ABSTRAK

Kajian Tentang Manifestasi Klinis, Respon Terapi dan Polimorfisme Gen *Merozoite Surface Protein* 1 dan 2 Penderita Malaria Falciparum di Provinsi Aceh

Latar Belakang: Sekitar 3.3 milyar penduduk dunia hidup di daerah berisiko malaria dan 1.2 milyar hidup di daerah berisiko tinggi, jumlah kasus lebih dari 1 per 1000 penduduk. Di Provinsi Aceh manifestasi klinis penderita malaria juga bervariasi, hal ini disebabkan oleh adanya variasi genetik, namun polimorfisme gen pada parasit di Provinsi Aceh sampai saat ini belum pernah diteliti.

Tujuan Penelitian: Penelitian ini bertujuan untuk menganalisis hubungan dari *gen msp1* dan *msp2* terhadap manifestasi klinis malaria dan respon terapi pasien malaria falciparum di beberapa Rumah Sakit di wilayah Provinsi Aceh.

Metode: Jenis penelitian observasional analitik, desain *cross-sectional.* Dimulai sejak 1 Januari 2013 sampai 31 Desember 2015. Sampel diperoleh dari 11 Kabupaten/Kota di Provinsi Aceh. Dilaksanakan dua tahap yaitu penelitian klinis dan laboratorium. Kriteria inklusi adalah pasien usia $\geq$ 18 tahun yang terdiagnosis malaria falciparum dengan pemeriksaan mikroskopis di Laboratorium Parasitologi FK-Unsyiah dan biomolekuler di Laboratorium Eijkman. Pasien diberikan terapi antimalaria dan dievaluasi respon terapi sesuai protokol WHO 2010. Analisis data menggunakan univariat dan bivariat.

Hasil: Sebanyak 90 malaria falciparum berjenis kelamin laki-laki 57,7% dan perempuan 42,2%, usia 21-30 tahun 46,7%. Seluruh isolat memiliki gen *msp1* dan *msp2*. Gen *msp1* yaitu 37,7% alel K1, 46,7% alel MAD20 dan 1,1% alel RO33. *Mixed infection* antara alel K1+MAD20 5,6%, alel K1+RO33 4,4%, alel MAD20+RO33 4,4%. Pada *gen msp2* yaitu 3D7 37,7% dan alel FC27 41,1%. *Mixed infection* pada msp1antara alel 3D7+FC27 21,2%. Hasil statistik pada msp1 alel K1+RO33 signifikan terhadap *severity* (OR: 28,50; 95% CI: 1,59–1532,32). Pada msp2 Alel multiple *FC27+3d7* signifikan terhadap gejala klinis malaria.

Kesimpulan: Ditemukan semua alel *msp1* dan *msp2.* Gangguan hati signifikan terhadap alel multipel *msp2* (FC27+3D7). Sementara tingkat *severity* signifikan hanya pada msp1 alel K1+RO33.

Kata kunci: msp1, msp2, manifestasi klinis, respon terapi, *P. falciparum,* Prov. Aceh

ABSTRACT

The Analysis Clinical Manifestation, Treatment Response, and the Polymorphism of Merozoite Surface Protein-1 and Merozoite Surface Protein-2 in *Plasmodium falciparum* Isolates From Aceh Province

Background: Estimated 3.3 million Indonesian population were infected with malaria including 1.2 million in the risk areas which *Plasmodium falciparum* dominant with *Annual Parasite Incidence* (API) 1.0/1,000 population. Unfortunatelly the manifestation of malaria are variated. However, extensive genetic polymorphism of the field isolates (msp1 and msp2) of *P. falciparum* represents a major obstacle for the development clinical manifestation and malaria treatment. In this study, genetic of msp1 and msp2 among *Plasmodium falciparum* field isolates from Aceh Province was analysed.

Methods: A observasional analytic methods (cross-sectional) was conducted. Survey of 90 participants enrolled in this study who were selected from positive malaria by microscopic test and 18 years of age from eleven General Hospitals in Aceh Province from 2013 due 2015. Malaria cases was an individual who had positive *P. falciparum* from microscopic examination. Data was collected by standard questionnaire, completed physical examination and laboratory tests (Hb, microscopic, and nPCR for msp1 and msp2 allele). All protocols of assignment and malaria treatment followed manufactures manual and WHO, 2010 guidelines. Univariate and bivariates statistical analysis (Odds Ratios, α: 0.05 with 95% CI) were performed with the SPSS 16.0 software package.

Results: Among 90 samples were 57,7% male and 42,2% female with the most cases ages between 21-30 years old 46,7%. Diverse allelic of msp1 and msp2 was identified in *P. falciparum* isolates from Aceh Province. Alelle analysis of msp1 revealed that 3 different alleles for msp1 47.8% (43/90) for K1 type, 57.9% (51/90) for MAD20 type, and 10% (9/90) for RO33, however 5.5% (5/90) for K1 and MAD20 and 4,4% (4/90) for K1 and RO33 finallly 4.4% (4/90) for MAD20 and RO33 were identified. For msp2, a total of 2 alleles 62,2% (56/90) for FC27 type and 58,9% (53/90) for 3D7 type) and 21,1% (19/90) for FC27 and 3D7 were identified. Statistical result for msp1 allele RO33 significant with severity (OR: 20,12; 95% CI: 3,15-209,56) and for msp2 3D7 allele were also. Early treatment failure (ETP) significant with K1 allele (OR: 8,94; 95% CI: 1,01-411,60).

Conclusion: Diverse allele types from Aceh Province was identified in msp1 and msp2 in *P. falciparum* patients. A high level of mixed allele was also observed, as was a high clinical manifestation and early treatment failure in msp1.

Key words; msp1, msp2, clinical manifestation, treatment response, *P. falciparum*, Aceh Province