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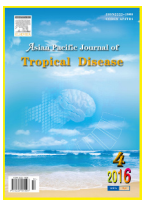

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The levels of *Toxoplasma gondii* profilin and adiponectin in obese patients complicated with or without metabolic syndrome as compared to non-obese patients

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ABSTRACT

Objective: To find out the levels of *Toxoplasma gondii* (*T. gondii*) profilin and adiponectin in obese patients complicated with or without metabolic syndrome as compared to non-obese patients.

Methods: This study was an observational analytic study using cross sectional design. After interview, the subjects were performed with a anthropometric test and then a metabolic syndrome panel. The levels of profilin and adiponectin were detected by using ELISA method.

Results: There was a significant difference of *T. gondii* profilin between the obese complicated with metabolic syndrome group and the non-obese group (P = 0.00; α = 0.05), as well as the metabolically healthy obese, in which the level of profilin was significantly higher in the group as compared to the non-obese group (P = 0.001; α = 0.05). Adiponectin level of the obese complicated with metabolic syndrome group was significantly lower as compared to the metabolically healthy obese and non-obese group (P = 0.001; α = 0.05).

Conclusions: The level of *T. gondii* profilin in obese patients was higher than that in the non-obese, whereas the level of adiponectin in obese patients complicated with metabolic syndrome was lower than that in the obese without metabolic syndrome and non-obese patients.

1. Introduction

Metabolic syndrome is a cluster of clinical cardiovascular risk factors including obesity, dyslipidemia and hypertension. This syndrome has a relationship with the pathologic mechanism of cardiovascular diseases. Obesity, a risk factor of metabolic syndrome, generally was abdominal or visceral obesity. The obesity prevalence around the world and its relationship with the metabolic syndrome increase rapidly. In the United States, the prevalence of overweight and obesity combined (body mass index (BMI) ⩾ 25) was 71.1% (95% *CI*: 68.0%–74.2%) among men and 65.5% (95% *CI*: 61.8%–69.3%) among women, and the prevalence of obesity (BMI ⩾ 30) was 33.3% (95% *CI*: 30.5%–36.2%) among men and 35.8% (95% *CI*: 32.3%–39.4%) among women[1]. The number of obesity increases rapidly year by year. It was reported that over 300 million of adults have obesity. In the United Stated, there are 280 000 people passing away every year[Please confirm my revision] as a result of obesity in which it becomes the trigger for some diseases such as heart attack, arthritis, diabetes mellitus type 2 and hypertension[2].

Apicomplexan parasites spur actin-dependent gliding movements, which are very important to invade the host cell. Profilin is a key contributor in actin polymerization. *Toxoplasma gondii* (*T. gondii*) has profilin-like protein which will be recognized by toll-like receptor (TLR-11) of the natural immune system and followed by inflammation of the host cell. The damage to the host cell is known correlated to a gene encoding profilin in *T. gondii* parasites. When profilin does not play a role in the cell growth, this protein will stimulate gliding motility to invade the host cell and cause virulence in mice. Besides, the parasites

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The study protocol was performed according to the Helsinki declaration and approved by Health Research Ethics Comittee of Medical Faculty of Brawijaya University with the number of 54/EC/KEPK/ 02/ 2012, and the informed written consent was obtained from the patients.

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which do not have profilin are not able to induce TLR-11 to produce interleukin (IL)-12 (cytokine defense of the host cell) both *in vivo* and *in vitro*. Thus, profilin is an important element of the two aspects of *T. gondii* infection. Profilin plays a role in motility when the ligand of the natural immune system is recognized by the microbial host cell[3].

Emerging researches on etiology of obesity has investigated the potential role of environmental infections, a concept referred to as "infectobesity", as well as gut microbiota in obesity pathogenesis. An understudied pathogen of the potential interest in obesity researches is the protozoan parasite *T. gondii*. Experimentally, in rats, *T. gondii* infection was associated with significant weight gain after 30 days of inoculation followed by weight loss over the next 60 days. The authors hypothesized that weight gain may have been due to direct central effects, *i.e.*, behavioral changes, such as increased food intake associated with *T. gondii* cysts in the brain and/or indicated central effects, *e.g.*, altered hypothalamic function (*e.g.*, appetite regulation) caused by peripheral tissue inflammation. Weight related effects of *T. gondii* infection may be influenced by strains. In another animal study, two different strains of *T. gondii* had opposite effects on body weight[4].

Reeves *et al.*, reported that individuals who were positive for *T. gondii* immunoglobulin G had approximately twice the odds of being obese as compared to seronegative individuals, but they were unable to determine if there is a causal relationship between *T. gondii* seropositivity and obesity[5]. However, how the changes in the quality of adipocytes in adipose tissue after exposure to the pathogen is still very little known. Besides, the prevalence of infectious diseases in developing countries is still high and it is mentioned that there is a relationship between infection and obesity. The study conducted by Susanto *et al.*[6] resulted that the exposure of *T. gondii* profilin on subcutaneous fat cell cultures can raise the levels of IL-6 and tumor necrosis factor-alpha (TNF-α) as well as lower the level of TLR-11, and the increase of the levels of IL-6 and TNF-α in the subcutaneous fat cells indicates the occurrence of adiposopathy and metabolic syndrome caused by *T. gondii* profilin infection.

The study conducted by Iskandar *et al.*[7] states that there is a significant difference between the level of profilin of the obese and healthy individuals. The study also mentions that the increase of profilin level in obese individuals is associated with the increase of IL-6 and IL-12 as well as inflammatory cytokines in obese individuals. Although the correlation is weak, it suggests that in obese individuals there are increases of the level of profilin triggering increases in inflammatory cytokines such as IL-6 and IL-12, which is an early marker of adipocyte dysfunction in obese individuals.

Adiponectin is an anti-inflammatory cytokine which is secreted exclusively by adipocytes in large quantities in plasma. Adiponectin, which is mainly produced in white adipose tissue, characteristically differs from most adipokines as it is negatively correlated with obesity. In healthy people, adiponectin plays a role in preventing the development of vascular changes and the failure of glucose and fat metabolism induced by various factors such as chemicals, excessive eating and so on. The physiological role of adiponectin has not yet been fully elucidated, but it is believed that it has the ability to reduce glucose, triglycerides, and free fatty acids and it plays a major role in the pathogenesis of metabolic syndrome. Adiponectin has a role in increasing the sensitivity of insulin receptors, *i.e.* as anti-inflammatory and anti-atherogenic. On the state of obesity and insulin resistance, the level of adiponectin decreases. While in the state of weight loss, there is an increase of the level of adiponectin. The increase and decrease of the level of adiponectin are influenced by various factors such as TNF-α and IL-6[8].

This study aimed to investigate the basic mechanism of metabolic syndrome pathogenesis, the role of *T. gondii* parasite infection, as well as determine the relationship between profilin increase and adiponectin as anti-inflammatory adipocytokine in obese individuals with or without metabolic syndrome.

2. Materials and methods

2.1. Ethical clearence and informed concent

The study protocol was performed according to the Helsinki declaration and approved by Health Research Ethics Comittee of Medical Faculty of Brawijaya University with the number of 54/ EC/KEPK/ 02/ 2012, and the informed written consent was obtained from the patients.

2.2. Study protocal

The research was conducted from May 2012 to September 2012. Sampling was collected consecutively, *i.e.* the obese patients who came to the central laboratory of Saiful Anwar Hospital Malang, from May to September 2012.

A patient is called an obese one if his/her BMI is greater than or equal to 27 in accordance with the criteria of World Health Organization-Western Pacific Region which are suitable for people of Asia, including Indonesia. The criteria for metabolic syndrome is taken from the National Cholesterol Education Program Adult Treatment Panel in 2001 in which there are at least three main features: the abdominal circumference is over 102 cm in men and more than 88 cm in women; the triglyceride blood level is over 150 mg/dL; the high-density lipoprotein (HDL) cholesterol is lower than 40 mg/dL in men and 50 mg/dL in women; the blood pressure is above 130/85 mmHg; and the fasting blood sugar is over 110 mg/dL.

The anthropometric examination, blood glucose, HDL cholesterol, total cholesterol and triglycerides were done in the central laboratory of Saiful Anwar Hospital Malang by using enzymatic method.

The level of *T. gondii* profilin and adiponectin were measured in the Molecular Physiology Laboratory of Medical Faculty of Brawijaya University by using ELISA method.

2.3. Processing and data analysis

The entire technical data processing were analyzed in computer software with Lavene's test and then followed by *t*-test and correlation test using software statistical product and solution service 17 PS (15 PS SPSS) ($P < 0.05$).