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**EFFECT OF D543N AND TGTG DELETION 3' UTR *Nramp1* GENE
POLYMORPHISMS AGAINST PULMONARY TUBERCULOSIS AT
MELAYU ETHNIC OF SOUTH SUMATERA**

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INTRODUCTION

Pulmonary tuberculosis is still a major health problem with incidence on the world each year 139/100000 population and caused 1,8 million people death. In Indonesia there are 234/100000 population incidence of tuberculosis, 515677 new cases and 88000 death each year¹. Immunological finding showed that only 10% of population infected by *Mycobacterium tuberculosis* will get pulmonary tuberculosis, 90% were not get the disease. It is indicated that genetic factors controlling immune responses have major role in the pathogenesis of tuberculosis². Some studies showed 3 kind of genes have major contribution: *Mbl* gene encoding surface protein in attachment process. *Nramp1* gene encoding protein in phagolysosome, responsible for phagocytosis process and *Vdr* gene encoding protein that regulate cellular immunity³. In Gambia and China, substitution of G to A at codon 543 *Nramp1* gene altering aspartate amino acid (D) to asparagines (N) and 4 bases deletion of TGTG at 3'UTR *Nramp1* gene cause

people susceptible to pulmonary tuberculosis. In contrast in Cambodia, these polymorphisms have protective effect. The studies in Jakarta Indonesia showed that these polymorphisms have no effect to susceptible for pulmonary tuberculosis but in Surabaya Indonesia 4 bases deletion of TGTG at 3'UTR was susceptible to pulmonary tuberculosis^{4,5}.

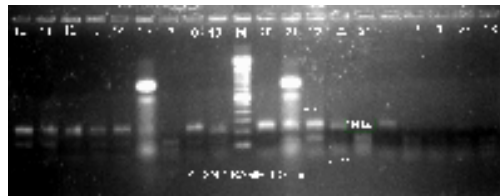
METHOD

The design of study was observational case control study. Pulmonary tuberculosis patients as case group were matched with healthy person group with tuberculin positive test as control group. The aims of the study was to analyze susceptible risk factor of Melayu ethnic of South Sumatera population to pulmonary tuberculosis. Polymorphism of D543N was detected by PCR-RFLP using *AvaII* enzyme and 4 bases deletion of TGTG at 3'UTR was detected by PCR-RFLP using *FokI* enzyme⁶.

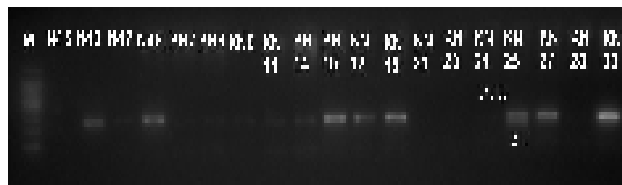
RESULT AND DISCUSSION

We recruited 40 cases and 40 controls subject. The results showed that genotype distribution of codon 543 Nrampl: GG:GA:AA were 20% : 37,5% and 42,5% in cases group, and 35% : 42,5% and 22,5% in control group respectively. Value of p 0,045, Odds Ratio 3,31 in confidence interval 95%. These results indicated that mutation G to A at codon 543 Nrampl gene has influence in susceptibility the South Sumatera Melayu to pulmonary tuberculosis. The genotype distribution of 4 bases deletion of TGTG at 3'UTR: +/+ : +/- : -/- were 40% : 32,5% and 27,5%

in cases group, and 22,5% : 27,5% and 50% in control group respectively Value of p 0,034, Odds Ratio 0,31 in confidence interval 95%. The results indicated that this deletion has protective effect to pulmonary tuberculosis. Both two results were different to previous studies. Genetic factor is a specific variable which related to race or ethnic of population. It is also influence with geographic and migration of pupolation⁷⁻⁹.



Picture 1. PCR-RFLP result digested by *AvaII* enzyme of D543N *Nrampl* gene. M is marker. Undigested 244 bp was homozygote wild type, digested 126 bp, 79 bp and 39 bp (not seen) was homozygote mutant and 4 band 244 bp, 126 bp, 79 bp and 39 bp was heterozygote.



Picture 2. PCR-RFLP result digested by *FokI* enzyme of TGTG Deletion 3'UTR *Nrampl* gene. M is marker. Undigested 244 bp was homozygote wild type, digested 240 bp, 211 bp and 29 bp (not seen) was homozygote mutant and 4 band 244 bp, 211 bp, 29 bp was heterozygote.

CONCLUSION

The polymorphism of codon D543N *Nrampl* gene have susceptible effect to pulmonary tuberculosis in Melayu South Sumatera but 4 bases deletion of TGTG at 3'UTR *Nrampl* gene in the population have protective effect.

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