

## The role of physical activity and body mass index in the development and prevention of COVID-19

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### Abstract

**Introduction:** Given the high spread and mortality rate of COVID-19, it is of great importance to find solutions to prevent it. In this study, the role of physical activity and body mass index in the development or prevention of COVID-19 was investigated.

**Materials and methods:** In this cross-sectional study, participants included 155 patients with coronavirus selected as the experimental group and 150 age-matched healthy people included in the control group. The participants' physical activity levels were assessed using Beck's physical activity questionnaire. Independent t-test and binary logistic regression were run to analyze the data.

**Results:** The findings showed a significant difference between the patient and control groups body mass index (BMI), and total physical activity ( $P < 0.05$ ). On the other hand, total physical activity had a significant effect on COVID-19 prevention ( $P < 0.05$ ), but BMI had a significant increasing effect on the risk of COVID-19 ( $P < 0.05$ ).

**Conclusion:** It seems that physical activity can be effective in the prevention of COVID-19, but a higher body mass index may increase the risk for the development of COVID-19.

**Keywords:** COVID-19, Physical activity, Exercise, Women, Men

### Introduction

Since the end of 2019, people in most countries of the world have faced a common problem. The rapid and progressive outbreak of Coronavirus disease 2019 (COVID-19) has endangered the health and lives of many people around the world and has created many problems for the countries' health care systems (1). Based on the literature, coronaviruses include Alpha CoV, Beta CoV,

Gamma CoV, and Delta CoV (2). Coronaviruses have primarily caused enzymatic infections in birds and mammals followed by humans (3). The outbreak of severe acute respiratory syndrome (SARS) in 2002 and Middle East Respiratory Syndrome (MERS) in 2012 have infected people and caused death in humans (3). The SARS-CoV and MERS-CoV belong to the beta-CoV family (4). Recently, a new flu-like CoV, called severe acute respiratory syndrome

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coronavirus 2 (SARS-CoV-2), related to MERS and SARS CoVs, was discovered in late 2019 in Wuhan, China (6, 5). This disease has a human-to-human transmission (7). Based on sequential analyses, SARS-CoV-2 has a typical genomic CoV structure and belongs to the family of beta- CoVs, including SARS-CoV and MRS-CoV (8). Consequently, SARS-CoV-2 shares 80% of its genome with SARS-CoV (9,10). Considering that COVID-19 has recently become a pandemic disease (11) and no specific treatment has ever been found for it, finding the right solution to prevent and control its spread is of great necessity.

Factors that increase the risk of COVID-19 and death include age (risk of death is higher in the elderly), gender (prevalence and mortality rates are higher among men), high blood pressure, chronic metabolic diseases such as diabetes, chronic lung diseases such as asthma, coronary artery disease, congestive heart failure, kidney disease, any conditions that suppress immunity, gastrointestinal/liver disease, and blood disorders. Although no definitive treatment has ever been discovered for COVID-19, it seems that any factor that can prevent or treat the above-mentioned Conditions and diseases can prevent or reduce the effects of COVID-19 and even speed up the recovery process (12).

One of the significant effective factors in improving people's health and well-being is physical activity. Physical activity and exercise have been shown to play a preventive role against diseases such as cardiovascular disease, type 2 diabetes, some cancers, as well as conditions such as obesity and overweight (13,14). Past studies have shown that physical activity and exercise are effective in preventing some viral infections (15). But, so far, no study has shown whether physical activity and exercise can be effective in preventing Covid-19. Therefore, the present study was conducted to

investigate the role of physical activity and body mass index in the development or prevention of COVID-19.

## Materials and Methods

The present cross-sectional study was conducted between two groups: Patients with Covid-19 and Healthy individuals as the control group. The experimental group included 155 patients (85 men and 70 women) with COVID-19. Patients who were referred to the emergency department of Yazd Shahid Sadoughi Hospital with symptoms such as fever, dry cough, and shortness of breath were visited by an emergency physician. The emergency physician prescribed blood tests [C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complete blood count (CBC), and real-time polymerase chain reaction (RT-PCR)] and chest computed tomography (CT) for these patients. The test results were checked by an infectious disease specialist; in the case that the person was diagnosed with COVID-19, s/he was admitted to the 'Corona ward'. These patients stayed in the Corona ward for about 4 to 6 days. If their symptoms improved, they were released from the hospital but were told to be quarantined at home for 14 days. During this period, patients were followed-up by phone calls or other means of communication.

Since COVID 19 is often transmitted through close human contact, to control the effect of contact history, on the selection of subjects for the control group, we tried to select people who have almost the same living conditions as the subjects in the patient group. Therefore, after collecting the patients' information, the subjects in the control group were selected from among the family members and close relatives, friends, and colleagues of the patients. Hence, the control group consisted of 150 healthy people who were selected from the patients' close friends and relatives (80 men and 70 women). The

two study groups were matched in terms of age and selected using the available sampling method.

First of all, participants were explained about the study procedures and asked to sign special consent forms if they were willing to take part in the research. After obtaining the necessary licenses and receiving the patients' consent, Beck's physical activity questionnaire was administered and the required information was obtained regarding the subjects' level of physical activity. This questionnaire is used internationally to assess the level of physical activity and consists of 16 items classified into three parts. These three sections include questions that examine the extent of leisure time, sports, and workplace physical activity. Most items of this questionnaire are set on a 5-point scale.

In this questionnaire, the levels of subjects' physical activity were estimated during work, sports, leisure time, and total physical activity. To calculate the amount of physical activity the following formulas were used:

Work physical activity index =  $[I_1 + (6 - I_2) + I_3 + I_4 + I_5 + I_6 + I_7 + I_8] / 8$ .

Sports activity index =  $[I_9 + I_{10} + I_{11} + I_{12}] / 4$ .

Leisure-time activity index =  $[(6 - I_{13}) + I_{14} + I_{15} + I_{16}] / 4$ .

Total physical activity index = Leisure-time physical activity index + Sports physical activity index + Work physical activity index.

The validity and reliability of this questionnaire were confirmed in previous studies (16,17).

BMI was calculated by participants' weight in kilograms divided by the square of height in meters.

Since the patients' medical records were confidential, the researchers were not allowed to access all the details. In other words, the researchers were only provided with the patients' contact phone numbers. Therefore, patients were asked about their blood type; however, we could not obtain the blood type information completely since

some patients were illiterate or did not remember their blood type.

To collect data in all stages of the research, the above-mentioned questionnaire was administered and the participants were provided with the necessary instructions in this regard. Patients were required to ask any questions about any part of the research from researchers. It was tried to respect all the participants' rights in all stages of the research. The participants were treated respectfully and politely so that their merits and dignity were fully preserved throughout the research. Given that the research data were collected using a questionnaire, no aggressive behavior or methods were applied against the participants. All participants' information was kept strictly confidential so that only the researchers accessed the data. Furthermore, it was tried to inform the participants about the final findings of the research. Ethical approval for this study was obtained from the ethics committee of Shahid Sadoughi University of Medical Sciences in Yazd, Yazd, Iran (approval number: IR.SSU.REC.1399.115). The inclusion criteria were aged 30-80 years old, definite confirmation of the disease as well as the ability to understand and answer the questions. The exclusion criteria included Patient dissatisfaction to participate in the study.

### Statistical Analysis

Data were analyzed by SPSS software version 22 using descriptive and inferential statistics. In descriptive statistics, the mean and standard deviation of the results were evaluated. In inferential statistics, the difference between the experimental and control groups concerning the means of physical activity and BMI was studied using an independent t-test. Moreover, adjusted binary logistic regression was applied to investigate the effect of participants' BMI and

physical activity levels on COVID-19. The significance level in study was set at  $P < 0.05$ .

## Results

Variables related to anthropometric characteristics and physical activity of the participants are reported in Table 1. As an ancillary finding, data analysis showed that diabetes, hypertension, and asthma were among the most common underlying diseases in people with COVID-19, respectively (Table 2). Also, the incidence of the disease was examined in terms of different blood types. It is also showed that the highest

incidence rates of the COVID-19 were in patients with O+, B+, and A+ blood types, respectively. However, the lowest incidence rates of the COVID-19 were observed in people with A- and AB blood types (Table 3). The findings indicated a significant difference between the two groups in terms of BMI and total physical activity ( $P < 0.05$ ; Table 4). The results of the adjusted binary logistics regression test showed that total physical activity had a significant effect on COVID-19 prevention ( $P < 0.05$ ). Conversely, body mass index had a significant effect on increasing the risk of COVID-19 ( $P < 0.05$ ; Tables 5 and 6).

**Table 1.** Measured variables of the patient and control groups under study.

Groups	Men		Women	
	Patient	Control	Patient	Control
Number	85	80	70	70
Age (year)	53 ± 16	56 ± 14	52 ± 15	56 ± 13
Height (cm)	172 ± 7	173 ± 4	161 ± 6	163 ± 3
Weight (kg)	79 ± 14	75 ± 6	75 ± 12	71 ± 7
Body mass index (kg/m <sup>2</sup> )	26 ± 4	25 ± 2	29 ± 4	24 ± 3
Total physical activity	6.2 ± 1.2	7.9 ± 1.6	5.2 ± 1	6.4 ± 1.6

**Table 2.** The underlying health conditions in the patients with COVID-19.

Underlying health conditions	Women	Men	Total
Diabetes	13	22	35
Hypertension	15	15	30
Heart disease	1	4	5
Asthma	7	9	16
Chemical Veteran	0	2	2
Anemia	1	0	1
Rheumatism	6	0	6
Kidney Diseases	0	1	1
Hypothyroidism	2	0	2
Hyperthyroidism	0	1	1
Seasonal allergies	1	0	1

**Table 3.** Blood types of some the patients with COVID-19 (some patients did not know their blood types, so they were not exhibited).

Blood type	Women	Men	Total
A <sup>+</sup>	11	15	26
A <sup>-</sup>	2	0	2
B <sup>+</sup>	9	13	22
B <sup>-</sup>	2	2	4
AB <sup>+</sup>	3	5	8
AB <sup>-</sup>	0	2	2
O <sup>+</sup>	14	18	32
O <sup>-</sup>	0	3	3

**Table 4.** Results of independent t-test between the means of the variables of the two groups under study.

	Men			Women		
	t	df	P	t	df	P
Age (year)	1.103	163	0.27	-1.906	138	0.59
Height (cm)	1.195	163	0.23	-2.861	138	0.001*
Weight (kg)	-1.948	163	0.53	2.372	138	0.019*
Body Mass Index (kg/m <sup>2</sup> )	-1.948	163	0.53	4.406	138	0.001*
Total physical activity	7.22	163	0.001*	-5.287	138	0.001*

\* indicates a significant difference between groups. BMI, Body Mass Index.

**Table 5.** Adjusted binary logistic regression analysis with COVID-19 as dependent variable and physical activity and BMI as the independent variables in men.

	B	S. E	P	OR	95% CI	
					Lower	Upper
BMI (kg/m <sup>2</sup> )	.130	.061	.033*	1.139	1.010	1.283
Total Physical activity	-1.584	.364	0.00*	.205	.100	.419

\* indicates a significant difference between groups. BMI, Body Mass Index

**Table 6.** Adjusted binary logistic regression analysis with COVID-19 as dependent variable and physical activity and BMI as the independent variables in women.

	B	S. E	P	OR	95% CI	
					Lower	Upper
BMI (kg/m <sup>2</sup> )	.321	.073	0.00*	1.379	1.195	1.591
Total Physical activity	-1.685	.381	0.00*	.185	.088	.391

\* indicates a significant difference between groups. BMI, Body Mass Index

## Discussion

COVID-19 has recently endangered the health of people in most countries of the world. This disease transmits by close contact with infected people, especially through droplets released from the mouth and nose of the patients. Given the high spread and mortality rate of this disease, finding a way to prevent or treat this disease is essential. So, the present study examined the role of physical activity and body mass index in development or prevention of COVID-19.

The findings of the present study showed that physical activity can have a significant effect on the prevention of COVID-19. In line with the results of this research, some studies mentioned that physical activity and exercise had anti-inflammatory effects (17,18). Interferons (IFNS) are divided into type I and type II. Interferon-alpha, a member of type I interferons, is produced in response to a viral infection as part of innate immune response.

Interferon-alpha inhibits the proliferation of human and animal CoVs (19,20). Laboratory research has also shown that type I interferons, including interferon beta, inhibit SARS-CoV replication (21). Kuri et al. (2009) reported that interferon copying was inhibited in SARS-CoV-infected tissue cells. They also found that after using a small number of interferons, cells could partially regain their innate immune response (22). Also, interferons were identified as potential inhibitors of MERS-CoV proliferation (23). These findings suggest that interferons may be effective in treating COVID-19. The results of some well-controlled laboratory studies reported that physical activity and exercise not only strengthened the cells against infection caused by the flu virus but also reduced the severity of infection in non-obese mice. In non-obese mice, IFNS gene expression could reduce viral load in early stages, and in obese mice, IFNS could

activate type I obesity-induced IFN $\gamma$  activation disorders and improved immune responses. Therefore, physical activity and exercise are effective in boosting the body's immune response to infections in both obese and non-obese mice, but through two different mechanisms (24).

On the other hand, the other part of the findings of the present study showed that BMI had a significant effect ( $P < 0.05$ ) on increasing the risk of COVID-19. As mentioned, obesity and overweight are among the factors that increase the risk of developing COVID-19. Furthermore, obesity exacerbates infectious diseases, disrupts the immune responses, and weakens them. In obese mice infected with type A influenza, the function of immune cells and the production of cytokines and chemokines in the mice lungs were delayed or reduced; as a result, the virus clearance process was disrupted (25, 26). Obesity even reduces ciliary movements, motile cilia found in the lungs are responsible for expelling foreign matters, including viruses, from the lungs in the form of mucus (24). Given the positive impact of physical activity and exercise on weight loss and obesity prevention, we may consider its potential effective role in preventing and controlling viral diseases, including COVID-19.

In non-obese rats, moderate-intensity exercise increased the cells' ability to defend against viruses such as influenza A, while intense exercise increased the severity of infection (27, 28). animal studies noted that moderate-intensity exercise prevented viral diseases such as the flu, reduced their symptoms, and decreased the mortality rate in the case of infection. Intrinsic immune mechanisms (including interferon-alpha or beta-1) prevent the virus reproduction so that the acquired immune responses (especially CD8 + cytotoxic T cells) can clear the infection, which takes 7 to 14 days (29).

Physical activity and exercise have a dual effect on the body's immune responses to inflammation caused by viral infections. In the early stages of infection, Physical activity and exercise may increase the inflammatory responses. These mediators are vital to fighting invasive viruses. When the inflammatory mediators increased sufficiently, anti-inflammatory response mediators increase to prevent further tissue damage and mortality. However, prolonged strenuous physical activity and exercise have the opposite effect and increase inflammation and its complications (30-32). This can be one of the possible causes of death in professional athletes with COVID-19.

In respiratory tract infections such as influenza, moderate-intensity physical activity and exercise reduce inflammation of the lungs by slightly decreasing the inflammatory response of type 1 T-cells and increasing the anti-inflammatory response of type 2 T-cells. Consequently, the mortality rate is reduced in patients. Consequences of influenza are essentially the result of a balance between type 1 and type 2 T-cell responses. Moderate-intensity physical activity and exercise can cause faster recovery after the flu and prevent death by increasing type 2 T-cell responses without significant suppression of T helper type 2 cells (29, 30). Therefore, this can be considered as a possible mechanism regarding the effect of physical activity and exercise on the prevention of viral diseases, which eliminates the symptoms of severe inflammation in the case of infection. People with a history of Appropriate Physical activity and exercise may develop the COVID-19, but the symptoms do not appear and the person recovers as a result of the above-mentioned mechanism.

Besides, exercise as well as other physical and physiological stressors increase stress hormones, especially catecholamines and glucocorticoids. Stress hormones can have a

dual effect on the immune system. Moderate-intensity physical activity and exercise increase the concentration of stress hormones slightly, which strengthens the immune system's response to fight viruses. If viruses enter the body and cause infection, stress hormones produce anti-inflammatory responses to prevent tissue damage from severe pro-inflammatory and inflammatory responses (33). Therefore, we can also point to the possible role of physical activity and exercise in preventing viral diseases and reducing their complications from the viewpoint of moderate secretion of stress hormones. However, strenuous physical activity and exercise release high levels of stress hormones suppress immune responses, and consequently expose the person to infection (33). This mechanism may be considered as another reason for the death of professional athletes with COVID-19.

One of the limitations of this study was the administration of a self-report data-collection instrument. Considering that the researchers had no control over the participants' daily physical activity, the accuracy of the findings may be affected. Another limitation was those blood variables indicating different stages of the inflammation were not evaluated. Consequently, future researchers

are recommended to examine the participants' physical activity and exercise levels more accurately, control the patients' blood variables at different stages of the disease, and evaluate the possible impact of physical activity and exercise on preventing the disease, reducing its symptoms, and accelerating the patients' recovery.

### Conclusions

In conclusion, the results showed that moderate-intensity physical activity and exercise can be effective in preventing COVID-19, but higher body mass index may increase the risk for the development of COVID-19. However, much more research is needed to prove the findings and Possibilities.

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### Conflicts of interest

The authors declare no conflict of interest.

### References

1. South AM, Diz DI, Chappell MC. COVID-19, ACE2, and the cardiovascular consequences. *Am J Physiol Heart Circ Physiol*. 2020;318(5):1084-90. doi: 10.1152/ajpheart.00217.2020.
2. Banerjee A, Kulcsar K, Misra V, Frieman M, Mossman K. Bats and coronaviruses. *Viruses*. 2019;11(1):41. doi: 10.3390/v11010041.
3. Schoeman D, Fielding BC. Coronavirus envelope protein: current knowledge. *Virol J*. 2019;16(1):69. doi: 10.1186/s12985-019-1182-0.
4. Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. *Lancet*. 2015;386(9997):995-1007. doi: 10.1016/S0140-6736(15)60454-8.
5. Cohen J, Normile D. New SARS-like virus in China triggers alarm. *Science*. 2020;367(6475):234-5. doi: 10.1126/science.367.6475.234.
6. Zhu N, Zhang D, Wang W, Xingwang L, Yang B, Jingdong S, et al. A novel coronavirus from patients with

- pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727-33. doi: 10.1056/NEJMoa2001017.
7. Qun L, Xuhua G, Peng W, Xiaoye W, Lei Z, Yeqing T, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New Engl J Med.* 2020;382(13):1199-207. doi: 10.1056/NEJMoa2001316.
  8. Chen Y, Liu Q, Guo D. Coronaviruses: genome structure, replication, and pathogenesis. *J Med Virol.* 2020;92(4):418-23. doi: 10.1002/jmv.25681.
  9. Naru Z, Lili W, Xiaoqian D, Ruiying L, Meng S, Chen H, et al. Recent advances in the detection of respiratory virus infection in humans. *J Med Virol.* 2020;92(4):408-17. doi: 10.1002/jmv.25674.
  10. Jasper Fuk-Woo C, Kin-Hang K, Zheng Z, Hin C, Kelvin Kai-Wang T, Shuofeng Y, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect.* 2020;9(1): 221-36. doi: 10.1080/22221751.2020.1719902.
  11. Lei Zh, Yunhui L. Potential interventions for novel coronavirus in China: A systematic review. *J Med Virol.* 2020; 92: 479–90. doi: 10.1002/jmv.25707.
  12. Shikha G, Lindsay K, Michael W, Alissa O, Charisse C, Rachel H, et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1–30, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(15):458-64. doi: 10.15585/mmwr.mm6915e3.
  13. Aviroop B, Paul Oh, Guy F, Ravi Bajaj, Michael Silver, Marc M, et al. Sedentary Time and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults A Systematic Review and Meta-analysis. *Ann Intern Med.* 2015;162(2):123-32. doi: 10.7326/M14-1651.
  14. Jakobsson J, Malm Ch, Furberg m, Ekelund U, Svensson M. Physical activity during the coronavirus (COVID-19) pandemic: prevention of a decline in metabolic and immunological functions. *Front. Sports Act. Living.* 2020, 2: 57. doi:10.3389/fspor.2020.00057.
  15. CollaoN , Rada I, Francaux M, Deldicq ue L, Zbinden-Foncea H. Anti-inflammatory effect of exercise mediated by Toll-Like receptor regulation in innate immune cells - A review. *Int Rev Immunol.* 2020;39(2):39-52. doi:10.1080/08830185.2019.1682569.
  16. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr.* 1982;36(5):936-42. doi: 10.1093/ajcn/36.5.936.
  17. Pols M A, Peeters P H, Bueno-De-Mesquita H B, Ocké M C, Wentink C A, Kemper H C, et al. Validity and repeatability of a modified Baecke questionnaire on physical activity. *Int J Epidemiol ACTIONS.* 1995;24(2):381-8. doi: 10.1093/ije/24.2.381.
  18. Sim YJ, Yu S, Yoon KJ, Loiacono CM, Kohut ML. Chronic exercise reduces illness severity, decreases viral load, and results in greater anti-inflammatory effects than acute exercise during influenza infection. *J Infect Dis.* 2009;200(9):1434-42. doi: 10.1086/606014.
  19. Pei J, Sekellick MJ, Marcus PI, Choi IS, Collisson EW. Chicken interferon type I inhibits infectious bronchitis virus replication and associated respiratory illness. *J Interferon Cytokine Res.* 2001;21:1071-7. doi: 10.1089/107999001317205204.
  20. Turner RB, Felton A, Kosak K, Kelsey DK, Meschievitz CK. Prevention of



- experimental coronavirus colds with intranasal alpha-2b interferon. *J Infect Dis.* 1986;154:443-7. doi: 10.1093/infdis/154.3.443.
21. Morgenstern B, Michaelis M, Baer PC, Doerr HW, Cinatl J Jr. Ribavirin and interferon-beta synergistically inhibit SARS-associated coronavirus replication in animal and human cell lines. *Biochem Biophys Res Commun.* 2005;326:905-8. doi: 10.1016/j.bbrc.2004.11.128.
22. Thomas K, Xiaonan Z, Matthias H, Martínez-Sobrido L, García-Sastre A, Zhenghong Y, et al. Interferon priming enables cells to partially overturn the SARS coronavirus-induced block in innate immune activation. *J Gen Virol.* 2009;90:2686-94. doi: 10.1099/vir.0.013599-0.
23. Mustafa S, Balkhy H, Gabere MN. Current treatment options and the role of peptides as potential therapeutic components for Middle East Respiratory Syndrome (MERS): a review. *J Infect Public Health.* 2018;11:9-17. doi: 10.1016/j.jiph.2017.08.009.
24. Warren K, Olson M, Thompson N, Cahill M, Wyatt T, Yoon K, et al. Exercise Improves Host Response to Influenza Viral Infection in Obese and Non-Obese Mice through Different Mechanisms. *PLoS ONE.* 2015; 10(6): e0129713. doi: 10.1371/journal.pone.0129713.
25. Easterbrook JD, Dunfee RL, Schwartzman LM, Jagger BW, Sandouk A, Kash JC, et al. Obese mice have increased morbidity and mortality compared to non-obese mice during infection with the 2009 pandemic H1N1 influenza virus. *Influenza Other Respir Viruses.* 2011; 5:418-25. doi: 10.1111/j.1750-2659.2011.00254.x.
26. O'Brien KB, Vogel P, Duan S, Govorkova EA, Webby RJ, McCullers JA, et al. Impaired wound healing predisposes obese mice to severe influenza virus infection. *J Infect Dis.* 2012;205: 252-61. doi: 10.1093/infdis/jir729.
27. Lowder T, Padgett DA, Woods JA. Moderate exercise protects mice from death due to influenza virus. *Brain Behav Immun.* 2005;19(5):377-80. doi: 10.1016/j.bbi.2005.04.002.
28. Davis JM, Kohut ML, Colbert LH, Jackson DA, Ghaffar A, Mayer EP. Exercise, alveolar macrophage function, and susceptibility to respiratory infection. *J Appl Physiol.* 1997;83(5):1461-6. doi: 10.1152/jappl.1997.83.5.1461.
29. Stephen A.M, Brandt D.P, Jeffrey A.W. Exercise and respiratory tract viral infections. *Exerc Sport Sci Rev.* 2009; 37(4): 157-64. doi: 10.1097/JES.0b013e3181b7b57b.
30. Lowder T, Padgett DA, Woods JA. Moderate exercise protects mice from death due to influenza virus. *Brain Behav Immun.* 2005;19(5):377-80. doi: 10.1016/j.bbi.2005.04.002.
31. Lowder T, Padgett DA, Woods JA. Moderate exercise early after influenza virus infection reduces the Th1 inflammatory response in lungs of mice. *Exerc Immunol Rev.* 2006;12:97-111. PMID: 17201075.
32. Kohut ML, Boehm GW, Moynihan JA. Prolonged exercise suppresses antigen-specific cytokine response to upper respiratory infection. *J Appl Physiol.* 2001;90(2):678-84. doi: 10.1152/jappl.2001.90.2.678.
33. Dhabhar FS. Stress-induced augmentation of immune function--the role of stress hormones, leukocyte trafficking, and cytokines. *Brain Behav Immun.* 2002;16(6):785-98. doi: 10.1016/s0889-1591(02)00036-3.