

## ABSTRACT

**Introduction:** Osteosarcoma is the most common primary bone tumor malignancy that accounts for 30% -80% of all primary bone tumors with a bimodal distribution, namely 10-20 years of age and over 60 years of age. The patient's prognosis is influenced by various factors, one of which is the expression of Cyclin-dependent kinase 4 (CDK4). Cyclin-dependent kinase 4 as a pathogenesis pathogenesis of osteosarcoma through inactivation of the Rb gene, from previous studies was considered to be associated with a good prognosis of osteosarcoma.

**Objective:** This study aims to determine the profile of CDK4 mutations in osteosarcoma cases and their relationship with gender, age, tumor location, metastases, histological grading, and pathologic staging in Dr. Sardjito.

**Methods:** This study was an observational analytic study using a retrospective cohort method. Data collection was performed by measuring CDK4 expression (BioCare Medical, USA, 1: 100) in paraffin block tissue assessed by immunohistochemical techniques. Samples taken were 50 osteosarcoma patients at RSUP Dr. Sardjito. The data that had been collected was then analyzed by using the Chi-Square statistical test, Fisher's exact test, and Mann Whitney.

**Results:** Of the 50 study subjects, 38 samples (76%) showed CDK4 overexpression, with 24 samples (63.2%) male, 24 samples (63.2%) having age <25 years, 31 samples (81.6%) tumors were located in the extremities, 17 samples (44.7%) with metastatic, 35 samples (92.1%) were high-grade osteosarcomas, and 21 samples (91.3%) were localized tumors. CDK4 mutation was not significantly related to sex ( $p = 1,000$ ), age ( $p = 0.729$ ), tumor location ( $p = 0.424$ ), metastasis ( $p = 0.750$ ), histological grading ( $p = 1,000$ ), and pathologic staging ( $p = 0.309$ ).

**Conclusion:** CDK4 overexpression was found in 76% of osteosarcoma patients, but it have no a significant association with gender, age, tumor location, metastasis, histological grading, and pathologic staging.

**Keywords:** CDK4 expression, osteosarcoma, metastasis, histological grading, and pathologic staging

## ABSTRAK

**Pendahuluan:** Osteosarkoma adalah keganasan tumor primer tulang yang paling umum menyumbang 30% -80% dari seluruh tumor primer tulang dengan distribusi bimodal yaitu usia 10-20 tahun dan usia lebih dari 60 tahun. Prognosis penderita dipengaruhi oleh berbagai faktor, salah satunya ekspresi *Cyclin-dependent kinase 4* (CDK4). *Cyclin-dependent kinase 4* sebagai salah satu jalur patogenesis osteosarkoma lewat inaktivasi gen Rb, dari penelitian sebelumnya dinilai berhubungan dengan prognosis osteosarkoma yang baik.

**Objektif:** Penelitian ini bertujuan untuk mengetahui profil mutasi CDK4 pada kasus osteosarkoma dan hubungannya dengan jenis kelamin, usia, lokasi tumor, metastasis, *grading* histologis, dan *pathologic staging* di RSUP Dr. Sardjito.

**Metode:** Penelitian ini merupakan penelitian analitik observasional dengan metode kohort retrospektif. Pengumpulan data dilakukan dengan pengukuran ekspresi CDK4 (BioCare Medical, USA, 1:100) pada jaringan blok parafin yang dinilai dengan teknik imunohistokimia. Sampel yang diambil yaitu 50 orang pasien osteosarkoma di RSUP Dr. Sardjito. Data yang telah dikumpulkan kemudian dianalisis dengan uji statistik *Chi-Square*, *Fisher's exact test*, dan *Mann Whitney*.

**Hasil:** Dari 50 subjek penelitian, 38 sampel (76%) menunjukkan overekspresi CDK4, dengan 24 sampel (63,2%) berjenis kelamin laki-laki, 24 sampel (63,2%) memiliki usia < 25 tahun, 31 sampel (81,6%) tumor berlokasi di ekstremitas, 17 sampel (44,7%) dengan metastasis, 35 sampel (92,1%) merupakan osteosarkoma derajat tinggi, dan 21 sampel (91,3%) tumor terlokalisasi. Mutasi CDK4 tidak berhubungan signifikan dengan jenis kelamin ( $p=1,000$ ), usia ( $p=0,729$ ), lokasi tumor ( $p=0,424$ ), metastasis ( $p=0,750$ ), *grading* histologis ( $p=1,000$ ), dan *pathologic staging* ( $p=0,309$ ).

**Kesimpulan:** Overekspresi CDK4 terdapat pada 76% pasien osteosarkoma, namun tidak memiliki hubungan yang signifikan dengan jenis kelamin, usia, lokasi tumor, metastasis, *grading* histologis, dan *pathologic staging*.

**Kata Kunci:** ekspresi CDK4, osteosarkoma, metastasis, *grading* histologis, dan *pathologic staging*