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# Effects of increasing aerobic capacity on improving psychological problems seen in patients with COVID-19: a review

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**Abstract. – OBJECTIVE: In response to the COVID-19 disaster, people have developed several psychological problems mainly stress, anxiety, and depression. These psychological problems have been seen in either normal people during the lockdown (who are waiting to get infected with COVID-19) and patients with COVID-19 (who are waiting for death). These psychological problems adversely affect immune functions causing more increase in the severity of COVID-19 associated disorders and death rates. Increasing the aerobic capacity is one of the effective methods that could be used to decrease stress, anxiety, and depression. Besides, increasing the aerobic capacity increases immune functions through autonomic regulation. Thus, this review was developed to summarize the effect of increasing the aerobic capacity on psycho-immune hormones commonly disturbed in people during the lockdown or patients with COVID-19 infection.**

**MATERIALS AND METHODS: This review was carried out by searching through Web of Science, Scopus, EBSCO, Medline databases. The search was conducted over clinical trials, literature reviews, and systematic reviews. The search included the possible effects of increasing the aerobic capacity on the functions of psycho-immune hormones.**

**RESULTS: This review found that increasing the aerobic capacity can decrease psychological problems commonly seen in people with COVID-19 and increase immune functions by modulating the levels of glucocorticoid, oxytocin, insulin, thyroid hormones.**

**CONCLUSIONS: This review demonstrated that increasing the aerobic capacity is a recommended treatment for decreasing the psychological problems commonly seen in people with COVID-19 because it has the potential for decreasing psychological problems and improving immune functions which would help counter COVID-19.**

*Key Words:*
Aerobic capacity, COVID-19, Hormones, Immune functions, Psychological problems.

## Introduction

Nowadays, the world faces a serious disaster called COVID-19. According to the WHO, more than 4,500,000 cases have been confirmed to be affected with COVID-19; among them, more than 300,000 cases died. COVID-19 started from Wuhan, China, and has spread across more than 220 countries[1]. COVID-19 is a subtype of enveloped RNA beta-coronaviruses and is known as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)[2].

As a response to this disaster, several psychological problems have been raised in patients with COVID-19 or even in normal people during lockdown[3]with over 720,000 cases and 33,000 confirmed deaths reported to date. Such widespread outbreaks are associated with adverse mental health consequences. Keeping this in mind, existing literature on the COVID-19 outbreak pertinent to mental health was retrieved via a literature search of the PubMed database. Published articles were classified according to their overall themes and summarized. Preliminary evidence suggests that symptoms of anxiety and depression (16–28%. The common reported psychological problems, in response to COVID-19, included stress, anxiety, and depression[3]with over 720,000 cases and 33,000 confirmed deaths reported to date. Such widespread outbreaks are associated with adverse mental health consequences. Keeping this in mind, existing literature on the COVID-19

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outbreak pertinent to mental health was retrieved via a literature search of the PubMed database. Published articles were classified according to their overall themes and summarized. Preliminary evidence suggests that symptoms of anxiety and depression (16–28%. All members of the medical team, particularly psychiatrists, across the world should be conscious of these psychological problems, their associates, and approaches to cope with them[4]. These psychological problems can significantly affect immune functions and increase the severity of COVID-19 associated disorders and death rates[5].

The strength of the immune system represents the key role to increase the defense of our body against COVID-19 because COVID-19 is a self-limited infection[6]viral diseases continue to emerge and represent a serious issue to public health. In the last twenty years, several viral epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV. Increasing the aerobic capacity has double-action by acting as a safe and effective approach to decrease the psychological problems and, at the same time, it increases immune functions[7-10]claims for the psychological benefits of physical exercise have tended to precede supportive evidence. Acutely, emotional effects of exercise remain confusing, both positive and negative effects being reported. Results of cross-sectional and longitudinal studies are more consistent in indicating that aerobic exercise training has antidepressant and anxiolytic effects and protects against harmful consequences of stress. Details of each of these effects remain unclear. Antidepressant and anxiolytic effects have been demonstrated most clearly in subclinical disorder, and clinical applications remain to be exploited. Cross-sectional studies link exercise habits to protection from harmful effects of stress on physical and mental health, but causality is not clear. Nevertheless, the pattern of evidence suggests the theory that exercise training recruits a process which confers enduring resilience to stress. This view allows the effects of exercise to be understood in terms of existing psychobiological knowledge, and it can thereby provide the theoretical base that is needed to guide future research in this area. Clinically, exercise training continues to offer clinical psychologists a vehicle for nonspecific therapeutic social and psychological processes. It also offers a specific psychological treatment that may be particularly effective for patients for whom more conventional psychological interventions are less acceptable. Copyright (C. The main advantage of increasing the aerobic capacity is that it can decrease the psychological problems in people with COVID-19 by producing an autonomic regulation; this autonomic regulation directly enhances immune functions[11,12].

Previously, we have written a review to summarize the effects of increasing the aerobic capacity on improving immune functions in patients with COVID-19[8]. In this paper, we discussed the effect of increasing the aerobic capacity on improving mood, anxiety, depression, and its valuable effects on enhancing the immune functions. This review demonstrates that psycho-hormonal changes occur in patients with COVID-19. Additionally, it demonstrates the effects of increasing aerobic capacity on regulating the psycho-immune hormones. These psycho-immune hormones mainly include the hormones involved in the fight or flight response, such as glucocorticoids (GCs), oxytocin (OX), catecholamines (CCs), thyroid hormones (THs), and insulin. Furthermore, this article explains the effect of restoring normal functions of these hormones on immune functions which are necessary for countering COVID-19 infection.

## *The Psycho-Hormonal Changes in Patients with COVID-19*

It has been demonstrated that psycho-hormones change in SARS-COV-1 survivors, without the occurrence of any endocrine disorders. These changes mainly include the hypothalamic-pituitary-adrenal (HPA) axis hypoactivity with hypercortisolism[13]many survivors were observed to suffer from psychosomatic symptoms reminiscent of various endocrine disorders. Hence, we sought to determine the existence of any chronic endocrine sequelae in SARS survivors. Design, patients, measurements: Sixty-one survivors of SARS prospectively recruited were analysed for hormonal derangements 3 months following recovery. Patients with pre-existing endocrine disorders were excluded. Any endocrine abnormalities diagnosed were investigated and treated where indicated up to a year. Serial evaluation facilitated characterization of trends and prognostication of any endocrinological aberrations. Results: Twenty-four (39-3%. These changes might be attributed to the increase in TNF-α and transforming growth factor-beta (TGF-β) in people with COVID-19, which may induce HPA axis hypoactivity[11,14]. Consequently, the increased cytokines in patients with COVID-19 can play a key role in COVID-19 associated hypercortisolism. Hypercortisolism could be due to the depressive symptoms that can occur in patients with COVID-19, which can cause both hypoactivity and hyperactivity of the HPA axis. Thus, studying and evaluating the axis HPA activity, cytokine levels, and psychiatric disturbances in patients with COVID-19 would positively enhance the current knowledge.

COVID-19 also could affect the adrenocorticotropic hormone (ACTH) by decreasing the host's cortisol stress reaction. The initial 24 amino acids of ATCH (ACTH1-24) highly preserve amid various mammalian kinds. Amino acids 26, 29, 31, 33, 37, and 39 play the dominant vital role in regulating mammalian ACTH. COVID-19, like the SARS virus, encompasses numerous variations of amino acid arrangements with homology to these probable ACTH key rests. Antibodies induced by the host to counter the COVID-19 virus would mistakenly destroy the host ACTH causing a blunting rise in cortisol levels. This might imply that COVID-19 would cause an associated cortisol insufficiency[15].

### *The Effect of Increasing the Aerobic Capacity on Decreasing Glucocorticoids Level*

GCs secretion starts through the stimulation of the hypothalamus to release arginine vasopressin (AVP) and corticotropin-releasing hormone (CRH). CRH-containing neurons, found in the paraventricular nucleus of the hypothalamus, make projections to noradrenergic centers in the brainstem and spinal cord. The locus coeruleus of the brainstem directly projects to the sympathetic and parasympathetic preganglionic neurons in the brainstem and the spinal cord[16]. In response to stressors, the locus coeruleus triggers the sympathetic activity by activating α1-adrenoceptors on preganglionic sympathetic neurons and inhibits the parasympathetic activity by activating α2-adrenoceptors on preganglionic parasympathetic neurons[16]. The activation of the sympathetic nervous system causes a release of CRH from the paraventricular nucleus of the hypothalamus[16].

The activation of CRF and VAP causes an activation of the HPA axis to release the ACTH from the anterior pituitary gland. The ACTH, in turn, stimulates the production and discharge of GCs from the adrenal cortex[17]. GCs receptors present in numerous brain areas (e.g., prefrontal cortex, hippocampus, amygdala, and other midbrain and limbic structures). These GCs receptors act as transcriptional factors to adjust cell functions, even following the termination of acute stress. The magnitude, type, and duration of the stress are important in determining the period and degree of HPA axis response[17]. GCs suppress immune functions and inhibit the central products of inflammation (prostaglandins and leukotrienes)[18,19]measured by increased glucocorticoid secretion, leads to profound reproductive dysfunction. In times of stress, glucocorticoids activate many parts of the fight or flight response, mobilizing energy and enhancing survival, while inhibiting metabolic processes that are not necessary for survival in the moment. This includes reproduction, an energetically costly procedure that is very finely regulated. In the short term, this is meant to be beneficial, so that the organism does not waste precious energy needed for survival. However, long-term inhibition can lead to persistent reproductive dysfunction, even if no longer stressed. This response is mediated by the increased levels of circulating glucocorticoids, which orchestrate complex inhibition of the entire reproductive axis. Stress and glucocorticoids exhibits both central and peripheral inhibition of the reproductive hormonal axis. While this has long been recognized as an issue, understanding the complex signaling mechanism behind this inhibition remains somewhat of a mystery. What makes this especially difficult is attempting to differentiate the many parts of both of these hormonal axes, and new neuropeptide discoveries in the last decade in the reproductive field have added even more complexity to an already complicated system. Glucocorticoids (GCs. This occurs through decreasing the activity and function of immune cells, including neutrophil, basophil, eosinophil, macrophages, mast cells T-lymphocytes, and B-lymphocytes.

Increasing the aerobic capacity produces short-term effects by decreasing serum GCs, AVP, and CRH levels. Lu et al[20] investigated the effects of aerobic exercises on GCs receptor expression located within the blood leukocytes in normal and asthmatic adolescents. They found that 8-week of mild aerobic exercise significantly decreased the GCs receptor expression within blood leukocytes. Hill et al[21] studied the effect of aerobic exercises on serum GCs levels in moderately trained men. They found that performing 30 minutes of low-intensity aerobic exercise significantly decreased the blood GCs levels. Silva et al[22] examined the effect of aerobic exercise on GCs receptor expression in mice. They found that performing mild aerobic exercises for 60 min at 50% of maximal exercise capacity significantly decreased the expression of the GCs receptors in mice. Fediuc et al[23] examined the effects of aerobic exercise on GCs levels and responsiveness of the HPA axis in Sprague-Dawley rats. They found that performing mild- intensity aerobic exercise for 5 weeks significantly decreased both GCs levels and responsiveness of the HPA axis. The characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on GCs levels are illustrated in Table I.

### The Effect of Increasing the Aerobic Capacity on Increasing Oxytocin Levels

OH is released from parvocellular and magnocellular neurons into the paraventricular nucleus and the supraoptic nucleus of the hypothalamus. Then, OH is passed to the posterior pituitary by axonal transport, where it is deposited till its release into the bloodstream. OH receptors present in numerous areas of the brain, including the cerebral cortex, hippocampus, hypothalamus, nucleus accumbens, and amygdala[24]. Several animal studies have reported that normal OH positively affects depression level[25,26]. In response to stress, anxiety, and depression; OH decreases[24].

The increase in serum OH levels can help in decreasing stress, anxiety, and depression; however, the actual mechanisms by which the OH system decreases these disorders are still unclear[24]. The effect of OH on decreasing anxiety disorders has been reported in several studies[27-29]. OH may decrease the stress and anxiety by facilitating the mitogen-activated protein/extracellular signal-regulated kinase signaling pathway and elevating brain-derived neurotrophic factor expressions in the hippocampus; this helps to produce neural plasticity in the hippocampus[24]. Also, OH itself has a significant role in decreasing immunological disturbances and restoring normal homeostasis because its secretion from oxytocin neurons is directly regulated by prostaglandins, nitric oxide, endocannabinoids, nitric oxide, and by several usual immune cytokines, such as IL-1β[30].

Increasing the aerobic capacity produces a short-term increase in blood OH, which helps in both decreasing stress, anxiety, and depression and increasing the immune functions. Yüksel et al[31] investigated the effect of aerobic exercises on serum OH levels in female rats. They found that performing a mild aerobic exercise for 6 weeks significantly increased serum OH levels and decreased anxiety. Tamer et al[32] examined the effect of aerobic exercises on oxytocinergic activity in rats. They observed that performing a continual 30 min moderate-aerobic exercise for 5 days significantly reversed the induced downregulated oxytocinergic activity. Martins et al[33] resulting in blunted exercise tachycardia. The objective of this study was to determine the effects of hypertension and training on oxytocin (OT studied the effect of aerobic exercise on blood OH levels in mice. They found that performing a mild-aerobic exercise for 3 months significantly increased blood OH levels. Irianti et al[34] investigated the effect of aerobic exercises on OH levels during women's labor. They detected that performing a regular mild aerobic exercise during the pregnancy significantly increased OH levels and resulted in an easy labor progression in humans. The characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on OH levels are illustrated in Table II.

### The Effect of Increasing the Aerobic Capacity on Increasing Thyroid Hormones Levels

The thyroid functions usually decrease during stressful conditions. With stress, there is a reduction in serum 3,5,3′,5′-tetraiodothyronine thyroxine (T4), and 3,5,3′-triiodothyronine (T3), and an inhibition of the thyroid-stimulating hormone (TSH) production *via* increasing GCs levels[35,36]. Thyroid hormones, mainly T4 and T3, are important hormones in regulating several functions in our body, such as oxygen consumption, carbohydrate, lipid, and protein metabolisms, puberty, seasonal breeding, and stress regulations[36].

In humans, several neurons in the paraventricular nucleus in the hypothalamus (PVN) controls the activity of the hypothalamic-pituitary-thyroid axis (HPT). The HPT stimulates the release of thyrotropin-releasing-hormone (TRH) in the median eminence. TRH activates the anterior pituitary gland to produce the TSH. TSH goes throughout the peripheral vasculature to activate the thyroid gland to secrete both T3 and T4. T4 usually converts to T3 by the action of deiodinase enzymes sited inside most body tissues. Thyroid hormones have negative feedback roles by acting on thyroid hormone receptors in the hypothalamus and pituitary to prevent the production of TSH[35,37].

Several studies[35,37] have proposed that stress produces a reduction in the release of thyroid hormones. The stress-produced reduction in thyroid hormones is facilitated by the decrease in the activity of the hypothalamus. This occurs due to increased production of GCs; which can stop the activity of the HPT axis, at the level of the hy-

**Table I.** Characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on GCs levels.

| Study | Participants | Methods | | | | Outcome measurement | Results | | Conclusions |
|---|---|---|---|---|---|---|---|---|---|
| | | Intervention group | | | Control group | | Within groups | Between groups | |
| | | Intensity | Frequency | Total duration | | | | | |
| [20] | Humans (14 healthy and 12 asthmatic adolescents) | 1-hour session | 3 days a week | 8 weeks | Same as the intervention group | GCs expression in leukocytes by flow cytometry | There was a significant decrease in baseline GCs expression in leukocyte and monocyte subtypes in both healthy and asthmatic adolescents. | There was a significant difference in GR expression among leukocyte subtypes, with the highest expression in eosinophils | Aerobic exercise training reduces GR expression on circulating leukocytes |
| [21] | Human (12 active moderately trained men | Cycling for 30 min of 40, 60, and 80% maximal oxygen uptake (VO2max) | 1 session | 1 session | N/A | Cortisol level | There was a significant increase in cortisol level at 60% and 80% only | N/A | Low-intensity aerobic exercise reduces circulating cortisol levels. |
| [22]aerobic training (AT; non sensitized/ trained | Animal (96 artificially-induce asthmatic men mice) | Mice are subjected to intraperitoneal (i.p.) injections of aluminum hydroxide (20 μg/mouse) on days 0, 14, and 28. On days 21 and 23: walking on the treadmill for 15 min at a speed of 0.2 km/h and inclination of 25%. On day 25, maximal exercise testing was performed. The treadmill training was performed for 60 min at 50% of maximal exercise capacity reached in the maximal exercise test. | 3 sessions | 28 days | The same aerobic exercises followed in the intervention group, however without intraperitoneal (i.p.) injections of aluminum hydroxide | GCs expression Cytokines (IL-4, IL-5, NF-κB, TGF-β, VEGF, ICAM-1, VCAM-1, and AR) | Aerobic exercise significantly decreased OVA-induced inhibition of GCs receptor and increased anti-inflammatory cytokines | There was a significant reduction in the expression of the GR when compared with the control group | Mild aerobic exercise reverses OVA-induced inhibition of GCs receptor and increases anti-inflammatory cytokines |
| [23] | Sprague-Dawley male rats | Voluntary wheel running (exercise specifications were not mentioned) | N/A | 5 weeks | No exercises | Serum corticosterone and ATCH, and HPA responsiveness | N/A | There was a significant difference between the two groups in corticosterone and ATCH and HPA responsiveness | 5 weeks of wheel running are accompanied by normal daily corticosterone activity and normal negative-feedback inhibition of the HPA axis, as well as with increased adrenal sensitivity to ACTH following restraint stress. |

GC: glucocorticoids, ATCH: adrenocorticotropic hormone, HPA: hypothalamus, pituitary gland, and adrenal glands interaction.

pothalamus and anterior pituitary. Furthermore, GCs can inhibit the peripheral transformation of T4 to T3, causing a stress-produced reduction in circulating T3 levels[35,37].

It has been demonstrated that thyroid hormones (T3 and T4) can produce changes in the activity of different immune cells (e.g., lymphocytes, natural killer cells, monocytes, macrophages); this consequently influences several infection-related processes, such as phagocytosis, chemotaxis, cytokines production, and reactive oxygen species generation. The actual mechanisms beyond this are still unclear[38,39]. Previous studies[40,41] examined the immune functions in patients with hyperthyroidism and they found that these patients had an increase in functions and levels of leukocytes, lymphocytes, and macrophages. In contrast, other studies[42,43] found the opposite results in patients with hypothyroidism.

Increasing the aerobic capacity can produce a short-term increase in serum T3. Altaye et al[44] studied the effect of regular aerobic exercise on thyroid hormonal alteration in adolescents with intellectual disabilities. They detected that performing a mild aerobic exercise for 12 weeks significantly increased plasma concentrations of T3, T4, and TSH. Masaki et al[45] investigated the effect of aerobic exercise on serum TSH levels in patients with subclinical hypothyroidism. They observed that performing a mild aerobic exercise significantly decreased serum TSH levels. Fathi et al[46] investigated the effect of aerobic exercises on thyroid hormones in obese postmenopausal women. They showed that mild aerobic exercises performed for 8 weeks significantly increased serum T3, T4, and TSH levels. Rone et al[47] studied the effect of serum T3 in men. They found that athletes had greater serum T3 than sedentary controls during kinetic analysis. Characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on thyroid levels are illustrated in Table III.

### *The Effect of Increasing the Aerobic Capacity on Decreasing Insulin Resistance*

Insulin is a peptide hormone produced by the β-cells of the pancreatic islets of Langerhans. The function of insulin is to maintain normal blood glucose levels by promoting cellular glucose, lipid, and protein metabolisms, and facilitating cell split by its mitogenic properties[48]. In early stress, there is an increase in serum insulin levels; however, insulin depletes afterward causing the occurrence of diabetes mellitus[48,49]. Thus, the continual release of GCs negatively affects the secretion of insulin. The increase in insulin levels occurs as a compensatory mechanism to the increase in insulin resistance to preserve normal plasma glucose concentrations. If this compensatory mechanism fails to maintain normal plasma glucose concentrations, diabetes mellitus might occur. Also, there is a connection between several hormones (e.g., NE, epinephrine (Epi), GCs, glucagon, and growth hormone) and insulin because both are involved in carbohydrate metabolism and blood glucose level regulation. Insulin and these hormones have been reported to be significantly influenced by psychological stress[50]. Several studies[51-53] have demonstrated that there is an association between persistent psychological stress and the development of diabetes which mainly occurs due to the depletion of insulin. Also, several studies have reported the relationship between diabetes mellitus and accompanied decrease in immune functions; however, the role of low insulin levels or increased insulin resistance on decreasing these immune functions is not clear yet[54-56]. It might be due that insulin has a key role in glucose metabolism which is important to provide energy to immune cells to counter body infections.

Increasing the aerobic capacity can increase insulin levels and glucose metabolism and decrease insulin resistance. The increase in insulin secretion might be attributed to the effect of increasing the aerobic exercise on decreasing serum GCs levels. There is extensive evidence in the literature[57-61] about the useful effects of aerobic exercise on increasing insulin sensitivity and glucose metabolism. Winnick et al[57] investigated the effect of aerobic exercise on insulin sensitivity in fat subjects with type 2 diabetes. They found that performing an aerobic exercise for only one week significantly increased insulin sensitivity. Schwaab et al[58] investigated the effect of aerobic and anaerobic exercises on glucose tolerance in patients with type 2 diabetes and coronary artery diseases. They found that performing a regular aerobic exercise for 16 weeks, in contrast to anaerobic exercises, significantly decreased glucose tolerance. Karstoft et al[59] investigated the effect of mild aerobic exercise on glycemic control, physical fitness, and body composition in patients with type 2 diabetes. They found that 4 months of aerobic exercise of alternate mild to high intensity significantly increased insulin sensitivity and decreased glycemic control. Short et al[61] investigated the effect of aerobic

**Table II.** Characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on oxytocin levels.

| Study | Participants | Methods | | | | Outcome measurement | Results | | Conclusions |
|---|---|---|---|---|---|---|---|---|---|
| | | Intervention group | | | Control group | | Within groups | Between groups | |
| | | Intensity | Frequency | Total duration | | | | | |
| 31 | Animal (32 mice) | Voluntary wheel running | 143 ± 5.18 min/day | 6 weeks | No exercises | Serum and brain OH levels, and empathy and anxiety levels | The brain and serum OT levels significantly increased in female mice; though OT levels increased in only the brain in males. Anxiety levels decreased in all the exercise groups | N/A | Voluntary aerobic exercises reduce anxiety and increases empathy-like performance in mice; which is associated with elevated oxytocin levels in female mice but not in male mice. |
| 32 | Animal (mice) | Swimming training<br><br>At the end of the 6-week exercise/sedentary protocol, rats were injected intraperitoneally with atosiban (0.1 mg/kg/day) or saline for 4 days | 30 min/day, 5 days | 6 weeks | No exercises | 1. Anxiety Level.<br>2. Serum corticosterone and gastric 8-hydroxy-2′-deoxyguanosine levels.<br>3. MDA, GSH, and MPO levels.<br>4. Cytokines ((TGF-β, TNF-α, IL-8, IL-6, and IL-10).<br>5. Gastric caspase-3 activity Caspase-3.<br>6. Serum OH levels | Having exercised before ulcer induction significantly:<br>1. Decreased anxiety levels<br>2. Eliminated the elevation in MDA levels, and reversed the changes in MPO activity and GSH content.<br>3. Increased TNF-α levels only<br>4. increased OT levels hypothalamus | N/A | Regular moderate aerobic exercises for 5 days decrease gastric oxidative damage in mice via the involvement of oxytocin receptors |
| | Animal (male mice) | 55% maximal exercise capacity | 1 hour/ day for 5 days/ week | 3 months | No exercises | Serum and OT receptor expression in the brain | Regular aerobic exercises significantly increased both serum OTand OT receptor expression in the brain | N/A | Training increased serum OT and OT mRNA expression in sedentary and hypertensive rats |
| 34 | Human (40 pregnant women (32-34 weeks)) | N/A | N/A | N/A | N/A | Serum OT | Aerobic exercise significantly increased serum OT levels | There was a significant difference between intervention and control groups in serum OT levels | Regular aerobic exercise in a pregnant woman increases serum OT levels and eases labor progress |

OT: oxytocin hormone, MDA: malondialdehyde, GSH: glutathione, MPO: myeloperoxidase activity

**Table III.** Characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on thyroid hormones.

| Study | Participants | Methods | | | | Outcome measurement | Results | | Conclusions |
|---|---|---|---|---|---|---|---|---|---|
| | | Intervention group | | | Control group | | Within groups | Between groups | |
| | | Intensity | Frequency | Total duration | | | | | |
| 44 | Human (36 adolescents with intellectual disabilities) | Moderate-intensity aerobic exercises (the specific intensity was not mentioned) | 30-45 min/ session for 3 sessions/week | 16 weeks | No exercises | Serum T3, T4, and TSH | Aerobic exercises significantly increased serum Serum T3, T4, and TSH | There were significant differences between both groups in serum T3, T4, and TSH | Moderat-intensity aerobic exercises increase the serum of thyroid and thyroid-stimulating hormones in adolescents with intellectual disabilities |
| 45 | Humans (108 patients (53 with subclinical hypothyroidism and 55 patients with euthyroid) | Cycling with the pedaling frequency of 60 rpm | 1 session | 1 session | Patients with euthyroid performed the same protocol performed for a patient with hypothyroidism | TSH | Aerobic exercises significantly increased serum TSH levels in both groups | There was a significant difference in serum TSH between subclinical hypothyroidism and euthyroid groups | Aerobic exercises significantly increased serum TSH levels in both hypothyroidism and euthyroid groups |
| 46 | Humans (21 obese women) | 30-60 minutes of aerobic exercise at 65-75% of maximum heart rate | 3 times/ week | 8 weeks | No exercises | Serum T3, T4, and TSH | Aerobic exercises significantly increased serum T3, T4, and TSH | There were significant differences between both groups in Serum T3, T4, and TSH | Aerobic exercises significantly increase serum levels T3, T4, and TSH |
| 47 | Humans (10 healthy men (5 athletes and 5 sedentary controls) | Submaximal exercise testing by cycle ergometry to determine VOZ | N/A | N/A | | T3 metabolism (MCR, TVD, DR, POOL) | The parameters MCR, TVD, DR, and POOL, when normalized for BSA were all significantly greater in the athletic group than in the sedentary controls. | There were significant differences between both groups for MCR, TVD, DR, and POOL | T3 metabolism is altered by physical conditioning |

T3: 3,5,3′-triiodothyronine, T4: 3,5,3′,5′-tetraiodothyronine thyroxine, TSH: the thyroid-stimulating hormone, MCR: metabolic clearance rate, TVD: total volume of distribution, DR: disposal rate, POOL: total body pool.

exercise on age-related alteration in insulin sensitivity. They found that performing a mild aerobic exercise for 16 weeks significantly decreased insulin sensitivity in middle-aged people. Nassis et al[60] examined the effects of aerobic exercise on insulin sensitivity among obese girls. They found that performing a mild aerobic exercise for 12 weeks significantly decreased insulin sensitivity. The characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on insulin levels are illustrated in Table IV.

### *The Effect of Increasing the Aerobic Capacity on Decreasing the Catecholamines Levels*

Catecholamines consist of norepinephrine (NE) and epinephrine (Epi). CCs play a significant role in enhancing hepatic glucose release during acute stresses[62]. The body, during stress and anxiety conditions, stimulates brainstem catecholaminergic neurons to send impulses to the spinal cord through the interomedial lateral column to stimulate preganglionic sympathetic neurons; this stimulates the sympathetic nervous system and adrenal medulla to increase the circulating NE and Epi[62].

The persistent high CCs levels affect almost all body functions, particularly immune functions. It has been usually demonstrated that high CCs levels significantly suppress immune functions63. Persistent high CCs levels obstruct the T-cell proliferation produced by mitogens or anti-CD3 monoclonal antibodies by the CD3/TCR complex. This is often associated with an elevation of cAMP in lymphocytes. The amount of cAMP is related to the extent of inhibition of T-cell proliferation[63,64]. The elevation of cAMP constrains IL-2 production occurs due to the T-cell proliferation via CCs which could cause the stoppage of the production of IL-2. IL-2; this plays an important role as a co-stimulatory molecule in T-cell proliferation[63,64].

Human or animal studies investigated the effect of increasing the aerobic capacity on decreasing CCs levels were little, old, and included other disorders besides psychological disorders (such as hypertension or mitochondrial myopathies); however, these studies[65-68] have demonstrated that mild to moderate aerobic exercise can produce a partial decrease in CCS levels. Thus, increasing aerobic capacity might have little or partial effects on decreasing CCs level. This partial effect could be combined with the decrease in serum GCs levels by increasing the aerobic capacity because both GCs and CCs are closely related to each other[69].

## Conclusions

In sumary, this review suggests that increasing the aerobic capacity plays an important role in decreasing the psychological problems commonly seen with COVID-19. Increasing the aerobic capacity could be a potent intervention to decrease these psychological problems because it produces an autonomic regulation. This autonomic regulation helps to improve immune functions important to counter COVID-19. Increasing the aerobic capacity can mainly decrease psychological problems commonly seen with COVID-19 through modulating GCs, OT, insulin, and thyroid hormones.

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#### Conflict of Interest

The Authors declare that they have no conflict of interests.

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**Table IV.** Characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on insulin hormone.

| Study | Participants | Methods | | | | Outcome measurement | Results | | Conclusions |
|---|---|---|---|---|---|---|---|---|---|
| | | Intervention group | | | Control group | | Within groups | Between groups | |
| | | Intensity | Frequency | Total duration | | | | | |
| 57 | Humans (18 subjects with type II diabetes) | On days 1-3 and 5-7, subjects performed 2×25 min bouts of aerobic exercise (treadmill walking) with a 10-min break between bouts. The intensity of the exercise was 70% VO2 max. On day four of exercise subjects performed exercises for 60 min at 60% of their age-predicted max heart rate. | 1 session/day | 7 days | No exercises | Whole-body, peripheral, and hepatic insulin sensitivity | 1-wk of exercise training significantly increased peripheral and whole-body peripheral insulin sensitivity during high-dose insulin. | There were significant differences between both groups in peripheral and whole-body peripheral insulin sensitivity | Short-term aerobic exercises improve the whole-body insulin sensitivity because of an increase in peripheral, not hepatic insulin sensitivity |
| | | Both groups subjected to an isocaloric diet consisting of 50% carbohydrate, 30% fat, and 20% protein | | | | | | | |
| 58 | Humans (10 patients with coronary heart disease and type 2 diabetes mellitus) | Aerobic exercise: cycle ergometer at a constant pedal velocity of 50-60 rpm for 30 min Anaerobic exercises: cycle ergometer exercise at a maximum tolerable intensity | 1 session | 1 session | No control group | Fasting plasma glucose and 2-hour plasma glucose in an oral glucose tolerance test | Only aerobic exercises significantly decreased 2-hour plasma glucose | N/A | Postprandial plasma glucose was decreased only by aerobic exercises |
| 59 | Human (32 subjects with type II diabetes) | 60 min/session of continuous or interval walking. Continuous walkers performed all training at moderate intensity, whereas interval walkers alternated 3-min repetitions at low and high intensity. Before and after the 4-month intervention, the following variables were measured: $VO2_{max}$ | 5 days/week | 16 weeks | No exercises | VO2max, body composition, and glycemic control (fasting glucose, HbA1c, oral glucose tolerance test, and continuous glucose monitoring | Interval walking only significantly increased $VO2_{max}$, insulin sensitivity and decreased body fat and glucose concentration | There were significant differences between the three groups in insulin sensitivity and glucose concentration with more difference to the interval-walking group | Both continuous and interval walking offset deteriorations in glycemic control. |
| | | Participants were randomized to a control (n = 8), continuous-walking (n = 12), or interval-walking group (n = 12) | | | | | | | |

*Table continued*

**Table IV.** ***(Continued).*** Characteristics, specifications, and results of the included studies concerning the effect of aerobic exercises on insulin hormone.

| Study | Participants | Methods | | | | Outcome measurement | Results | | Conclusions |
|---|---|---|---|---|---|---|---|---|---|
| | | Intervention group | | | Control group | | Within groups | Between groups | |
| | | Intensity | Frequency | Total duration | | | | | |
| 61 | Human (102 Healthy men and women who exercised more than30 min twice per week during the previous 9 months) | Stationary bicycle. The training began with 20 min/day for 3 sessions/week, at 70% of maximal heart rate. Duration, intensity, and the number of sessions were gradually raised so that the end month of training was composed of 40 min/day for 4 sessions/week at 80% of maximal heart rate. | | 16 weeks | N/A | Plasma insulin and glucose | Aerobic exercises significantly decreased fasting insulin levels in middle-aged people only, while nonsignificantly decreased fasting glucose in any age-group | N/A | Aerobic exercises significantly decrease insulin sensitivity in middle-aged people |
| | | This study compared the effect of aerobic exercises on three different age groups | | | | | | | |
| 60 | Human (19 obese girls) | 40 minutes od mild aerobic exercises | 3 days/week | 12 weeks | No control group | Body composition (dual-energy x-ray absorptiometry), insulin sensitivity (oral glucose tolerance test and homeostasis model assessment estimate of insulin resistance; n = 15), adiponectin, C-reactive protein (CRP), interleukin (IL) 6, insulin-like growth factor-1, soluble intercellular adhesion molecule-1, and soluble vascular cell adhesion molecule-1 serum levels, and blood lipids and lipoproteins factor-1 | Aerobic exercises significantly increased insulin sensitivity, cardiorespiratory fitness, and lower limb fat-free mass and decreased insulin-like growth factor-1 was | N/A | 12 weeks of aerobic exercises improved insulin sensitivity in obese girls |

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