

# Kemampuan Fagositosis Makrofag yang Berasal dari Monosit Pasien Tuberkulosis Tulang dan Hubungannya dengan Ledakan Oksigen dan Aktivitas Enzim Lisosom = Phagocytosis Abilities of Monocytes Derived Macrophages In Spondylitis Tuberculosis Patients and Their Correlation with Oxygen Burst and Lysosomal Enzyme Activities

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## Abstrak

Tuberkulosis (TB) sampai dengan saat ini masih merupakan salah satu masalah kesehatan utama di Indonesia. Sepuluh persen dari TB ekstraparu adalah TB tulang, dan sekitar 50% penderita TB tulang menyerang tulang belakang (Spinal Tuberkulosis). Respon tubuh terhadap *Mycobacterium tuberculosis* (M.tb) sehingga menimbulkan penyebaran ekstraparu, khususnya respon makrofag sebagai pertahanan lini pertama, masih belum sepenuhnya dimengerti. Makrofag menghasilkan molekul reactive oxygen species (ROS) sebagai hasil dari oxygen burst untuk mengeliminasi antigen. Nitrat Oksida (NO) dan mieloperoksidase (MPO) berperan pada oxygen burst Selain itu, Pada fagositosis terdapat organel lisosom yang di dalamnya terdapat enzim hidrolase (fosfatase asam dan beta glukuronidase) berguna pada pencernaan intraseluler. Penelitian ini menguji hipotesis bahwa ada gangguan fungsi makrofag pada pasien TB tulang belakang. Monosit diisolasi dari peripheral blood mononuclear cells (PBMC) dari lima pasien TB tulang belakang dan lima orang sehat sebagai kontrol. Monosit yang terisolasi dikultur dengan stimulasi dari macrophage colony-stimulating factor (M-CSF) selama tujuh hari untuk pematangan. Kemampuan fagositosis makrofag dinilai aktivitasnya terhadap sel darah merah domba (SDMD). Sedangkan nitrat oksida (NO), mieloperoksidase (MPO), betaglukuronidase, dan aktivitas fosfatase asam diselidiki dengan metode spektrofotometer.

Analisis data dengan menggunakan aplikasi SPSS versi 20. Kami menemukan bahwa monosit yang diisolasi dari PBMC pasien TB tulang belakang secara signifikan lebih sedikit dibandingkan dengan kelompok kontrol (2992.103 vs 6474.103 (sel / mL)) dan juga lebih sedikit makrofag yang melekat pada sel darah merah domba (SDMD) (264.103 vs 598.103 (sel / mL)). Namun, produksi NO (2346 vs 325,17 ( $\mu\text{mol}$  / gram protein)), dan MPO (570,7 vs 17,4 (unit / mg), beta-glukuronide (0,149 vs 0,123 (unit / mg)), dan asam fosfatase aktivitas (1776,9 vs 287,9 (unit / mg)) dari makrofag kelompok TB tulang belakang lebih tinggi daripada kelompok yang sehat serta korelasi negatif kuat dan bermakna antara fagositosis makrofag dengan tiap variabel tersebut. Selain itu, Terdapat korelasi positif lemah dan tidak bermakna antara kejadian fagositosis dan uji WST. Meskipun pengenalan rendah pada benda asing, proses makrofag intraseluler, termasuk aktivitas oksidatif dan fungsi lisosom, tinggi secara signifikan. Hasil ini menunjukkan penurunan fungsi makrofag pada pasien TB tulang belakang serta terdapat kemungkinan adanya dominasi imunitas non-spesifik bawaan pada infeksi TB tulang belakang

Tuberculosis (TB) is still one of the main health problems in Indonesia. Ten percent of extrapulmonary TB is bone TB and about 50% of people with bone TB affected to the spine. The immune response against *Mycobacterium tuberculosis* (M.tb), which causes extrapulmonary spread, particularly the response of macrophages as a first-line defense, is still not fully understood. Macrophages produce reactive oxygen species (ROS) molecules as a result of oxygen bursts to eliminate antigens. Nitric Oxide (NO) and myeloperoxidase (MPO) play a role in oxygen burst. Also, phagocytosis process involved lysosomal organelles in which there are hydrolase enzymes (acid phosphatase and betaglucuronidase), which have important role in intracellular digestion. This study examined the hypothesis about impairment of macrophage function in spondylitis TB patients. Monocytes were isolated from peripheral blood mononuclear cells (PBMC) collected from five spinal TB patients and five healthy people as controls. Isolated monocytes were cultured by stimulation of macrophage colony-stimulating factor (M-CSF) for seven days for maturation. The phagocytic ability of macrophages is assessed as to their activity on sheep red blood cells. Whereas nitric oxide (NO), myeloperoxidase (MPO), betaglucuronidase, and acid phosphatase activity were investigated by spectrophotometer methods. Data was analyzed using SPSS version 20. We found that monocytes isolated from PBMC of spondylitis TB patients were significantly less than in the control group (2992,103 vs 6474,103 (cells / mL)) and also fewer macrophages attached to red blood cells sheep (264,103 vs 598,103 (cells / mL)). However, NO production (2346 vs 325.17 ( $\mu\text{mol} / \text{gram protein}$ )), MPO (570.7 vs. 17.4 (units/mg), beta-glucuronide (0.149 vs 0.123 (units/mg)), and acids phosphatase activity (1776.9 vs 287.9 (units/mg)) of macrophages in the spondylitis TB group were higher than in the healthy group. There was a strong and significant negative correlation between phagocytosis of macrophages with each of the previous variables. There was no significant difference between phagocytic ability and the WST test. Although the recognition against foreign bodies was low, intracellular macrophage processes, including oxidative activity and lysosomal function, were significantly higher than control. This result showed a decrease of macrophage function in spondylitis TB patients as well as a possible dominance of non- specific immunity.