FAKTOR-FAKTOR YANG MEMPENGARUHI KEJADIAN EFEK SAMPING KEMOTERAPI DERAJAT BERAT DAN SANGAT BERAT PASIEN KANKER PAYUDARA METASTATIK DI RSDK TAHUN 2021–2024

Latar Belakang: Efek samping kemoterapi derajat berat dan sangat berat membatasi manfaat paliatif kemoterapi sistemik pada kanker payudara metastatik (KPM), sementara data faktor prediktor toksisitas derajat 3–5 dari pusat onkologi Indonesia masih terbatas.

Tujuan: Mengidentifikasi faktor-faktor terkait pasien, penyakit, dan terapi yang berhubungan dengan terjadinya efek samping kemoterapi derajat berat dan sangat berat (CTCAE grade 3–5) pada pasien KPM yang dirawat di RSUP Dr. Kariadi Semarang periode 2021–2024.

Metode: Studi kasus–kontrol senter tunggal, menggunakan rekam medis elektronik pasien perempuan dengan kanker payudara stadium IV (de novo maupun rekuren) yang menerima kemoterapi di RSUP Dr. Kariadi Semarang antara Januari 2021–Desember 2024. Kasus adalah pasien yang mengalami ≥1 efek samping kemoterapi akut paska kemo (onset ≤2 minggu), derajat keparahan CTCAE grade 3–5 (n=60), sedangkan kontrol hanya mengalami efek samping grade 0–2 (n=60). Variabel yang dikumpulkan meliputi usia, status performa ECOG, komorbiditas, parameter hematologi dan biokimia dasar, subtipe molekuler, jumlah dan lokasi metastasis, kepatuhan terhadap pedoman, serta penggunaan rejimen tunggal versus kombinasi pada setiap lini kemoterapi. Perbandingan kelompok menggunakan uji T *Welch* dan uji χ^2. Rasio odds (OR) dengan *confidence interval* (*CI*) 95% didapat dari analisis bivariat uji χ^2; prediktor bermakna dari analisis bivariat kemudian dimasukkan ke regresi logistik multivariat dengan metode *backward likelihood ratio* (LR).

Hasil: Karakteristik dasar (usia, jumlah lokasi metastasis, komorbiditas, dan parameter laboratorium baseline) sebanding antara kelompok (seluruh p>0,05). Pada analisis bivariat, status performa ECOG (ECOG PS) >2 (OR 4,09; p=0,002), kemoterapi lini pertama kombinasi (OR 3,27; p=0,003), kemoterapi lini kedua kombinasi (OR 17,50; p=0,009), serta ketidaktaatan terhadap pedoman klinis (OR 4,00; p=0,001) berasosiasi dengan kejadian ESO berat, sedangkan subtipe molekuler tidak bermakna. Pada analisis multivariat, hanya kemoterapi lini kedua kombinasi yang tetap menjadi prediktor independen (OR 17,50; IK95% 1,88–163,01; p=0,012).

Kesimpulan: Dalam studi kasus–kontrol retrospektif KPM ini, ESO kemoterapi derajat berat dan sangat berat berasosiasi dengan faktor terkait pasien dan faktor terkait terapi pada analisis bivariat. Pada regresi logistik multivariat, kemoterapi lini kedua kombinasi merupakan satu-satunya prediktor independen kejadian ESO derajat tinggi (OR 17,50; IK95% 1,88–163,01; p=0,012). Penguatan kepatuhan tatalaksana terhadap pedoman serta pemilihan (atau menghindari) rejimen kemoterapi kombinasi terutama setelah lini pertama dan pada pasien dengan status performa menurun berpotensi menurunkan toksisitas derajat tinggi. Temuan ini mendukung kehati-hatian penggunaan kemoterapi kombinasi setelah lini pertama dan memprioritaskan strategi monoterapi sekuensial sesuai pedoman bila memungkinkan.

Kata kunci: kanker payudara metastatik; kemoterapi; efek samping.

FACTORS ASSOCIATED WITH THE OCCURRENCE OF SEVERE AND VERY SEVERE CHEMOTHERAPY ADVERSE EVENTS IN PATIENTS WITH METASTATIC BREAST CANCER AT KARIADI CENTRAL GENERAL HOSPITAL, 2021–2024

Background: Severe and very severe chemotherapy adverse events (AEs) limit the palliative benefit of systemic treatment in metastatic breast cancer (MBC), yet data on real-world predictors of grade 3–5 toxicity from Indonesian oncology centers remain limited.

Objective: To identify patient-, disease-, and treatment-related factors associated with the occurrence of severe and very severe (CTCAE grade 3–5) chemotherapy AEs in patients with MBC treated at Kariadi Central General Hospital during 2021–2024.

Methods: Single-center, hospital-based, matched case–control study using electronic medical records of women with de novo or recurrent stage IV breast cancer who received cytotoxic chemotherapy at Kariadi Central General Hospital between January 2021 and December 2024. Cases were patients who experienced ≥1 acute post-chemo chemotherapy adverse event (onset within 2 weeks after chemotherapy), CTCAE grade 3–5 (n=60), while controls only experienced grade 0–2 side effects (n=60). Group comparisons were performed using the Welch's T-test and the χ^2 test. Odds ratios (ORs) with 95% confidence intervals (CIs) were obtained from bivariate analysis using the χ^2 test; significant predictors from the bivariate analysis were then entered into multivariate logistic regression using the backward likelihood ratio (LR) method.

Results: Baseline characteristics (age, number of metastatic sites, comorbidities, and baseline laboratory parameters) were comparable between groups (all $p>0.05$). In bivariate analyses, ECOG performance status (ECOG PS) >2 (OR 4.09; p=0.002), first-line combination chemotherapy (OR 3.27; p=0.003), second-line combination chemotherapy (OR 17.50; p=0.009), and non-adherence to clinical guidelines (OR 4.00; p=0.001) were associated with severe AEs, while molecular subtype was not significant. In multivariable analysis, only second-line combination chemotherapy remained an independent predictor (OR 17.50; 95%CI 1.88–163.01; p=0.012).

Conclusion: In this retrospective MBC case–control study, severe and very severe chemotherapy AEs were associated with both patient-related and therapy-related factors in bivariable analyses. In multivariable logistic regression, second-line combination chemotherapy was the only independent predictor of high-grade AEs (OR 17.50; 95%CI 1.88–163.01; p=0.012). Strengthening guideline adherence and carefully selecting (or avoiding) combination regimens, particularly beyond first line and in patients with reduced performance status may reduce high-grade toxicity. These findings support cautious use of combination chemotherapy beyond first line and prioritization of guideline-recommended sequential single-agent strategies whenever feasible.

Keywords: metastatic breast cancer; chemotherapy; adverse events.