Effect of smoking and alcohol consumption on pulmonary tuberculosis among Batak ethnic population in Medan, Indonesia

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Abstract. Simultaneous consumption of tuak, a traditional alcoholic beverage, and smoking is prevalent among Batak ethnic group in Indonesia. This research was to find out the association between smoking and alcohol consumption with the risk of Pulmonary Tuberculosis (PTB) in Batak ethnic group in Medan, Indonesia. A matched case-control study was conducted on 100 PTB patients and 100 healthy individuals group. Smoking and alcohol consumption was self-reported. Data were analyzed with Epi Info program. Smoking and alcohol consumption habit is a significant difference in case and control group (p<0.01). After conditional logistic regression analysis with non-smoking and non-alcohol consuming as a comparative, the Odds Ratio (OR) for the smoking-only group was 4.08 (95% CI: 1.28-13.05). For the alcohol-only consuming group was 1.83 (95% CI: 0.11-28.95) and for the smoking and alcohol consuming group was 13.7 (95% CI: 4.02-46.94). There is an association between smoking and alcohol consumption and the risk of PTB in Batak ethnic group in Medan, Indonesia.

1. Introduction
Previous studies showed an association between smoking, alcohol and the increased risk of PTB[1-4]. Smoking may lower the immune system by affecting the function of epithelial permeability, cilia movement and macrophage[5]. Alcohol consumption weakens the immune system via direct or indirect toxic effect of alcohol through nutrient deficiency and the other alcohol-related medical condition such as cancer and depression[5]. It is common for Batak ethnic group to consume tuak, a traditional beverage containing alcohol. Tuak is usually enjoyed in a lapo, a traditional coffee shop while smoking cigarettes[6]. Based on this condition, this study was conducted to find out the association between smoking and consuming alcohol and the risk of PTB in the Batak ethnic group in Medan, Indonesia.
2. Method

2.1. Cases and controls
It is a matched case-control study. Cases were PTB patients who were recruited from several TB centers in Medan, Indonesia, from November 2012 to November 2013. The inclusion criteria in the case group were the newly diagnosed PTB patients, age 16-55 years old, Batak ethnic, have symptoms of PTB, positive sputum smear and chest radiography consistent with the active disease. The exclusion criteria in the case group were HIV positive, have diabetes mellitus and other severe diseases, and taking immunosuppressive drug.

The sample size used a matched case and control formula. The sample size was 100 for case group and 100 for the control group. Cases were found by continuous sampling and control group matched in sex, age and ethnicity were healthy subjects with ordinary chest X-ray and no prior history of PTB.

All of the subjects were interviewed, and informed consents were obtained. Smoking and alcohol consumption were self-reported. The habits of matter were into smoking-only, alcohol-only consuming, smoking & alcohol drinking and non-smoking & non-alcohol drinking. This research has been approved by the Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.

2.2. Statistical analysis
The association between smoking and alcohol consumption and PTB was through Odds Ratio (OR) calculation with 95% confidence interval (95% CI) with p-value <0.05 to be statistically significant. The conditional logistic regression analysis was conducted by separating the study population into smoking-only, alcohol-only consuming, smoking and alcohol-consuming, with non-smoking and non-consuming alcohol group was used as a control. The data obtained were processed and analyzed by using Epi Info program.

3. Results

Table 1. Characteristic of the subject in case and control group.

| Characteristics | TB (Case) | Non-TB (Control) |
|----------------|-----------|------------------|
|                 | n   %    | N   %            |
| Sex            |         |                  |
| Male           | 70 70   | 70 70            |
| Female         | 30 30   | 30 30            |
| Age (Years)    |         |                  |
| 16-25          | 32 32   | 32 32            |
| 26-35          | 39 39   | 39 39            |
| 36-45          | 20 20   | 20 20            |
| 46-55          | 9 9     | 9 9              |
| Ethnic         |         |                  |
| Batak          | 100 100 | 100 100          |

The characteristics of the subjects comprising age, sex, and ethnic group in the case and control groups were in table 1. Gender, age and racial characteristic between case and control group, were matched.

Table 2. Smoking and alcohol consumption habits in case and control group.

| Habits                          | TB (case) | Non-TB (control) | x²   | p-value |
|--------------------------------|-----------|------------------|------|---------|
|                                | n   %    | N   %            |      |         |
| Non-smoking & non-alcohol consuming | 37 37   | 61 61            |      |         |
| Smoking-only                    | 19 19   | 22 22            | 21.85| < 0.01  |
| Alcohol-only consuming          | 1 1     | 3 3              |      |         |
| Smoking & alcohol consuming     | 43 43   | 14 14            |      |         |
| Total                           | 100 100 | 100 100          |      |         |

MxN table epi info
There was a significant difference in smoking and alcohol consumption habits in case and control group (p<0.01).

**Table 3. It is an association between smoking and alcohol consumption with PTB.**

| Habits                              | TB (Case) | Non-TB (Control) | OR  | 95% CI       | p-value |
|-------------------------------------|-----------|------------------|-----|--------------|---------|
| Non-smoking & non-alcohol consuming | 37        | 61               | 1   | 1            |         |
| Smoking-only                        | 19        | 22               | 4.08| 1.28-13.05   | 0.01    |
| Alcohol-only consuming              | 1         | 3                | 1.83| 0.11-28.95   | 0.66    |
| Smoking and alcohol consuming       | 43        | 14               | 13.7| 4.02-46.94   | <0.01   |

Conditional Regression Logistic

The conditional logistic regression test was conducted by separating the study population into four different group such as smoking-only, alcohol-only consuming, smoking and alcohol consuming, with the non-smoking and non-alcohol consuming group as the control. The Odds Ratio (OR) for the smoking-only group was 4.08 (95% CI: 1.28-13.05); for the alcohol-only consuming group was 1.83 (95% CI: 0.11-28.95), and for the smoking and alcohol consuming group was 13.7 (95% CI: 4.02-46.94) (Table 3).

4. **Discussion**

This study found a difference in smoking and alcohol consumption habits between pulmonary tuberculosis patients compared to healthy subjects in the Batak population. Similar to previous studies, this study also showed an association between smoking and alcohol consumption and the risk of PTB. Review of 34 previous studies from various countries, it was found out that smoking increased the risk of infection caused by *Mycobacterium tuberculosis*, tuberculosis development, and tuberculosis-caused mortality. Meta-analysis study of 24 previous studies was in a separate analysis: TB infection (6 studies), TB development (13 studies), and tuberculosis-caused mortality (5 studies) - showed a relationship between smoking and TB infection and TB development after sex, age, and the other confounding factors were adjusted. The relationship between smoking and TB development was also found in the passive smokers.

Regarding alcohol consumption, in a meta-analysis study, Lömroth concluded that Relative Risk (RR) for heavy drinkers consuming more than 40 grams of alcohol per day was 2.94 (95% CI: 1.89-4.59). Rehm reported similar results in a meta-analysis study and found that alcohol influences the incident of TB, TB treatment outcomes, increased risk of re-infection, and drug-resistant TB. A meta-analysis by Imtiaz found alcohol increased TB incident, death and TB risk rose as ethanol intake increased.

The specific mechanism of cigarette smoke on respiratory infections and inflammation is further study. Smoking directly affects the integrity and permeability of the respiratory alveolar macrophages to produce the inflammatory mediators, reactive oxygen species and proteolytic enzymes. Cigarette smoke also minimizes alveolar macrophages phagocytic ability. Mice exposed to cigarette smoke during experiment has more *M. tuberculosis* in their lungs and spleens compared to the control group. An increased number of intracellular *M. tuberculosis* in human macrophages was in smokers compared to non-smokers.

Alcohol can cause the direct toxic effect on the human immune system causing susceptibility to TB. Alcohol lowers the response of Nitric Oxide system against mycobacterial infection and inhibits phagocytosis. The result of the experiments carried out on mice indicates that alcohol may inhibit granuloma formation, produce IL-2, IFN-gamma, and proliferation of CD4. Migration Inhibition Factor (MIF) is a cytokine whose production is inhibited by the presence of alcohol. Alcohol also lowers the production of cytokines such as TNF-alpha, IL-1, and IL-6. Alcohol can also affect the activation of T cells causing Th2 population (humoral immunity) to dominate the Th1 population (cellular immunity responsible for TB infection). These changes disrupt the balance between the two
basic types of immune system, and therefore, lowering the immune defense and increasing the susceptibility to TB[13].

This study was explicitly carried out on Batak ethnic group based on the consideration of their habit of drinking tuak, a traditional alcoholic beverage. Most subjects said that they drink tuak in the lapo, traditional coffee shop while smoking. Tuak is from mayangenauc also known as aren (Arengapinnata). The enau or aren tree is tapped to collect its juice known as nira. After this nirais mixed with raru, a kind of wood to add more taste and alcohol content. Raru is the main ingredient in the fermentation process. Since enau or arenis not in Medan, tuak can also be made from the tapped coconut tree[6]. The alcohol content found in tuak is quite high compared to other alcoholic beverages, especially the tuak made from the mixture of nira and raru. The previous study revealed that the content of ethanol in pure tuak ranges from 12.07 to 21.88%, and in tuak made from the mixture of nira and raru the alcohol content can be up to 47.04%[15].

Study about smoking and alcohol consumption as a risk factor for tuberculosis based on ethnic has been done in India and the results were similar to this study. Among Tribal population in India, a person who was both smoker and alcohol-consuming increased the risk of pulmonary tuberculosis than smoking and alcohol consumption only[16].

There was some limitation when conducting this study. The amount of the alcohol consumed, alcohol content and smoking severity index could not be determined. Though sex, age, and ethnicity of the case and control groups were matched, other confounding factors such as education level, nutrition, drug abuse, air pollution, occupation and socio-economic status remain unmatched. The limitation of the analysis in this study was related to the sample size especially the sample size for the alcohol-only consuming group.

Further study on the association between smoking, alcohol consumption and the risk of PTB using a large sample size is needed to be conducted with a careful assessment of the confounding factors to obtain a better understanding of the possible causal pathways between smoking and alcohol consumption and pulmonary tuberculosis.

5. Conclusion
Smoking and alcohol consumption are risk factors for pulmonary tuberculosis occurring in Batak ethnic group in Indonesia. This information is essential for TB control and the strategy to prevent the incidence of tuberculosis in Indonesia whose population comprising various ethnic backgrounds and cultures.

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