(3):264-72. https://doi.org/10.1089/sur.2017.217
17. Claridge JA, Banerjee A, Kelly KB, Leukhardt WH, Carter JW, Haridas M, *et al*. Bacterial species-specific hospital mortality rate for intra-abdominal infections. Surg Infect 2014; 15(3):194-9. https://doi.org/10.1089/sur.2011.039
18. Mikamo H, Yuasa A, Wada K, Crawford B, Sugimoto N. Optimal treatment for complicated intra-abdominal infections in the era of antibiotic resistance: A systematic review and meta-analysis of the

efficacy and safety of combined therapy with metronidazole. Open Forum Infect Dis 2016; 3(3):ofw143. https://doi.org/10.1093/ofid/ofw143
19. Piano S, Singh V, Caraceni P, Maiwall R, Alessandria C, Fernandez J, *et al*. Epidemiology and effects of bacterial infections in patients with cirrhosis worldwide. Gastroenterology 2019; 156(5):1368-80.e10. https://doi.org/10.1053/j.gastro.2018.12.005
20. Asim M, Amin F, El-Menyar A. Multiple organ dysfunction syndrome: Contemporary insights on the clinicopathological spectrum. Qatar Medical J 2020; 2020(1):2. https://doi.org/10.5339/qmj.2020.22
21. Cosentino F, Viale P, Giannella M. MDR/XDR/PDR or DTR? Which definition best fits the resistance profile of Pseudomonas aeruginosa? Curr Opin Infect Dis 2023; 36(6):564-71. https://doi.org/10.1097/QCO.0000000000000966
22. Kurniawan E, Wibowo MD, Danardono E. Predictor of mortality in complicated intraabdominal infection patients at Dr. Soetomo General Hospital Surabaya. Bali Medical Journal 2023; 12(2):2338-44. https://doi.org/10.15562/bmj.v12i2.4584
23. Sartelli M, Viale P, Koike K, Pea F, Tumietto F, Van Goor H, *et al*. WSES consensus conference: Guidelines for first-line management of intra-abdominal infections. World J Emerg Surg 2011; 6:2. https://doi.org/10.1186/1749-7922-6-2
24. Farajzadeh M, Nasrollahi E, Bahramvand Y, Mohammadkarimi V, Dalfardi B, Anushiravani A. The use of APACHE II scoring system for predicting clinical outcome of patients admitted to the intensive care unit: A report from a resource-limited center. Shiraz E-Med J 2021; 22(5). https://doi.org/10.5812/semj.102858
25. Chern YB, Ho PS, Kuo LC, Chen JB. Lower education level is a major risk factor for peritonitis incidence in chronic peritoneal dialysis patients: a retrospective cohort study with 12-year follow-up. Perit Dial Int 2013; 33(5):552-8. https://doi.org/10.3747/pdi.2012.00065
26. Silva-Nunes J, Cardoso T. Intra-abdominal infections: the role of different classifications on the selection of the best antibiotic treatment. BMC Infect Dis 2019; 19(1):980. https://doi.org/10.1186/s12879-019-4604-0
27. 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 2017; 18(1):1-76. https://doi.org/10.1089/sur.2016.261
28. Holzheimer RG, Gathof B. Re-operation for complicated secondary peritonitis – how to identify patients at risk for persistent sepsis. Eur J Med Res 2003; 8(3):125-34.
29. Lin TL, Chang PH, Chen IL, Lai WH, Chen YJ, Li WF, *et al*. Risk factors and mortality associated with multi-drug-resistant Gram-negative bacterial infection in adult patients following abdominal surgery. J Hosp Infect 2022; 119:22-32. https://doi.org/10.1016/j.jhin.2021.09.021
30. World Health Organization (WHO). Who bacterial priority pathogens list 2024: Bacterial pathogens of public health importance, to guide research, development, and strategies to prevent and control antimicrobial resistance, 1st edition. Geneva: World Health Organization; 2024.
31. Perhimpunan Ahli Mikrobiologi Klinik Indonesia (PAMKI). Pola pathogen dan antibiogram di Indonesia tahun 2022; 2023.
32. World Health Organization (WHO). Infection prevention and control: Guidance to action tools. Geneva: World Health Organization; 2021.