

Curcumin: Boosting the immunity of COVID-19-vaccinated populations

Sry Suryani Widjaja,
Rusdiana Rusdiana, Rina Amelia¹

Department of Biochemistry, Faculty of Medicine, Universitas Sumatera Utara, Medan, ¹Department of Community Medicine/Public Health, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

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ABSTRACT

The ongoing, highly infectious COVID-19 pandemic has prompted various drugs, vaccines, and phytochemical research to control the disease. The accelerated development of vaccines showed the importance of immune boosters against the virus. This study aims to elucidate the role of curcumin, a phytochemical with an immunomodulatory profile potentially able to boost immunity after vaccination. Eighty participants were enrolled to receive curcumin supplementation ($n = 40$) and without ($n = 40$) after the first vaccination until 4 weeks after the second vaccination. Total antibody formation for SARS-CoV-2 was measured using an enzyme-linked immunosorbent assay 4 weeks after the second vaccination. The average antibody formed in groups treated with curcumin supplementation showed a statistically significant increase compared to the control group (262.6 ± 324.2 vs. 42.8 ± 53.5 , $P < 0.01$). Age, sex, and comorbidities did not affect the production of antibodies within groups. Curcumin showed potential as a complementary supplementation during the period of vaccination as it can increase antibodies produced post vaccinations. Further investigation should be conducted on more subjects and a longer period in concordance to vaccine boosters and emerging new variants.

Key words: COVID-19 vaccines, curcumin, neutralizing antibodies, receptor-binding domain SARS-CoV-2 antibody

INTRODUCTION

The emerging novel coronavirus disease or known as COVID-19 was first discovered in China, Wuhan City, in December 2019, rapidly turned into a global pandemic. The high transmissibility and its varying spectrum of severity cause high mortality and morbidity in infected patients.^[1,2] COVID-19 was announced by the WHO as an international health emergency as the number of cases

surged to 352 million cases worldwide, with the death toll exceeding 1.6 million cases in late January 2022.^[3] COVID-19 is a disease caused by RNA betacoronavirus which has similarities to SARS-CoV.^[4,5] In Indonesia, COVID-19 was detected in early March 2020. Insofar, as more than 4.2 million cases have been recorded, with a death toll of 144,000 cases.^[6] The colossal effect of COVID-19 in every aspect of life has urged the world to immediately develop various types of vaccines and treatment plans which were expected to control the disease.

Our body's immune system is by far the best defense against various microorganisms invasions. With a properly functioning immune system, infections would be resolved appropriately.^[7] The COVID-19 treatment plans, apart from antivirals, are accompanied by the provision of nutrients

Address for correspondence:

Dr. Sry Suryani Widjaja,
Jl. Joserizal No. 33E/51, Medan 20214, Indonesia.
E-mail: sry.suryani@usu.ac.id

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Table 1: Characteristics of patients, antibody levels, and clinical parameters

	Number of patients (n)	RBD SARS-CoV-2 antibody	
		Mean±SD	P
Age (years)			
18-59	65	171.5±278.2	0.161
>60	15	68.4±77.0	
Sex			
Male	39	128.8±281.0	0.965
Female	41	174.4±230.5	
BMI			
Normal weight	65	150.8±254.2	0.963
Overweight	12	149.9±299.4	
Obese	3	192.5±141.8	
Comorbidities			
Present	18	281.9±349.5	0.13
Breast cancer	2		
CAD	2		
CKD	1		
Dyslipidemia	3		
DM	1		
Hypertension	6		
Rheumatoid arthritis	1		
Stroke	1		
Tuberculosis	1		
No comorbidities	62	114.5±210.3	
Turmeric			
Treatment group	40	262.6±324.2	<0.01
Control group	40	42.8±53.5	

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RBD: Receptor-binding domain, SD: Standard deviation, BMI: Body mass index, CKD: Chronic kidney disease, CAD: Coronary artery disease, DM: Diabetes mellitus

and supplements aimed to overcome inflammation, oxidative stress, and cytokine storms.^[8] Several types of phytochemicals can reduce the severity of viral infections, their anti-inflammatory, antioxidants, and antiviral effects, thus improving immunity.^[8,9] These nutrients are utilized to overcome various pathological effects caused by COVID-19 infection, so the use of these natural components can be alternative prevention or supportive treatment of COVID-19.^[10]

The curcumin (diferuloylmethane) found in turmeric (*Curcuma longa*) has antibacterial, antiviral, antifungal, as well as antioxidant and anti-inflammatory effects.^[11] The antioxidant effect of curcumin is obtained by neutralization of free radicals and increasing antioxidant enzyme production, thus hinting at a potential for COVID-19 treatment.^[2,10,12] In a systematic review of six randomized controlled trials on 558 patients, curcumin as an adjunct therapy in COVID-19 patients improved clinical outcomes and reduced hyperinflammatory effects.^[13]

The dose-dependent immunoeediting potential of curcumin to suppress or increase T-cell production has also been

recognized in several cases.^[14] Not only Treg inhibition but curcumin also increase the function of effector T-cells. Curcumin treatment on myeloid-derived suppressor cells showed an increment in CD8+ T-cell number and reduction of Treg cells, enhancing antitumor immune response.^[15] The role of curcumin in enhancing immunity has also been documented in several clinical investigations. In both colon and lung cancer studies, curcumin therapy increases Th1 cells by promoting Treg cell conversion to Th1 cells and markedly decreases Treg cells through Foxp3 suppression and expression of IFN- γ .^[16,17]

More studies were put on the effects of curcumin on T-cells and the immune system. However, very few nonanimal studies can be found to support the effect of curcumin on B memory cell production, which contributed to humoral immunity producing antibodies. This study aims to elucidate the difference in antibody formation between vaccinated populations subjected to routine turmeric powder supplement compared to subjects who did not receive turmeric supplementation.

MATERIALS AND METHODS

This investigation was performed in a cohort of 80 recipients of the COVID-19 vaccine enrolled from March to October 2021. In the test group ($n = 40$), each subject was given 5 g of turmeric powder to be consumed daily for 8 weeks by diluting the powder in 150 ml of room-temperature water. The control group ($n = 40$) did not receive any supplementation. Exclusion criteria included COVID-19, pregnancy, or malignancy during the study period. All subjects were administered two doses (0.5 ml each) of CoronaVac[®] vaccine 4 weeks apart. The assessment for quantitative COVID-19 spike receptor-binding domain antibodies (S-RBD) was carried out using the enzyme-linked immunosorbent assay 4 weeks after the second dose.

Blood sera samples from patients were obtained under the protocols approved by the Ethical Committee through the Institutional Review Board of Universitas Sumatera Utara, Indonesia (Ethical Clearance No. 526/KEP/USU/2021). All participants had signed the informed consent and the research had been carried out according to the Declaration of Helsinki.

RESULTS

Among the total of 80 participants enrolled, 40 postvaccinated patients were given a solution of 5 g of turmeric powder. Measurement of quantitative RBD SARS-CoV-2 antibody was carried out 4 weeks after the second vaccine administration. "Characteristic of patients were shown in Table 1.

The results showed a statistically significant difference in the value of the quantitative RBD SARS-CoV-2 antibody

level between the postvaccine group that was given turmeric powder compared to the control group ($P \leq 0.01$), while age, sex, body mass index, and the presence of comorbidities did not. The average antibody level measured across the subjects was 152.2 IU/ml.

DISCUSSION

Amid the COVID-19 pandemic, it is essential to keep up with the urgency on preventive measures, cures, and a keener effort to elucidate the role and formulations of herbs. The health-promoting effect of curcumin has been well established in traditional medicine practices. Curcumin shows a significant role in the immune system through gene and enzyme modulations for disease prevention as well as a supplementary treatment. This study is the first study to investigate the effectiveness of curcumin on immune system stimulation in the vaccinated COVID-19 population.

Curcumin exerts its immune-boosting effects through free radical neutralization and antioxidant enzyme enhancement.^[10] The inflammatory modulation actions of curcumin in COVID-19 pathogenesis commenced by inhibition of inflammatory transcription factors such as signal transducer and activator of transcription-3, nuclear factor kappa B, and downregulation of proinflammatory cytokines.^[18,19] During SARS-CoV-2 infection, curcumin inhibits angiotensin-converting enzyme 2 synthesis, which further promotes anticoagulation and fibrinolysis to prevent severe COVID-19.^[8,9,20,21] Curcumin has also shown promising effects on numerous viral infections including human immunodeficiency virus, influenza, herpes simplex virus, and hepatitis.^[18,19,22-24] Despite plenty of research on the role of curcumin as a potential treatment, supplement, and safe option for improving COVID-19 disease outcomes, the effect on curcumin supplementation postvaccine has not been demonstrated.^[19]

To combat the outbreak, there were loads of developed COVID-19 vaccines, including mRNA vaccine, inactivated vaccine, and viral vector vaccine.^[25] After immunization, the antigen presented in the vaccine triggers B-cells which divide and mature into memory B-cells and polyclonal plasma B-cells. Antibodies would then be produced into IgM, the first antibody to emerge during the primary immune response, and IgG, a more effective antibody for opsonization and neutralizing antibody.^[26] The number of B-cells producing antibodies could be T-cell-dependent or independent. During the extrafollicular process of IgM production, T-cells contribute during B- and T-cell crosstalk at the germinal center; B-cells would be then able to switch from IgM to other isotopes as well as to improve B-cell receptor affinity against antigens. These antibodies would then efficiently neutralize the SARS-CoV-2 virus.^[27,28]

The present study showed a significant increase in SARS-CoV-2 antibody production in the test group consuming 5 g of curcumin powder. Studies have reported varying levels of antibody response as a measure of the effectiveness of the vaccine.^[29,30] After COVID-19 vaccination, a study reported an increment of antibody observed after 2 weeks, with a median of 234–580 IU/ml. However, it is also observed that 66% of subjects demonstrated <10 IU/ml antibody after the first vaccination dose. Similar to this study, the second dose of vaccination improves the antibody level from a median of 40–4320 IU/ml without any nonresponders (<10 IU/ml). The variability of vaccines is also attributed to sex, with females producing higher antibodies compared to males in which the gap shortens after 1 month. In regard to age, the antibodies produced were found to be inversely correlated with age.^[30]

CONCLUSION

In summary, this study was the first to explore the effect of curcumin to improve antibody produced post-COVID-19 vaccination. Curcumin supplementation yields a higher measured antibody after vaccination which is independent of age, sex, and comorbidities. Further research with more subjects and variables has to be accounted for to establish a proper causal relationship between curcumin supplementation with antibody produced post-COVID-19 vaccination.

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Conflicts of interest

There are no conflicts of interest.

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