INTISARI

Latar belakang: Prevalensi infeksi *Enterobacteriaceae* penghasil AmpC β-laktamase dilaporkan beragam 10-30% dan memiliki makna klinis yaitu kegagalan terapi antimikroba. Tingkat resistensi *Enterobacteriaceae* penghasil AmpC β-laktamase terhadap antibiotik beta laktam, khususnya *cephalosporin* generasi ketiga dilaporkan mencapai 60-80%. Identifikasi faktor risiko penyebab munculnya infeksi *Enterobacteriaceae* penghasil AmpC β-laktamase dapat membantu mencegah penyebaran infeksi atau resistensi. Beberapa penelitian menyebutkan riwayat terapi antibiotik *cephalosporin* dalam waktu 1-3 bulan dapat menjadi faktor risiko munculnya AmpC β-laktamase. Penelitian tentang hubungan riwayat terapi antibiotik *cephalosporin* dengan kejadian AmpC β-laktamase di Indonesia masih terbatas.
Tujuan: Mengevaluasi riwayat terapi *cephalosporin* sebagai faktor risiko infeksi *Enterobacteriaceae* penghasil AmpC β-laktamase.
Metode: Penelitian ini merupakan *unmatched case-control* yang dilakukan di RSUP Dr. Sardjito Yogyakarta. Kelompok kasus adalah pasien rawat inap di RSUP Dr. Sardjito dengan infeksi *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella pneumoniae*, dan *Proteus mirabilis)* penghasil AmpC β-laktamase, sementara kelompok kontrol adalah infeksi oleh isolat yang sama tetapi tidak menghasilkan AmpC β-laktamase. Identifikasi *Enterobacteriaceae* menggunakan Vitek 2, dan produksi AmpC β-laktamase menggunakan uji inhibisi *Phenyl boronic acid* (PBA). Kelompok kasus dan kontrol kemudian ditelusuri faktor risiko masing-masing terhadap penggunaan terapi *cephalosporin* dalam 90 hari sebelumnya. Uji beda median dan proporsi antar kelompok kasus dan kontrol dengan uji *Mann Whitney*, uji *Chi Square* dan *Fisher Exact test*. Hubungan faktor risiko dianalisis menggunakan uji bivariat dan multivariat (regresi logistik). Uji stastistik menggunakan perangkat lunak SPSS v.27 dengan batas kemaknaan $p<0,05$.
Hasil: Analisis dilakukan terhadap 72 pasien infeksi *Enterobacteriaceae*, 36 subjek masing-masing kelompok kasus dan kontrol. Tidak ada perbedaan usia, jenis kelamin, komorbid, tempat perawatan, dan alat intervensi medis yang digunakan antar kedua kelompok. Riwayat terapi *cephalosporin* dalam 90 hari terakhir berhubungan signifikan dengan infeksi *Enterobacteriaceae* penghasil AmpC β-laktamase (OR = 5,80; IK 95%: 2,01–16,72; p = 0,001). Setelah penyesuaian, riwayat terapi *cephalosporin* dalam 90 hari terakhir tetap menjadi faktor risiko signifikan (aOR = 5,58; IK 95%: 1,81–17,19; p = 0,003). Analisis lanjutan pada jenis *cephalosporin* didapatkan peningkatan risiko pada riwayat terapi *ceftriaxone* OR=6,40 (IK95%: 1,87-21,89, p=0,002) dan *cefixime* OR 1,77 (IK 95%:0,52-6,05, p=0,358).
Simpulan: Pasien dengan riwayat terapi antibiotik *cephalosporin* dalam 3 bulan sebelumnya memiliki risiko terinfeksi *Enterobacteriaceae* penghasil AmpC β-laktamase sebesar 5,58 kali dibanding yang tidak memiliki riwayat terapi *cephalosporin*. Riwayat terapi *cephalosporin* generasi ketiga, khususnya *ceftriaxone* memberikan peluang risiko infeksi *Enterobacteriaceae* penghasil AmpC β-laktamase sebesar 6,40 kali.

Kata kunci: *Enterobacteriaceae*, AmpC β-laktamase, riwayat terapi *cephalosporin*, faktor risiko

ABSTRACT

Background: The prevalence of AmpC β-lactamase-producing *Enterobacteriaceae* infections has been reported to vary between 10-30% and has clinical significance in terms of antimicrobial therapy failure. The level of resistance of AmpC β-lactamase-producing *Enterobacteriaceae* to beta-lactam antibiotics, particularly third-generation cephalosporins, has been reported to reach 60-80%. Identifying risk factors for the emergence of AmpC β-lactamase-producing *Enterobacteriaceae* infections can help prevent the spread of infection or resistance. Several studies have mentioned that a history of cephalosporin antibiotic therapy within 1-3 months can be a risk factor for the emergence of AmpC β-lactamase. Research on the relationship between a history of cephalosporin antibiotic therapy and the occurrence of AmpC β-lactamase in Indonesia is still limited.
Objective: To evaluate the history of cephalosporin therapy as a risk factor for infection with AmpC β-lactamase-producing *Enterobacteriacea*e.
Methods: An unmatched case-control study conducted at Dr Sardjito General Hospital in Yogyakarta. The case group consisted of inpatients at Dr Sardjito General Hospital with *Enterobacteriaceae* infections (*Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*) producing AmpC β-lactamase, while the control group consisted of patients who did not produce AmpC β-lactamase. *Enterobacteriaceae* were identified using Vitek 2, and AmpC β-lactamase production was determined using the phenyl boronic acid (PBA) inhibition test. The case and control groups were then traced for risk factors associated with cephalosporin therapy use in the previous 90 days. The difference in median and proportions between the case and control groups was tested using the Mann Whitney test, Chi Square test, and Fisher Exact test. The relationship between risk factors was analysed using bivariate and multivariate tests (logistic regression). Statistical tests were performed using SPSS v.27 software with a significance level of $p<0.05$.
Result: The analysis was conducted on 72 patients with *Enterobacteriaceae* infections, 36 subjects in each case and control group. There were no differences in age, gender, comorbidities, place of care, and medical intervention tools used between the two groups. A history of cephalosporin therapy within the last 90 days was significantly associated with infection of AmpC β-lactamase-producing *Enterobacteriaceae* (OR = 5,80; 95% CI: 2.01–16.72; p = 0.001). After adjustment, a history of cephalosporin therapy within the last 90 days remained a significant risk factor (aOR = 5.58; 95% CI: 1.81–17.19; p = 0.003). Further analysis of cephalosporin types revealed an increased risk in the history of ceftriaxone therapy OR=6.40 (95% CI: 1.87–21.89, p=0.002) and cefixime OR 1.77 (95% CI: 0.52–6.05, p=0.358).
Conclusion: Patients with a history of cephalosporin antibiotic therapy within the previous 3 months had a 5.58 times higher risk of infection with AmpC β-lactamase-producing *Enterobacteriaceae* compared to those without a history of cephalosporin therapy. A history of third-generation cephalosporin therapy, particularly ceftriaxone, increases the risk of infection with AmpC β-lactamase-producing *Enterobacteriaceae* by 6.40 times.

Keywords: *Enterobacteriaceae*, AmpC β-lactamase, history of cephalosporin therapy, risk factors