

## FULL ABSTRACT

Effect of Vitamin D Supplementation on Tuberculosis Infection among Under-Five Healthy Children Exposed to *Mycobacterium tuberculosis*.

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The dissertation is written in Indonesian.

**Background.** Prevalence of tuberculosis (TB) in Indonesia remains high that directly increase the risk of infection among under-five healthy children, whose immune systems are not fully developed. This children can suffer severe illness, disability, and death. It is important to boost the immune system among under-five healthy children, but it has not yet be a concern in the TB control program now. Vitamin D is known to affect innate and adaptive immunity, inhibit bacterial invasion, therefore will protect from tuberculosis infection. **Aim.** This study aims to evaluate the effects of vitamin D supplementation towards the incidence of tuberculosis infection among under-five healthy children with *Mycobacterium tuberculosis* contact through levels of vitamin D, IFN- $\gamma$ , cathelicidin, phagocytic activity of macrophages, and vitamin D receptor genetic polymorphisms in vivo and in vitro. **Method.** A randomized, double-blind, placebo-controlled trial was conducted. Initial screening among 225 under-five children with TB contact in 22 primary health cares in Padang was done. Among 136 children were eligible for this study, only 66 of them were analyzed. The inclusion criteria was under five children whose tuberculin skin test were negative (healthy). Vitamin D3 supplementation was given two times, each 25.000 IU, with an interval of 6 weeks, and monitored until 12 weeks. Measurements were performed at baseline and repeated after 12 weeks towards the indicators levels of vitamin D, IFN- $\gamma$ , cathelicidin (ELISA) and macrophage phagocytosis activity. RVD gene was also assessed (PCR). Categorical variables were assessed with chi-square test and continuous variables were compared by using independent t-test. Ethics approval was obtained from the Ethics Committee from Faculty of Medicine, Andalas University. **Results.** There were no difference of TB infection between intervention and placebo groups ( $p=0.855$ ). Baseline characteristics showed, the mean levels of vitamin D  $<30$  ng / ml, low IFN- $\gamma$ , normal cathelicidin, and phagocytic activity  $> 80\%$ . Most of the subjects have mutant FokI (93.9%), ApaI (72.7%), TaqI (94%), and mutant BsmI was found fewer (25.8%). Vitamin D supplementation significantly increased vitamin D level with the average of  $28.47 \pm 7.19$ ,  $p = 0.003$ . There were no significant differences in mean levels of vitamin D, IFN- $\gamma$ , cathelicidin, and macrophage activity between the two groups. BsmI has a role in the alteration of vitamin D level, this study showed significant differences between the two groups ( $p = 0,003$ ). **Conclusion.** Supplementation of vitamin D for 12 weeks among under-five healthy children with TB contacts did not affect to the incidence of TB infection, but it has increased of vitamin D serum levels. There was an association between mutant genes of VDR BsmI to the rise of vitamin D levels.