

# Keragaman karakteristik molekular faktor virulensi dan hubungan genotipe isolat cryptococcus dengan kepekaan terhadap obat antijamur = Biodiversity molecular characteristic virulence factors of cryptococcus and its relation to antifungal pattern / Robiatul Adawiyah

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## Abstrak

### <b>ABSTRAK</b><br>

Cryptococcus sp. adalah jamur yang sering menginfeksi penderita imuno-kompromis, termasuk AIDS. Jamur tersebut tersebar luas dan memiliki keragaman hayati (bio-diversity). Penelitian ini bertujuan untuk mengetahui keragaman karakteristik molekular, faktor virulensi dan hubungan kepekaan isolat Cryptococcus dengan obat antijamur. Metode: Penelitian ini menggunakan desain eksploratif-analitik dan dilakukan di Departemen Parasitologi FKUI dan CBS, Utrecht, Belanda pada tahun 2011-2014. Sebanyak 148 isolat tunggal Cryptococcus yang berasal dari 108 cairan otak pasien dan 291 isolat multipel Cryptococcus dari 48 sampel klinik (cairan otak, darah, cairan perikard) dilakukan penentuan spesies dan serotype. Sampel tunggal diidentifikasi menggunakan PCR dan sampel multiple dengan MALDI-TOF MS. Identifikasi genotipe pada sampel tunggal menggunakan RFLP-URA5 dan sampel multipel dengan AFLP. Uji kepekaan amfoterisin B, flusitosin, flukonazol, vorikonazol dan ketokonazol dilakukan dengan metode difusi cakram. Hasil: Sampel tunggal: Seluruh isolat tunggal adalah C. neoformans. Hasil identifikasi serotipe/varietas menunjukkan serotipe A 136 (91,9%) dan serotipe AD 12 (8,1%). Matingtype &#945; (85,8%) lebih banyak dibanding matingtype a (14,2%). Dari identifikasi genotipe diperoleh AFLP1/VN I (86,5%), genotipe AFLP3/VN III (8,1%), dan AFLP1A/VN II (5,4%). Pada umumnya genotipe masih sensitif terhadap antijamur, kecuali terhadap flusitosin (100% resisten). Terhadap amfoterisin B terdapat isolat yang susceptible dose dependent (SDD), yaitu AFLP1/VN I (10,2%) dan AFLP1A/VN II (25%), sedangkan terhadap flukonazol diperoleh isolat SDD dan resisten. Sampel multipel: Seluruh isolat multipel adalah C. neoformans; 269 isolat serotipe A, 6 isolat serotipe D, 16 serotipe AD dan 1 isolat serotipe AB. Sebanyak 18 (60%) pasien disebabkan oleh strain yang sama, 10 pasien (33,3%) disebabkan dua strain dan dua pasien (6,7%) disebabkan oleh tiga strain. Uji kepekaan menunjukkan 100% isolat sensitif terhadap amfoterisin B dan ketokonazol, 16 (21%) isolat resisten terhadap vorikonazol, 19 (24%) isolat resisten terhadap flukonazol dan 100% isolat resisten terhadap flusitosin. Kesimpulan: Terdapat keragaman karakteristik molekular dan faktor virulensi Cryptococcus. Seluruh isolat sensitif ketokonazol, namun resisten terhadap flusitosin. Terhadap amfoterisin B ada isolat yang SDD dan terhadap flukonazol ada yang resisten.

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### <b>ABSTRACT</b><br>

Cryptococcus sp. is a fungus that commonly infect immunocompromised patients, including AIDS. The fungus is cosmoplite and known has biodiversities. This study aim is to determine the characteristics of molecular diversity, virulence factors and its relation to Anti fungal Pattern. Methods: This study use exploratory-analytical design and performed at the Department of Parasitology, Faculty of Medicine and CBS, Utrecht, the Netherlands in 2011-2014. Out of 148 single Cryptococcus isolates originated from 108 patients and 291 cerebrospinal fluid Cryptococcus multiple isolates of 48

clinical samples (cerebrospinal fluid, blood, pericardial fluid) is the determination of the species and serotype. Single isolates were identified using PCR and multiple isolates were identified by MALDI-TOF MS. Identification of genotype on a single isolates using RFLP-URA5 and multiple isolates by AFLP. Susceptibility testing amphotericin B, flucytosine, fluconazole, voriconazole and ketoconazole performed by disc diffusion method. Results: Single sample: The entire single isolates are *C. neoformans*. Identification of serotype/variety shows serotype A 136 (91.9%) and the serotype AD 12 (8.1%). Matingtype  $\phi$  (85.8%) more than matingtype a (14.2%). Identification of genotypes obtained AFLP1/VN I (86.5%), genotype AFLP3/VN III (8.1%), and AFLP1A/VN II (5.4%). In general, all isolates are still sensitive to the anti-fungal, except against flucytosine (100% resistant). Some isolates show susceptible dose-dependent (SDD) to amphotericin B, they are AFLP1/VN I (10.2%) and AFLP1A/VN II (25%). Some isolates also obtained SDD and resistant to fluconazole. Multiple samples: The whole samples are *C. neoformans*; 269 isolates of serotype A, 6 isolates of serotype D, 16 serotype AD and 1 isolate serotype AB. 18 (60%) patients caused by the same strain, 10 patients (33.3%) due to two strains and two patients (6.7%) is caused by three strains. Susceptibility testing showed 100% of isolates are sensitive to amphotericin B and ketoconazole, 16 (21%) isolates were resistant to voriconazole, 19 (24%) isolates were resistant to fluconazole and 100% of isolates were resistant to flucytosine. Conclusion: There is a diversity of molecular characteristics and virulence factors of *Cryptococcus*. All isolates are susceptible to ketoconazole, but resistant to flucytosine. Some isolates SDD to amphotericin B and resistant to fluconazole.