ABSTRACT

MECHANISM of HOST IMMUNE RESPONSE INCREASED AND VIRULENCE MYCOBACTERIUM AFTER ADDITION OF IRON IN THE GRANULOMA IN VITRO MODEL of INFECTION *Mycobacterium tuberculosis*

Anik Handayati

Background. *Mycobacterium tuberculosis* (*M. tuberculosis*), pathogenic bacteria is the cause of tuberculosis (TB) that infects nearly a third of the population of the world. More than 90% of those who are infected with m. tuberculosis develop asymptomatic infections are latent TB (LTBI), the ability to control the body's immune response to infection was strongly influenced by nutrition, especially intake of iron (Fe) and homeostasis of Fe host. The status of the host and the Fe infection m. tuberculosis complex because in addition to being important for the immune function of Fe, Fe is also required for growth and virulence of *M. tuberculosis*. This research aims to gain a comprehensive understanding of the influence of Fe against host immune responses during infection with *M. tuberculosis* with special emphasis on the latent TB, using in vitro model of granuloma infection *M. tuberculosis.*

Method. This research using in vitro culture model of granuloma infection m. tuberculosis, coupled with FeCl3 concentration 25 μ μ M, 50 M and control without the addition of FeCl3, which are incubated for 24 hours, 72 hours 168 hours. In vitro model of granuloma by peripheral blood mononuclear cell infect (PBMC) and MOI 1:10. Furthermore each end of incubation time culture is harvested, supernatant culture in measuring the levels of IFN-γ, TNF-α and IL-10 with Elisa method, whereas mRNA expression of icl, pfkA and katG analyzedfrom the cell lysat.

Result. The addition of iron (FeCl3) increases the levels of pro-inflammatory cytokines (IFN-γ, TNF-α) which significantly to the time of incubation ($p < 0.05$) and a wide range of concentrations ($p < 0.05$). Iron lowers the anti-inflammatory cytokines (IL-10) are significant with respect to time of incubation ($p < 0.05$) but not significantly to various concentrations of Fe. The addition of iron 50 μM, the effect on the levels of TNF-α, which showed a decrease in the incubation time of 168 hours. In addition iron 50 μM, the levels of IL-10 shows the increase is not significant. The addition of iron Fe concentration between groups does not affect the expression of genes of the icl, but there was a significant increase in incubation for 24 hours against 72 hours, while the incubation time is 24 hours and 72 hours against 168, decreased significantly. PfkA gene expression decreased significantly between control and concentration of iron 25 μM, the increase was not significant between the control and the concentration of iron 25 μM, increased significantly between iron 25 μM and 50 μM, decreased significantly between incubation time. KatG gene expression increases significantly at concentrations of 50 μM, decreasing significantly to incubation time.

Conclusion. It can be concluded that the addition of iron concentration of 25 μM and 50 μM increases the immune response, through increased pro-inflammatory cytokines (IFN-γ, TNF-α) and anti-inflammatory cytokines (IL-10). The addition of iron 25 μM and 50 μM does not affect virulence of mycobacterium, through the expression of the icl and pfkA.

Key words: Iron, IFN-γ, TNF-α, IL-10, icl gene, gene pfka gene and katG