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ROLE OF PHYSICAL ACTIVITY DURING QUARANTINE IN COVID-19 PANDEMIC; A MULTI-LEVEL ACTION AND OUTCOME FRAMEWORK

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Abstract

Physically active individuals maintain a superior immune system even through altered WBC levels. Macrophages play an important role in immune response, tissue damage repairing, and repairing of skeletal muscle. Moderate intensity physical training reduces macrophage impaired function and lymphocytes percentage expressing intracellular IL-2 in the body. Post-exercise observation showed an increase in CD163+ and CD11b+ cells number in young people. The complete training program helps in increasing NK cell activity, viral infection controls, and malignant cell formation controls. Also, physical activity of low intensity increases the secretory immunoglobulin-A secretion rate by affecting surface immune defense. Whereas, immunoglobulin-A concentration and Saliva flow rate affect the secretion rate of secretory immunoglobulin-A. This may donate to a lower risk of prospectus chronic disease expansion such as COVID-19. The present study reflected the data of a couple of previous decades to clearly illustrate the readers with the most prominent evidence of physical activity in boosting up the immune system thus playing a vital role in this era of coronavirus.

Keywords
Physical Activity, COVID-19, Neutrophils, Cytokines, Macrophages, Immunoglobulin-A.

1. Introduction

Here are two main reasons for coronavirus to become a drastic threat. Firstly the aged population can die having other health issues but young ones can die as well. Virus as being virulent, having a mortality rate of 1% that enhanced its severity from the proposed data as compared to seasonal influenza pandemics. Two Seasonal influenza pandemics were reported in 1957 and 1918 with a mortality rate of 1% and

0.6% respectively. Secondly, an infected person has multiple ratios of two to three others. Duggal *et al.,* in 2019 strongly evidenced that even pre-symptomatic and slightly fever person can spread this disease. That's why it will be difficult to control as compared to middle east respiratory syndrome and Severe acute respiratory syndrome. Covid-19 is highly contagious due to its multiplication in a short duration as compared to a severe acute respiratory syndrome that was only symptomatically contagious (Shephard & R. J. 1998).

Quarantine word was taken from the Italian word quarantina which means "forty days", used in the 14th-15th-century Venetian language and designating the period that all ships were required to be isolated before passengers and crew could go ashore during the Black Death plague epidemic. Depression and tension are highly influenced by quarantine. Western health care system assembled patient-centered care but in this pandemic condition now it would be community-centered care. This would be increased in health-conscious people. Survey studies showed that quarantine had been reported a high number of psychological issues including depression, fear, anxiety, mood swings, restlessness, and insomnia. Thus, a balanced set of good physical activities (exercise) can help to boost the immune system in such a trend shown in figure 1.

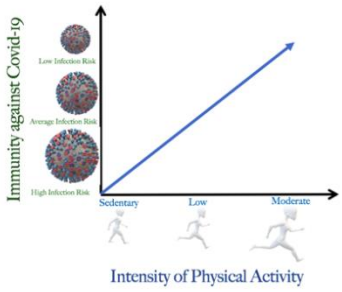

Figure 1: Impact of Physical Activities (Exercise) On Immune System

1.1 Exercise versus Enriched Foods to Prevent COVID-19

Chin with his coworkers in 2000 examined the effects of enriched foods and physical activity on the cellular immune response of weak elderly people. He concluded that no interactive or independent effect of enriched foods was experienced. Thus, exercise groups were compared with those of non-exercises ones, and micronutrients (pyridoxine, folate, and zinc) in their blood have been checked. Results revealed that non-exercising groups showed 38.5µmol/L of pyridoxine, 17.7nmol/L of folate, and 43.2 mg/L of zinc while a prominent increase in absorption of nutrients is observed in the exercising group which resulted as 39.1µmol/L of pyridoxine, 19.1nmol/L of folate, and 44.2 mg/L of zinc. The increase in micronutrients present in the blood of the exercising group as compared to that of the no-exercising groups is illustrated prominently in figure 2 (Chin *et al.,* 2000).

However, in this review study, we are trying to make it clear to the readers that exercise directly or indirectly plays a promising role in boosting up the immune system either by increasing white

blood cells (WBCs) or by increasing nutrient absorption which ultimately directs the body toward strong immunity.

The up-mentioned study of Chin *et al.*, clearly revealed that the micronutrient enriched foods reflected no effect but exercise does, so exercise may slow down or even prevent the decline in an immune response. However, this is the reason that physical activity can help in the prevention of COVID-19 by making a body strong enough to fight coronavirus on its own.

1.2 Effects of Stress and Anxiety on Physical Activity:

The "Global Action Plan on Physical Activity 2018-2030" specified that physical activity is compulsory for the prevention of non-communicable diseases published by WHO. Chances of Cardiovascular diseases are also reduced by regular physical activity (Gleeson *et al.*, 2004). The 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease 2019 suggested that the average person must do adequate intensive exercise of a minimum of two and half hours in seven days and vigorous-intensity aerobic physical activity of a minimum of one and half hours in 7 days or equivalence of both physical activities may minimize the chances of ASCVD (Class I LOE B-NR) Chances of ASCVD can be positively minimized by doing physical activity less than recommended by an average person in case if he feels difficult to do recommended. (Class IIa LOE B-NR). Watching Television for a long period increases the chances of cardiovascular disease, type 2 diabetes and all diseases that enhance mortality rate (Simpson *et al.*, 2020). A sedentary lifestyle is also linked with harmful health risks irrespective of levels of physical activity (Tudor-Locke *et al.*, 2004). Government restricted outdoor exercise like gym and social activities, physical activity of an average person is limited. Inflammation is a pathophysiological phenomenon that occurs in chronic diseases like cardiovascular, T2 diabetes, and obesity.

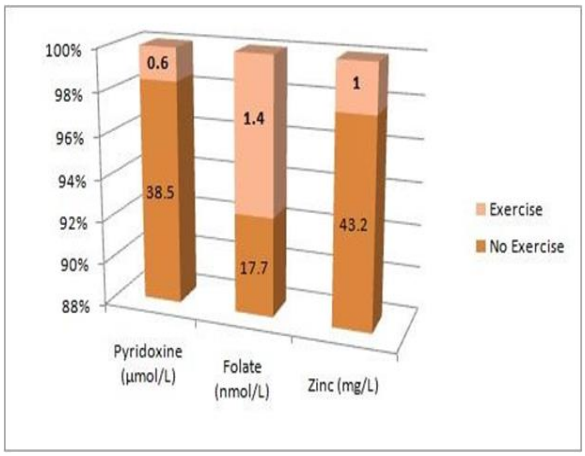

Figure 2: Level of micronutrients present in the blood of the exercising group and no-exercising groups

Regular physical activity helps to maintain a normal weight, adipose tissue reduction, and oxidative stress with inflammation reduction (Ströhle & A. 2009). Physical inactivity and sedentary life may enhance the chance of getting the cardiovascular disease with metabolic effects as a consequence of sharing quarantine. Physical inactivity may raise blood pressure, metabolic effects, and cardiovascular modification in just 14 days. In muscle tissues, there is a quick start of insulin resistance and reduction of glucose utilization that results in an inability of muscle performance by stopping the Physical activity

(Hammami *et al.,* 2020). Regular physical exercise will be helpful for both mental and physical health during quarantine (Bouchareb *et al.,* 2020). The WHO has just announced guidelines on how to remain physically active during quarantine for patients of acute respiratory illness and pre-symptomatic. They recommended subsequent online exercise lectures, online sessions containing videos and applications that guide and train aerobic exercises. Table 2 summarizes the WHO indication "Stay physically active during self-quarantine" (Rodríguez *et al.,* 2020).

Today across social media and the web, there are several videos elaborating exercises to help people carry out physical activity on their own. Also, sometimes it's difficult to perform all the alignments and pose in a workout, that is to say, in fear of permanent and long-term joint and muscles related injuries (Hall *et al.,* 2020). Additionally, Billions of people having nutrition and step-counting applications in smartphones, nowadays, are getting benefits with these applications. More advanced and community beneficial apps are yet to be developed for the changed lifestyle and behaviors of people. Many people use these nutrition-related applications for maintaining ideal body weight and diet. With each day, the number of nutrition and health applications. The number and availability of these nutrition and health applications increase on Apple App and Google Play Store. This concludes the increasing healthy lifestyle awareness in people in the modern era. These applications, along with social support, are a great source to minus the negative effect of quarantine that is cast on lifestyle due to COVID-19 (Parnell *et al.,* 2020). Other than nutrition-related smartphone applications, telemedicine is another important tool, for patients that are quarantined, to monitor nutritional, motor, psychological and psychiatric conditions.

Epidemiological studies reveal the relation between infections and other diseases occurrence and intensity of physical exercise. Acute exercise develops chronic stress in the body due to which elevated activity of Natural killer cells and reduces the function of neutrophils occurs in the body (Jiménez-Pavón *et al*., 2020). Several factors related to exercise, like intensity duration and type of exercise, total timing of physical activity session, and type and dose of immune modulator for stimulating the cell, are responsible for casting complex effects on the innate immune system (Yancy & C. W. 2020). Exercise concerning infection is related to some medical risks which include infected persons and athletes who can get infected. These types of risks are greater in sports teams where athletes are in close contact during, before, and after different physical sessions.

2. Physical Activity and Immune Function

Immune function role in the onset of diseases like cancer, inflammatory state, and autoimmune disease is well known. These diseases are very frequent in older adults. An elevated level of

respiratory tract infections, including influenza and cold, are due to innate immunity compromised function (Lippi *et al*., 2020). Studies revealed that moderate and regular physical activity can lead to increased innate immune functions. It also leads to a reduced rate of mortality and incidence for some known types of cancer including tumors of the female reproductive tract and colon (World Health Organization, 2020). Complete physical training casts a favorable effect on some clinical courses. The immune system role seems to be restricted and depends on exercise program type, specific cytolysis tumors' sensitivity, the stage at which cancer was reached, and several other complex factors (Livingston *et al.,* 2020). Regular exercise of moderate intensity lessens upper respiratory tract infections, whereas hard and chronic physical workout has the opposite effect. A number of studies report that the infection gets worse with strenuous exercise inpatients (Leung *et al.*, 2020). Factors like blood flow, hydration status, intensity, changes in body temperature, duration and mode of exercise, and cytokines play a role in immune cells interchanging between circulation and peripheral lymphoid tissues with and as a result of strenuous exercise (Wang *et al.,* 2020). Macrophages, NK cells, and neutrophils show more response towards acute exercise to function and number. In contrast, various immune measures and T-cell counts show no elevation. NK-cell shows a higher level of activity in response to long-term physical training, whereas functions of neutrophils get reduced during acute exercise. Comparatively to strenuous exercise bouts of high intensity, average intensity and duration lead to less reduced immune system stress as illustrated in figure 3 (Rundle *et al.,* 2020).

3. Neutrophil Granulocytes

In elderly people, the most frequent infectious diseases, because of lowered immune defense, increase the mortality risk with higher susceptibility and affect the upper respiratory tract within the population (Galea *et al.,* 2020). The polymorph nuclear cells are represented as a primary barrier to fungi and bacteria attacks. Comparing the old population with the young population, numerous studies have shown that the numbers of neutrophils are still the same in the bone marrow and blood. Moreover, in old adults, vascular adhesion and chemotaxis did not show changes. Therefore, compromised neutrophil granulocytes function which deals with superoxide generation and degradation could be due to decreased capacity of bactericidal and altered phagocytosis (Chen *et al.*, 2020).

This inability explanation has been given as CD16, CD32, CD64, and CD11b, by studying the expression of such membrane markers. in detail, the Fc-gamma receptor that is called CD16, which declines along with age has been identified by Butcher *et al.,* Neutrophilia has been noticed by them but with lowered CD16 level. It has been suggested that the origin of alteration arises in the bone marrow. These

findings could give more information about the decreased superoxide anion production in response to Gram-positive bacteria, like *Staphylococcus aureus*. Probably, these kinds of microbes require a complement bond and Fc-receptor (Mattioli *et al.*, 2020). *Escherichia coli*, conceivably not affected by aging, depends on the binding of CD14, thus the elderly people are more susceptible to other Gram-positive infections and *S. aureus*. Within this last mechanism the ion calcium existence is not required, therefore, the intermediates of reactive oxygen don't undertake any kind of changes (Mattioli *et al.*, 2020). The concentration of calcium intracellularly influences the capability of killing microbes and phagocytosis. The activation of neutrophils granulocytes is because of an increase in calcium levels, therefore, Wenisch *et al.*, hypothesized that may be the inability of the neutrophils is due to raised resting ion calcium levels, furthermore, along with aging, after the stimulation with f-Met-Leu-Phe the calcium extrusion is reduced (Orgilés *et al.*, 2020). Certainly, the same group found that the functionality of these cells might be reduced with the decreased transport, a fuel for neutrophils. In elderly people, reduced neutrophil numbers could not be the reason for severe and long-lasting URTI but for the lowered expression of some membrane markers involving the reactive species production and signaling of transmembrane that intervene in microbes killing (Martin *et al*., 2009).

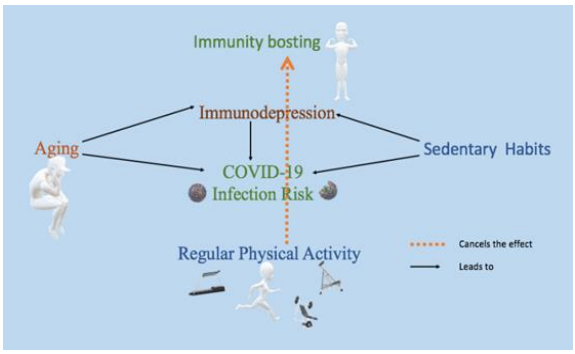

Figure 3: Relation of Exercise Intensity on Immune System

4. Exercise and Neutrophils

Relatively few studies have been carried out to study neutrophil's role during exercise on various athletes. Depending on the increase in the level of cortisol and catecholamine, exercise stimulates the neutrophil's release into the circulation. When stimulated in vitro, mobilized neutrophils have a heightened capacity to generate some kind of reactive oxygen species (ROS) after exercise (Maedaniyan *et al.*, 2020). ROS may lead to damage of DNA within leukocytes that should be generated during intense exercise but it is unidentified if this happened as a result of the activation of neutrophils. Following prolonged and intensive training of exercise the neutrophil's function appears to be impaired (Sood & S., 2020). In elite swimmers that undergo intense training, the neutrophil's oxidative activity is significantly lower as compared to controls. Instead, before a World Championship, alterations have not been shown by the elite female rowers in monocyte phagocytosis, oxidative burst, and granulocyte (Singhal & T. 2020). Furthermore, alterations were not present in respiratory burst activity and

degranulation, in well-trained runners after downhill running. At present, however, variation in exercise-induced alterations in the function of neutrophils could be reliant on the differences in training status and exercise protocols (Shereen *et al.*, 2020).

Table 2 elaborates the rapid increase in neutrophil, leukocyte, monocyte, and eosinophil count promptly after physical activity in a control group of normal physically active. The swift change in WBCs can also be seen in the Physical active group directly after physical activity. The total drops to some extent after 2 hours of exercise in both groups, whereas, the total count after 2 hours of exercise in a lateral group is greater as compared to the same count in a control group of normal physically active.

Table 1. White Blood Cells Count In Normal Physical Active (Control) and Physically Active Group

		Neutrophil counts		**Leukocyte count**	**Monocyte count**		**Eosinophil counts**	
Groups	**Count of cells at rest**	(1/µl)	(%)	(1/µl)	(1/µl)	(%)	(1/µl)	(%)
		3, 663± 571	62 ±8	5,940± 967	133±41	2.0± 0.7	54±65	0.9± 1.0
Control group/normal Physical activity	promptly After exercise	5,726± 1,087	63 ±7	8,921± 1,560	209±78	2.0± 0.7	74±76	0.8± 0.9
	After 2 hours	5,396± 1,972	76 ± 6	6,841± 2,068	147±85	2.0± 1.1	60±62	0.9± 0.9
	Cells count at rest	3,884± 655	62 ±3	6,364± 1,201	166±52	3.0± 0.7	69±65	1.1± 1.0
Physical active Group	promptly After exercise	6,168± 1,246	66 ±4	9,224± 1,724	207±76	2.0± 0.7	151±82	1.7± 0.9
	After 2 hours of exercise	5,322± 1,376	71 ±11	7,483± 1,358	150±50	2.0± 0.6	52±42	0.7± 0.5

4.1 Macrophages

Macrophages play a significant role in the immune response by acting through several mechanisms. These mechanisms include the elimination of microbes, phagocytosis, and releasing of mediators. Macrophages also play an essential role in repairing tissue damage. Monocyte numbers remain considerably constant with increasing age. A number of experimental studies demonstrated that, as the age of hematopoietic stem cells increases, their functional lifespan gets limited (Rodriguez-Morales *et al.,* 2020). These studies demonstrate hypo cellularity in the macrophage precursors noticed and detected in older adults. According to early works, macrophages give rise to alike levels of cytokines. The difference in function can be adjusted through changes in T- and B-cell responses. Some studies also found elevated levels of TNF-α, IL-8, IL-6, and IL-1 by macrophages in the body, whereas reduced synthesis was also found by some others. The reduced generation of TNF-α and IL-6, because of monocytes, and lipopolysaccharide stimulation in elderly people has been correlated with not sufficient activation of mitogen-activated protein kinase, protein kinase C β1, protein kinase C β11 and protein kinase C α, and also a deficiency in expression of c-Jun and c-FOS (Salehi *et al.,* 2020).

Gon *et al.,* described that human macrophages cause a reduced release of chemokine macrophage inflammatory protein 1 α, granulocyte-macrophage colony-stimulating factor, and granulocyte colony-stimulating factor. These results can be demonstrated by not having the same experimental conditions, the health status of subjects, and methods used for the measurement of cytokines levels (World Health Organization, 2020). Defects like damaged DNA and repair capacity of impaired DNA in genomic DNA become the cause of macrophage aging. This leads to a number of functional activities lost. A fresh study conducted on the effect of the elevated generation of TNF-α in splenic macrophages incubated in vitro models demonstrated that macrophage activation is affected by age-specific external milieu (World Health Organization, 2020). Macrophages or monocytes are usually exposed to a number of agents including fatty acids, hormones, and cytokines. These can act on function and phenotype leading to adjusting to changing microenvironments and functional plasticity. These agents' levels can change in older adults affecting macrophages (Ludvigsson & J. F. 2020).

4.2 Physical Activity and Macrophages

Other than immune response and tissue damage repairing, macrophages also play an important role in repairing skeletal muscle. These skeletal muscles are repaired through alternative and pro-inflammatory functions. Due to aging, change in properties and abundance of macrophages of skeletal muscle leads to an effect on the response to acute resistance exercise. Pre-exercised muscles of young people show an abundance of macrophages whereas

higher levels of IL-1Ra, IL-1 beta, and IL-10 are usually found in elderly pre-exercised muscles. Comparatively, post-exercise observation showed an increase in CD163+ and CD11b+ cell numbers in young people, whereas macrophage abundance remained the same in both young and old groups. These findings give the results that the regulation of muscle macrophage function becomes defective with aging. This defective regulation takes place in response to resistance exercise. All these limits hypertrophy of muscle in older adults. A study on the murine model suggested that macrophages' impaired function is due to acute restraint stress whose effects reduce with the physical training of moderate-intensity involving the mechanism of increased macrophages tolerance (Heymann *et al.,* 2020).

4.3 Natural Killer

Natural killer (NK) helps the innate immune, to respond against infections. Natural killer (NK) cells do not require an antigen sensitization to lyse targets. This ability differs from natural killer (NK) cells (cytotoxic cells) from cytotoxic T cells. Recent studies have suggested that, with aging, the cytotoxic ability of NK cells changes with an increase in number and decrease in the activity of cells. These results contradicted the early studies' suggestion, which suggests that aging brings no change in the NK cell's ability (Zheng *et al.,* 2020). Factors like increased responses and decreased responses to the negative modulating adenosine triphosphate and IL-2, IL-12, and interferon (IFN)-α, respectively, are all due to the NK cell's functional decline. Moccheggiani *et al.* described that the neuroendocrine-immune pathway has an exceptional role in immune senescence. Many immune cells and NK cells affect the adaptive immune responses because of stimulating the production of cytokines. This is due to the presence of some hormone receptors on them. These hormone receptors include pituitary, gonadal, thyroid, and hypothalamic hormones' receptors. In some cases, impaired immune responses in elderly people are caused by hormone deficiency and also the availability of zinc ions. The bioavailability of the ion zinc helps in the maintenance of effective neuroendocrine-immune networks in elderly people (Fang *et al.,* 2020). In the majority of healthy older people of less than 80 years, the NK cells system is found to be very active. High activity of NK cells in this age group suggests a slow incidence of age-specific cancer, whereas it declines in the elderly over 80 years (Hollander *et al.,* 2020).

4.4 Physical Activity and NK

Exercise intensity affects activity and the number of natural killers (NK) cells. One hour of bout exercise leads to a decrease in cell functions resulting in inhibition of lysis of tumor cells. In athletes, NK cell activity is increased in response to chronic stress caused by intensive exercise whereas in elderly people NK cell activity does not change in response to moderate exercise. A complete physical training program has a good effect on resting NK cell activity. This also increases the malignant cell formation

and viral infection controls (Velavan *et al.,* 2020). A study done by Flynn *et al*. gave the results that, elderly women who completed resistance training of 10 weeks showed a short-term increase of NK cell number after exercise. A comparative study was done on the relation and difference between the active and inactive way of life and immune competence on a group of elderly people doing exercise and by keeping other groups as control groups. The results showed increased NK-cells concentration in the group doing exercise compared to another controlled group. Also, a reduction in phagocytic activity in neutrophils was observed in relation to age, in older people doing exercise. All these results conclude that daily moderate-intensity exercise leads to lowering the reduction of innate immunity and circulating T-cell, related to age (Recalcati & S. 2020). Another study about NK-cells and exercise described that NK-cells show an immediate response after exercise. The response is normal in a single challenge of exercise (Zu *et al.,* 2020). Older people showed slighter elimination of phytohemagglutinin-induced lymphocyte regeneration or growth than younger subjects. The number of cross-sectional immune status comparisons done between a controlled group of young people having a sedentary lifestyle and elderly people, who were physically fit, showed increased activity of NK-cell due to persistently done physical activity (Liu *et al.,* 2020). Also, NK-cell percentage was recorded more in elderly people practicing regular physical activity for up to 16 years, than in control groups (Sohrabi *et al.,* 2020). Generally, moderate exercise alone can increase the activity of oxidative burst, monocyte phagocytosis, and blood granulocytes. In another study, Neil with his coworkers in 2012 created an experiment in which a group of some women was randomly directed to a non-exercise control assembly or one of mentioned three specified exercise groups. These groups include the control group and the energy expenditure groups of 4, 8, or 12 Kcal/KW (kcal kg^{-1}·$week^{-1}$) for the time of 6 months at 50% VO_{2peak} intensity which is shown in Table 2 (Willis *et al.,* 2018).

Table 2. Effect of Exercise on VO_{2peak} And WBC Count

Content	**Treatments**				
	All	Control	4 Kcal/KW	8 Kcal/KW	12 Kcal/KW
VO_{2peak}, mL·kg^{-1}·min^{-1}	15.5	15.7	15.4	14.9	15.9
Total WBC, cells/ìL	5662	5619	5718	5776	5526
Lymphocytes, cells/µL	1926	1901	1962	1976	1854
Monocytes, cells/µL	383	376	386	368	396
Neutrophils, cells/µL	3144	3128	3151	3230	3074

Basophils, cells/μL	34.9	35.3	34.5	37.9	32.8
Eosinophils, cells/μL	175	179	185	164	169

WBC (White blood cells)
VO2 (Volume of oxygen consumed)
Kcal/KW (kcal kg−1·week−1)

4.5 Cytokines

CD28−CD8+ T lymphocytes are seen to be responsible for increased cytokine type 1 production in old adults as TNF-α and IFN-γ are responsible for supporting the status of chronic inflammatory and also have control of defense activity (Hellewell *et al.,* 2020). Chronic antigenic load causes this status called "inflame-aging" which leads to an increase in the production of acute-phase protein and an increase in inflammatory cytokines. Inflammatory cytokines improve responses to the vaccine by improving the survival of CD4+ T cell effectors (Tian *et al.,* 2020). This is due to an increase in the production of IL-2 by overcoming the activation of a reduced transcription factor, leading to an increase in the generation of CD4 effector, in aged CD4 cells (Andersen *et al*. 2020). A number of studies concluded increased IL-4 production, produced by activated CD4+ cells, and decreased IL-2 is an anti-inflammatory cytokine, type 2 cytokines pattern (Van Doremalen *et al*. 2020). Alberti *et al*. reported a decrease in IFN-γ / IL-4 ratio, in aging. This suggests an increased pattern 2 roles comparative to pattern 1 (Walls *et al.,* 2020).

Being an inflammatory mediator, IL-6 can cause pathogenesis, like many lymphoproliferative disorders. For this purpose, elevation in the level of IL-6 serum is necessary to stimulate the hypothalamus. A study performed on IL-15 in ultra-longeval subjects concluded that interleukin provokes the growth of both CD8 and CD4, memory T cells, in the elderly (Livingston *et al.,* 2020). IL-15 also plays a role in the differentiation of NK CD56+ cells. NK CD56+ cell helps in the defense against pathogens like bacteria and viruses (Novel & C. P. E. R. E. 2020).

4.6 Physical Activity and Cytokines

Various Studies conducted on marathoners and runners illustrate the increased concentration of anti-inflammatory and inflammatory types of cytokines in the blood. While little change in levels of cytokines was detected in subjects doing physical activity of moderate intensity of only one hour (Guan *et al.,* 2020). IL-6 has the highest level in cytokines, achieved only after six hours of running (Zhu *et al.,* 2020). IL-6 increases 5.5-fold after running for 2.5 hours while it reaches up to 100-fold in marathoners. It has been observed that the IL-1Ra level increases, mainly due to various cytokines like IL-6, two hours after the exercise. Being an inhibitor of IL-1, IL-1Ra reduces the damaging effects of IL-1. IL-6 is observed to increase during running while IL-1Ra rises in the post-run (Perlman & S. 2020).

IL-6 plays an inhibitor role on TNF-α. IL-6 is released due to muscle damage because of

induced exercise. The inhibitor role of IL-6 prevents a number of negative effects which results in lower blood pressure, better lipid profile, and elevated insulin sensitivity (Mehta *et al.,* 2020). An anti-Inflammatory activity can also be the result of the inhibitor role of IL-6 but it can be due to preformed exercise. A hypothesis states that, if older adults maintain the IL-5 release during exercise then exercise exerts a beneficial effect on the anti-inflammatory state of these subjects (Jiang *et al.,* 2020). Although resistance exercise brings decreased levels of TNF-α (Phan *et al.,* 2020). Cytokine expressions are affected by exercise intensity. Examination on older adult women performing the exercise of moderate-intensity showed that the lymphocytes percentage that was expressing intracellular IL-2 was elevated as compared to the controlled group of women having a sedentary lifestyle. The results were the same for young people (Memish *et al.,* 2013). The intracellular IL-4, which was demonstrating lymphocytes, was reduced. This plays a role in controlling elevated levels of memory cells than other naive cells (Peiris *et al.,* 2003).

4.7 Secretory Immunoglobulin-A

Secretory immunoglobulin-A are found to play a basic role, in the body, against pathogens. These pathogens get into the body through the mucosa. Secretory immunoglobulin-A are found in Broncho alveolar and intestinal secretions, and in some other mucosal fluids. Abundant quantities of Secretory immunoglobulin-A are also found in mother's milk, tears, and saliva (van der Hoek *et al.,* 2004). Immunoglobulins protect against pathogens, like bacteria and viruses, for upper respiratory tract infections. Immunoglobulins binding with pathogens, like bacteria and viruses, is the inability of the pathogens to colonize and avoid adhesion (Wang *et al.,* 2020). These findings suggest that decreases in secretory immunoglobulin-A levels, especially in the elderly, will cause more chances of infections for upper respiratory tract infections, like cold or influenza. A number of studies have also concluded that elderly people who are at rest have lower secretory immunoglobulin-A secretion, in both genders (Cui *et al.,* 2019).

4.8 Physical Activity and Immunoglobulins

Low-intensity physical activity gives useful effects to surface immune defense, which results in an increased secretory immunoglobulin-A secretion rate (Li *et al.,* 2020). Saliva flow rate and immunoglobulin-A concentration affect the rate of secretory immunoglobulin-A secretion. Whereas increased secretory immunoglobulin-A concentration is observed in old adults, after an increased rate of secretory immunoglobulin-A secretion caused due to 12 months exercise program (Xinhua *et al.,* 2020). Sakamoto *et al*. suggested activation of the parasympathetic nervous system after physical activity, after finding an increase in saliva flow rate (Cheng ZJ & Shan J. 2019). While, after the physical activity of low intensity, increased secretory immunoglobulin-A secretion and saliva flow rate is found to be temporary (Brian *et al.,*

2005). Other studies also show, after training for 12 months, a high level of immunoglobulin-A is found in the body with unknown mechanisms (Holmes & K. V. 2003). Another study reported improvement in mucosal immune function in old adults, after taking 7,000 steps/day as physical activity of moderate intensity (Ziebuhr & J. 2005).

5. References

Abdurachman, A., &Herawati, N. (2018). The role of psychological well-being in boosting immune response: an optimal effort for tackling infection. *African Journal of Infectious Diseases*, *12*(1S), 54-61.

Andersen, K. G., Rambaut, A., Lipkin, W. I., Holmes, E. C., & Garry, R. F. (2020). The proximal origin of SARS-CoV-2. *Nature Medicine*, *26*(4), 450-452.

Bouchareb, R., & Laadjal, Z. Coronavirus (COVID-19) and the benefits of physical activity during quarantine.

Brian, D. A., & Baric, R. S. (2005). Coronavirus genome structure and replication. In *Coronavirus replication and reverse genetics* (1-30). Springer, Berlin, Heidelberg.

Brines, R., Hoffman-Goetz, L., & Pedersen, B. K. (1996). Can you exercise to make your immune system fitter?.*Immunology today*, *17*(6), 252-254

Chen, Q., Liang, M., Li, Y., Guo, J., Fei, D., Wang, L. & Wang, J. (2020). Mental health care for medical staff in China during the COVID-19 outbreak. *The Lancet Psychiatry*, *7*(4), e15-e16.

Cheng ZJ, Shan J. (2019). Novel coronavirus: where we are and what we know. Infection. 2020:1–9. https://doi.org/10.1007/s15010-020-01401-y.

Chin, M. A. P., Pallast, E. G., Kloek, G. C., Schouten, E. G., & Kok, F. J. (2000). Immunity in frail elderly: a randomized controlled trial of exercise and enriched foods. *Medicine and science in sports and exercise*, *32*(12), 2005-2011.

Codella, R., Luzi, L., & Terruzzi, I. (2018). Exercise has the guts: how physical activity may positively modulate gut microbiota in chronic and immune-based diseases. *Digestive and Liver Disease*, *50*(4), 331-341.

Cui, J., Li, F., & Shi, Z. L. (2019). Origin and evolution of pathogenic coronaviruses. *Nature Reviews Microbiology*, *17*(3), 181-192.

Duggal, N. A., Niemiro, G., Harridge, S. D., Simpson, R. J., & Lord, J. M. (2019). Can physical activity ameliorate immunosenescence and thereby reduce age-related multi-morbidity?. *Nature Reviews Immunology*, *19*(9), 563-572.

Fang, L., Karakiulakis, G., & Roth, M. (2020). Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?. *The Lancet. Respiratory Medicine*, *8*(4), e21.

Galea, S., Merchant, R. M., & Lurie, N. (2020). The mental health consequences of COVID-19 and physical distancing: The need for prevention and early intervention. *JAMA Internal Medicine*.

Gleeson, M., Nieman, D. C., & Pedersen, B. K. (2004). Exercise, nutrition and immune function. *Journal of Sports Sciences*, *22*(1), 115-125.

Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., & Du, B. (2020). Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine*, *382*(18), 1708-1720.

Hall, G., Laddu, D. R., Phillips, S. A., Lavie, C. J., & Arena, R. (2020). A tale of two pandemics: How will COVID-19 and global trends in physical inactivity and sedentary behavior affect one another?. *Progress in Cardiovascular Diseases*.

Hammami, A., Harrabi, B., Mohr, M., &Krustrup, P. (2020). Physical activity and coronavirus disease 2019 (COVID-19): specific recommendations for home-based physical training. *Managing Sport and Leisure*, 1-6.

Hellewell, J., Abbott, S., Gimma, A., Bosse, N. I., Jarvis, C. I., Russell, T. W., & Flasche, S. (2020). Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *The Lancet Global Health*.

Heymann, D. L., & Shindo, N. (2020). COVID-19: what is next for public health?. *The Lancet*, *395*(10224), 542-545.

Hollander, J. E., &Carr, B. G. (2020). Virtually perfect? Telemedicine for COVID-19. *New England Journal of Medicine*, *382*(18), 1679-1681.

Holmes, K. V. (2003). SARS-associated coronavirus. *New England Journal of Medicine*, *348*(20), 1948-1951.

Jiang, F., Deng, L., Zhang, L., Cai, Y., Cheung, C. W., & Xia, Z. (2020). Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). *Journal of General Internal Medicine*, 1-5.

Jiménez-Pavón, D., Carbonell-Baeza, A., & Lavie, C. J. (2020). Physical exercise as therapy to fight against the mental and physical consequences of COVID-19 quarantine: Special focus in older people. *Progress in Cardiovascular Diseases*.

Leung, C. C., Lam, T. H., & Cheng, K. K. (2020). Mass masking in the COVID-19 epidemic: people need guidance. *Lancet*, *395*(10228), 945.

Li, G., Fan, Y., Lai, Y., Han, T., Li, Z., Zhou, P., & Zhang, Q. (2020). Coronavirus infections and immune responses. *Journal of Medical Virology*, *92*(4), 424-432.

Lippi, G., Henry, B. M., & Sanchis-Gomar, F. (2020). Physical inactivity and cardiovascular disease at the time of coronavirus disease 2019 (COVID-19). *European Journal of Preventive Cardiology*, 2047487320916823.

Liu, Y., Yan, L. M., Wan, L., Xiang, T. X., Le, A., Liu, J. M., & Zhang, W. (2020). Viral dynamics in mild and severe cases of COVID-19. *The Lancet Infectious Diseases*.

Livingston, E., & Bucher, K. (2020). Coronavirus disease 2019 (COVID-19) in Italy. *Jama*, *323*(14), 1335-1335.

Livingston, E., & Bucher, K. (2020). Coronavirus disease 2019 (COVID-19) in Italy. *Jama*, *323*(14), 1335-1335.

Ludvigsson, J. F. (2020). Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatrica*, *109*(6), 1088-1095.

Maedaniyan, M., Banitalebi, E., Faramarzi, M., Ghorbanpoor, M., & Earnest, C. (2020). 2019 novel coronavirus: Emphasis on maintaining optimal levels of physical activity under self-quarantine conditions. *International Journal of Epidemiologic Research*.

Martin, S. A., Pence, B. D., & Woods, J. A. (2009). Exercise and respiratory tract viral infections. *Exercise and sport sciences reviews*, *37*(4), 157.

Mattioli, A. V., Puviani, M. B., Nasi, M., & Farinetti, A. (2020). COVID-19 pandemic: the effects of quarantine on cardiovascular risk. *European Journal of Clinical Nutrition*, 1-4.

Mattioli, A. V., Sciomer, S., Cocchi, C., Maffei, S., & Gallina, S. (2020). Quarantine during COVID-19 outbreak: changes in Diet and physical activity increase the risk of cardiovascular disease. *Nutrition, Metabolism and Cardiovascular Diseases*.

Meek, R. (2013). *Sport in prison: exploring the role of physical activity in correctional settings*. Routledge.

Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., Manson, J. J., & HLH Across Speciality Collaboration. (2020). COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet (London, England)*, *395*(10229), 1033.

Memish, Z. A., Zumla, A. I., Al-Hakeem, R. F., Al-Rabeeah, A. A., & Stephens, G. M. (2013). Family cluster of Middle East respiratory syndrome coronavirus infections. *New England Journal of Medicine*, *368*(26), 2487-2494.

Nieman, D. C. (2001). Exercise immunology: nutritional countermeasures. *Canadian Journal of Applied Physiology*, *26*(S1), S45-S55.

Nieman, D. C. (2011). Moderate exercise improves immunity and decreases

illness rates. *American Journal of Lifestyle Medicine*, *5*(4), 338-345.

Novel, C. P. E. R. E. (2020). The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghualiuxingbingxue za zhi= Zhonghualiuxingbingxuezazhi*, *41*(2), 145.

Orgilés, M., Morales, A., Delvecchio, E., Mazzeschi, C., & Espada, J. P. (2020). Immediate psychological effects of the COVID-19 quarantine in youth from Italy and Spain.

Parnell, D., Widdop, P., Bond, A., & Wilson, R. (2020). COVID-19, networks and sport. *Managing Sport and Leisure*, 1-7.

Peiris, J. S. M., Lai, S. T., Poon, L. L. M., Guan, Y., Yam, L. Y. C., Lim, W., ... & Cheng, V. C. C. (2003). Coronavirus as a possible cause of severe acute respiratory syndrome. *The Lancet*, *361*(9366), 1319-1325.

Perlman, S. (2020). Another decade, another coronavirus. https://www.nejm.org/doi/full/10.1056/NEJMe2001126

Phan, L. T., Nguyen, T. V., Luong, Q. C., Nguyen, T. V., Nguyen, H. T., Le, H. Q., & Pham, Q. D. (2020). Importation and human-to-human transmission of a novel coronavirus in Vietnam. *New England Journal of Medicine*, *382*(9), 872-874.

Recalcati, S. (2020). Cutaneous manifestations in COVID-19: a first perspective. *Journal of the European Academy of Dermatology and Venereology*.

Rodríguez, M. Á., Crespo, I., & Olmedillas, H. (2020). Exercising in times of COVID-19: what do experts recommend doing within four walls?. *Revista Espanola De Cardiologia (English Ed.)*.

Rodriguez-Morales, A. J., Cardona-Ospina, J. A., Gutiérrez-Ocampo, E., Villamizar-Peña, R., Holguin-Rivera, Y., Escalera-Antezana, J. P., &Paniz-Mondolfi, A. (2020). Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel medicine and infectious disease*, 101623.

Rundle, A. G., Park, Y., Herbstman, J. B., Kinsey, E. W., & Wang, Y. C. (2020). COVID-19–Related School Closings and Risk of Weight Gain Among Children. *Obesity*.

Salehi, S., Abedi, A., Balakrishnan, S., & Gholamrezanezhad, A. (2020). Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *American Journal of Roentgenology*, 1-7.

Schwartz, M., London, A., & Shechter, R. (2009). Boosting T-cell immunity as a therapeutic approach for neurodegenerative conditions: the role

of innate immunity. *Neuroscience*, *158*(3), 1133-1142.

Shephard, R. J. (1998). Immune changes induced by exercise in an adverse environment. *Canadian Journal of Physiology and Pharmacology*, *76*(5), 539-546.

Shereen, M. A., Khan, S., Kazmi, A., Bashir, N., & Siddique, R. (2020). COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research*, *24*, 91–98.https://doi.org/10.1016/j.jare.2020.03.005

Simpson, R. J., Campbell, J. P., Gleeson, M., Krüger, K., Nieman, D. C., Pyne, D. B., & Walsh, N. P. (2020). Can exercise affect immune function to increase susceptibility to infection?. *Exercise Immunology Review*, *26*, 8-22.

Singhal, T. (2020). A review of coronavirus disease-2019 (COVID-19). *The Indian Journal of Pediatrics*, 1-6.

Sohrabi, C., Alsafi, Z., O'Neill, N., Khan, M., Kerwan, A., Al-Jabir, A., & Agha, R. (2020). World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International Journal of Surgery*.

Sood, S. (2020). Psychological effects of the Coronavirus disease-2019 pandemic. *Research & Humanities in Medical Education*, *7*, 23-26.

Ströhle, A. (2009). Physical activity, exercise, depression and anxiety disorders. *Journal of neural transmission*, *116*(6), 777.

Tian, S., Hu, N., Lou, J., Chen, K., Kang, X., Xiang, Z., & Chen, G. (2020). Characteristics of COVID-19 infection in Beijing. *Journal of Infection*.

Tudor-Locke, C., & Bassett, D. R. (2004). How many steps/day are enough?. *Sports medicine*, *34*(1), 1-8.

Van der Hoek, L., Pyrc, K., Jebbink, M. F., Vermeulen-Oost, W., Berkhout, R. J., Wolthers, K. C., &Berkhout, B. (2004). Identification of a new human coronavirus. *Nature medicine*, *10*(4), 368-373.

Van Doremalen, N., Bushmaker, T., Morris, D. H., Holbrook, M. G., Gamble, A., Williamson, B. N., & Lloyd-Smith, J. O. (2020). Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *New England Journal of Medicine*, *382*(16), 1564-1567.

Velavan, T. P., & Meyer, C. G. (2020). The COVID-19 epidemic. *Tropical medicine & international health*, *25*(3), 278.

Walls, A. C., Park, Y. J., Tortorici, M. A., Wall, A., McGuire, A. T., &Veesler, D. (2020). Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell*.

Wang, C., Horby, P. W., Hayden, F. G., & Gao, G. F. (2020). A novel coronavirus

outbreak of global health concern. *The Lancet*, *395*(10223), 470-473.

Wang, C., Horby, P. W., Hayden, F. G., & Gao, G. F. (2020). A novel coronavirus outbreak of global health concern. *The Lancet*, *395*(10223), 470-473.

Wang, G., Zhang, Y., Zhao, J., Zhang, J., & Jiang, F. (2020). Mitigate the effects of home confinement on children during the COVID-19 outbreak. *The Lancet*, *395*(10228), 945-947.

Willis, E. A., Shearer, J. J., Matthews, C. E., & Hofmann, J. N. (2018). Association of physical activity and sedentary time with blood cell counts National Health and Nutrition Survey 2003-2006. *PloS one*, *13*(9), e0204277.

World Health Organization. (2020). Coronavirus disease 2019 (COVID-19) situation report, 88.

World Health Organization. (2020). Coronavirus disease 2019 (COVID-19): situation report, 85.

World Health Organization. (2020). *Mental health and psychosocial considerations during the COVID-19 outbreak, 18 March 2020* (No. WHO/2019-nCoV/MentalHealth/2020.1). World Health Organization.

Xinhua. China's CDC detects a large number of new coronaviruses in the South China seafood market in Wuhan. Available at: https://www.xinhuanet.com/2020-01/27/c_1125504355.htm.

Yancy, C. W. (2020). COVID-19 and African Americans. *Jama*.

Zheng, Y. Y., Ma, Y. T., Zhang, J. Y., &Xie, X. (2020). COVID-19 and the cardiovascular system. *Nature Reviews Cardiology*, *17*(5), 259-260.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., &Niu, P. (2020). A novel coronavirus from patients with pneumonia in China, 2019. *New England Journal of Medicine*.

Ziebuhr, J. (2005). The coronavirus replicase. In *Coronavirus replication and reverse genetics* (pp. 57-94). Springer, Berlin, Heidelberg.

Zu, Z. Y., Jiang, M. D., Xu, P. P., Chen, W., Ni, Q. Q., Lu, G. M., & Zhang, L. J. (2020). Coronavirus disease 2019 (COVID-19): a perspective from China. *Radiology*, 200490.