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Exploring the Potential Role of Magnesium in Mitigating COVID-19 Among Athletes: A Narrative Review

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ABSTRACT

The lingering effects of COVID-19 continue to exert an impact on different populations, particularly athletes, facing a potential decrease in performance due to prolonged inflammation. Due to disrupted training, competition schedules, isolation, and uncertainty, athletes also experience mental health challenges, including stress, anxiety, and depression. Optimal nutrition is therefore essential for maintaining energy balance, immunity, and mental health. One such vital micronutrient Magnesium (Mg) serves more than 300 physiological functions including signaling molecules, regulating ATP synthesis, storage, and transport. Low or below optimal levels of Mg can have a negative impact on various metabolic processes. Search for literature was performed using various databases, including Google Scholar, PubMed, and ScienceDirect using various keywords. The literature analysis revealed compelling evidence indicating an inverse relationship between Mg levels and the severity of COVID-19. Mg was found to play a potential role in the regulation of Angiotensin-Converting Enzyme (ACE) 2 receptors and the same pathway is used by the SARS-CoV-2 virus to enter and infect the cells. Among athletes, Mg supplementation has demonstrated positive effects on recovery, stress, sleep, and the reduction of inflammation. From the findings of this narrative review, we summarize that Mg supplementation emerges as a potential strategy for mitigating post-COVID-19 syndrome, particularly in athletes. However, it is crucial to note that the intake of supplements should only be done under the guidance of healthcare professionals or nutritionists, considering individual body requirements and needs.

INTRODUCTION

COVID-19 infection caused by SARS-CoV-2, first appeared in December 2019 in China (1), resulting in affecting millions of people globally. The pandemic reported over 5.2 million cases and nearly 50,0000 deaths between January and February 2023, statistical data showed a reduction of 89% and 62 % of death respectively when compared to December 2022. However, as of February 2023, more than 750 million confirmed cases and nearly 7 million deaths were registered worldwide (2).

SARS-CoV-2 spreads mainly through respiratory droplets (1) (3). The virus enters the body, binds to ACE2 receptors on the upper lining of the respiratory system, and slowly enters the cells (4) (5). This could cause a sudden shift in the body's mechanism and result in multiplication, which further results in infecting neighboring cells, causing symptoms such as anosmia, ageusia, dyspnea, hyperthermia, and cough (3). To fight against the virus, the body's defensive mechanism gets activated, and in extreme cases of infection, overexpression of immune cells triggers a cytokine storm. This sudden septic shock could affect multiple organs and leads to death (6).

COVID-19 can generally occur in three phases: Phase 1 -

asymptomatic or mild symptoms, lasting for 5-7 days; Phase 2 - moderate symptoms such as shortness of breath and pneumonia, occurring around day 7-10 and may require hospitalization; and Phase 3 - severe or critical symptoms such as acute respiratory distress syndrome (ARDS), septic shock, and multiple organ failure, which can be life-threatening and require intensive care. Individuals with metabolic syndrome, atherosclerosis, hypertension, hyperglycemia, and hypertriglyceridemia were at higher risk of developing severe illness (7) (8) (9).

Moreover, depending on the body's immune function and adaptability, each person could experience different symptoms and risk of severity It's important to note that not all people with COVID-19 will experience all three phases, and some people may progress rapidly through the phases, while others may not experience any symptoms at all (10) (11) Additionally, some people may experience long-term effects of the disease, known as "post-COVID-19 syndrome," even after the infection has resolved (12) (11).

The COVID-19 pandemic has affected health, society, and lifestyles worldwide. Lockdowns and social distancing were used by various nations to curb the outbreak. These regulations have postponed many professional sports league games. Professional sporting organizations resumed games without spectators for months after the COVID-19 pandemic. (13).The COVID-19 pandemic has resulted in the closure of many facilities where people engaged in physical activities, which has eventually led to decreased physical activity (PA), increased screen time, irregular sleep patterns, and unhealthy diets. The World Health Organization recommends 150 minutes of moderate or 75 minutes of vigorous PA per week for optimal health. Lack of PA could lead to challenges to the immune system and physical health, exacerbating sedentary lifestyle - related diseases. Further results in increased stress and anxiety caused by pro-longed social isolation (14).

Evidence from clinical studies showed the inverse relationship between PA and body composition by increasing fat mass (FM) and reducing muscle mass (MM)alongside affecting maximal oxygen uptake (VO_{2max}) (15). This situation could be aggravated in athletes who have undergone SARS-CoV-2 infection. Apart from the metabolic and psychological effects associated with physical inactivity, it is crucial to acknowledge the respiratory implications. Numerous athletes have reported experiencing persistent symptoms for several months following an initial COVID-19 infection. These lingering symptoms often include a persistent cough, tachycardia (rapid heart rate), and fatigue. These respiratory alterations contribute to the overall burden and impact on athletes' well-being and athletic performance even after recovering from the initial infection (10) (12) (16). In this context, physical inactivity decreases the muscle mass and size of muscle fibers that consequently leads to weakening.

In a normal physiological state, a sustained high intense PA releases muscle protein causing inflammation of myocytes and disturbance in muscle integrity. Further inflammatory response by immune system increases circulating muscle proteins such as Creatine Kinase (CK), Lactate dehydrogenase (LDH) (a type of protein), myoglobin and pro-inflammatory markers such as Tumor Necrosis Factor (TNF-α) and Interleukin-6 (IL-6) (17) (18) this response could appear concomitantly with albumin and muscle protein degradation. However this area needs further research (19) (20). In presences of COVID-19 infection a similar reaction occurs by increasing ferritin and C-Reactive Protein (CRP). Increased cytokines are involved in the initial and effector stage of all immune and inflammatory response (21) (22) (23).

Altogether, COVID-19 has an impact on metabolic adaptation during moderate-intense activity. Therefore, athletes with COVID-19 disease or post COVID-19 displayed an increased risk of reduced maximal and submaximal performance as well as altered cardiovascular and muscle metabolic adaptations (15) (24). SARS-CoV-2 is capable of infecting different cells of the body particularly, pulmonary epithelium and immune cells. As a result, muscle pain (myalgia) and fatigue occurred in 35% of COVID-19 patients (25) (26) (27). Thus, it can be hypothesized that the acute inflammatory response to COVID-19 infection would consume the proteins that work as building blocks for muscle activity (19).

Nutritional therapy appears as the first-line treatment and should be implemented into standard practice (28) (29). Athletes may need more nutrients than physically inactive people due to their higher energy consumption. Athletes' nutritional intake levels have not been identified, leading to insufficient calorie intake, and micronutrient deficiencies. Supplementation may be an effective strategy to achieve dietary requirements in athletes (30). Optimal to higher intake of all nutrients, those playing crucial roles in immune system, should be assured through a diverse well-balanced diet. Nevertheless, in order to reduce the risk and consequences of infections (31), the intakes for some micronutrients can exceed the recommended dietary allowances (32).

COVID-19 causes significant metabolic changes, including depletion of antioxidant defenses, along with negative effects on energy, fat, carbohydrate, protein, and micronutrient metabolism due to elevated pro-inflammatory cytokines (33). The immune response also has a high metabolic cost, emphasizing the need for essential vitamins and minerals to support the body's needs (34) (35). One such key micronutrient is Mg (36) (37) (38). Evidence from clinical studies suggests that Mg have a potential role in the regulation of ACE 2 receptors (39). ACE 2 is a protein that controls arterial pressure and maintains fluid balance (4) in Renin-Angiotensin-Aldosterone System (RAAS). ACE2 is also the receptor that the SARS-CoV-2 virus uses to enter and infect the cells (40) (41). Mg has been shown to modulate the expression and function of ACE2 receptor in several ways (42) which may limit the entry of SARS-CoV-2 into the lung and prevent the development of severe respiratory symptoms. Mg supplementation has been found to increase the expression of ACE2 in the heart and kidneys, which may have beneficial effects on cardiovascular and renal health(4) (43). More studies are needed to understand the relationship between Mg and ACE2, and their underlying metabolic pathway, specifically in severity of COVID-19 infection. Mg could have a potential therapeutic role in mitigating COVID-19. However, it is not an alternative measure for vaccination or social distancing in prevention.

With this context, this paper examines in its initial section on the effect of COVID-19 on sports and athletic performance. It then delves into the impact of Mg deficiency on acute inflammation and the inflammatory response, highlighting the implication of low levels of Mg on COVID-19. The review also explores the potential benefits of Mg supplementation in reducing its adverse effects in athletes. Therefore, this review would enumerate various health benefits of Mg, with a primary focus on alleviating COVID-19 symptoms among athletes.

METHODOLOGY

A systematic approach was performed to extract recent relevant evidence using three databases, Google scholar, PubMed and Science Direct. The search process consisted of three distinct sections, each targeting specific aspects of Mg in relation to athletic performance, COVID-19 outcomes, and other health outcomes. Search terms used were “Mg AND performance” OR “Mg AND recovery” OR “Mg AND sports” OR “athletes AND supplementation” OR “Mg AND COVID-19” OR “Mg AND inflammation” OR “Mg AND other outcomes”. The titles and abstracts were scanned to exclude any irrelevant studies. A total of 115 papers that focused on the importance of Mg in different settings, especially in athletes and COVID-19, were screened, and articles containing relevant data were reviewed. These articles provided insights into the benefits of optimal to higher Mg status in athletes, the relationship between Mg levels and COVID-19 outcomes, and the beneficial effects of Mg on other health outcomes. Articles that encompassed both genders and were published in English with access to the full text were included. while articles lacking clarity or sufficient information were excluded.

A detailed screening and selection process of methodology is presented below through PRISMA flow diagram:

COVID-19 a threat to athletes and their performance

Physicians examining athletes often evaluate and address COVID-19 symptoms that impacts performance and well-being (12) (13) (19) (44) Dyspnea on exertion, resting tachycardia and/or exaggerated heart rate response to intensity of PA, lightheadedness, nonspecific chest tightness, headaches, sleep disturbances, and difficulty concentrating may be common despite the absence of overt pathologic cause. Even mild-moderate cases have had prolonged “long-hauler” symptoms including profound fatigue, and PA intolerance that could be multi-factorial (12)

Athletes are high-performing individuals, pushing their bodies to excel at their sports. COVID-19 can be a threat to athletes and their performance due to its potential impact on respiratory and cardiovascular health(20), which are essential for athletic performance. COVID-19 pandemic has been recognized as a psychologically stressful event by itself (32) as it can cause fatigue, muscle weakness, affect an athlete's ability to train and compete (45) disrupt training and competition schedules. COVID-19 has been found to have impact on multiple organs. It could impact the athlete's performance as they return to sport (46). While some athletes have been able to return to training and competition after recovering from COVID-19, others have

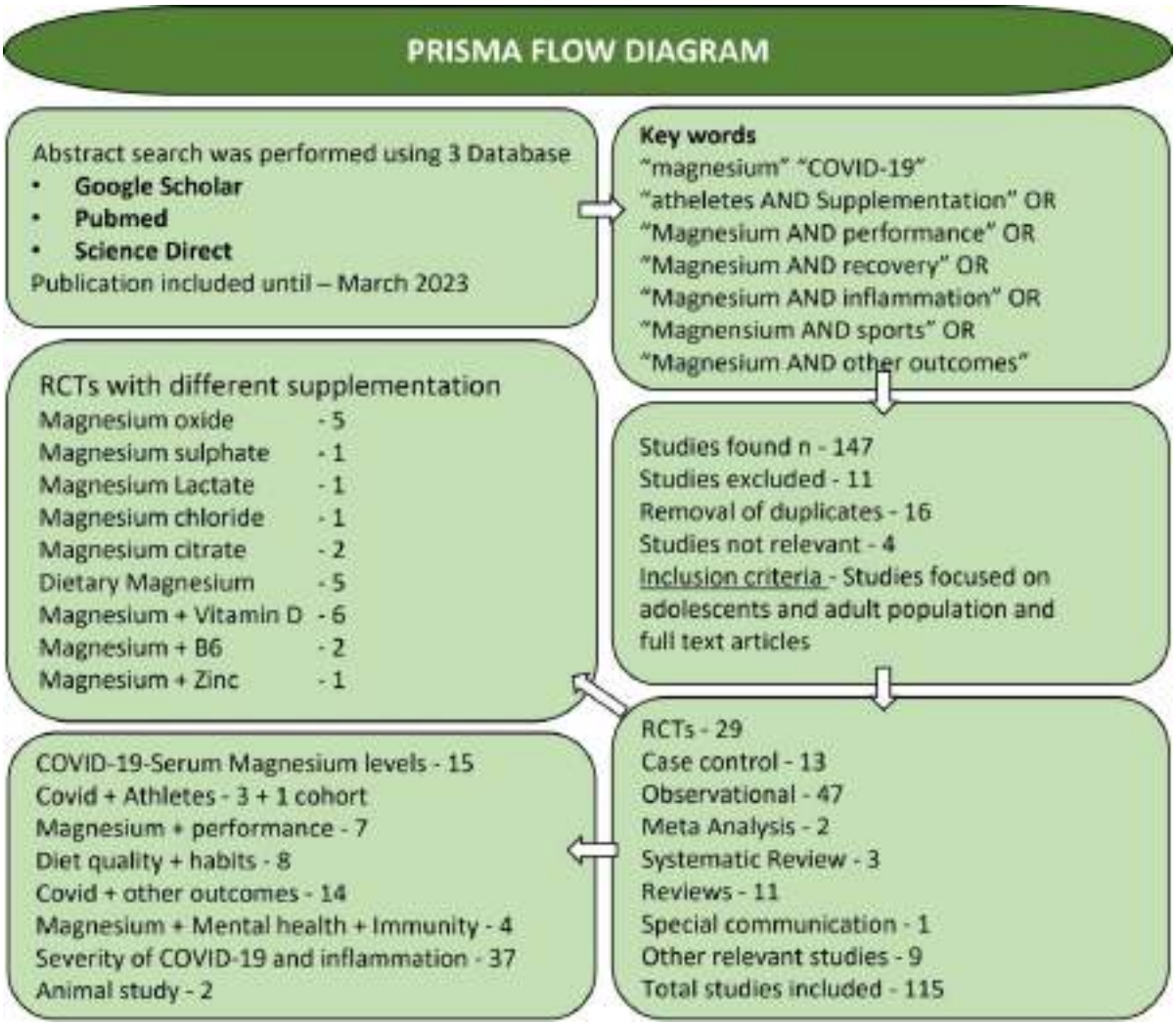

Figure 1 :

experienced long-term effects of the disease, which highlights the need for caution and careful monitoring (47).

According to a recent study on the impact of COVID-19 on cardio-pulmonary exercise test (CPET) on performance of the athletes, COVID-19 infection resulted in deterioration of PA and body anthropometric parameters both among professional and amateur Endurance Athletes (48). According to the studies, infection was significantly related to an increased Heart Rate (HR), and Maximal Oxygen Consumption (VO_2 max), disrupting their performance. Hence even a mild form of COVID-19 infection should be considered as a limiting factor for any kind of PA (16). All these disruptions might influence an athletes' ability to perform well in sports, especially among professional athletes. In this context, physical performance is a complicated concept that is affected by factors (17) including 1. the energy system (both aerobic and anaerobic), 2. Neuromuscular dynamics (strength and technical skills) and 3. Psychological features (17). COVID-19 pandemic has been found to break this framework (18).

Further, COVID-19 can trigger inflammatory reactions including a cytokine storm, which may damage the organs, especially the heart. This can result in myocarditis, a condition characterized by inflammation of the heart muscle, which can be fatal (41). Therefore, athletes must take precautions to reduce their chance of contracting the virus and to monitor any relative symptoms.

Maintaining adequate levels of Mg may be particularly important for athletes during this time. Mg plays a crucial role in immune function and can help reduce inflammation and oxidative stress (49) which are common characteristics of COVID-19 (50). Athletes should maintain their Mg levels in the body by increasing their intake of Mg-rich foods or taking Mg supplements under the guidance of a healthcare professional. Proper hydration and adequate rest are also important for maintaining immune function and optimizing athletic performance (51).

Role of Mg and its physiological function

Mg as an enzymatic activator is essential for various physiological functions such as cell cycle, metabolic regulation, muscle contraction, and vasomotor tone (52). A growing body of evidence supports that Mg supplementation in the form Mg sulfate and Mg oxide helps in preventing or treating various types of disorders or diseases related to respiratory, reproductive, nervous, digestive, and cardiovascular systems also including kidney injury, diabetes, and cancer (53) (27). Mg predominantly performs its function by binding to organic compounds such as proteins, nucleic acids, and nucleotides. It is involved in the synthesis and replication of RNA and DNA, as well as the secretion of enzymes and hormones (54) Mg plays a significant role in metabolic processes, including oxidative phosphorylation and muscle contraction. Furthermore, Mg stabilizes membrane structures and its potential. It also facilitates transmembrane movement of ions through the modulation of iron transporters (54) (23).

Role of Mg in athletes' performance

The concentration of mineral elements is usually under strict homeostatic control; however, intensity of PA alters this mechanism and brings changes in the athletes serum levels (55) Mg is the second most common intracellular cation, that acts in numerous metabolic processes related to PA (56). The underlying mechanism of Mg-induced strength improvement, performance, energy production, effective role in activating other nutrients essential for recovery in COVID-19 could relate to its function in protein synthesis and energy metabolism (57) This in turn aids in the process of muscle contraction and relaxation (58). Scientists predict that an adequate Mg supply may decrease the exercise induced oxygen demands of muscle cells, thereby optimizing physical performance (59).

Mg depletion is caused by inadequate intake, excessive alcohol consumption and increased perspiration rates during PA. This depletion can be examined through plasma and/or serum concentrations (56). One of the most common findings in a few investigations was a decrease in plasma Mg levels after an activity (60). Maintaining adequate concentrations of Mg is necessary for athletes to sustain an appropriate level of performance because, this element utilizes high energy molecules for muscle contraction and to maintain the properties of cell membrane (57) (61). Moreover, it is assumed that only about 30-40% of the ingested Mg is absorbed through the intestines. An increase in Mg requirements is deemed to be necessary for athletes during PA, particularly after strenuous training sessions. However, the extent to which supplementation is necessary must be empirically proved through future clinical trials(62) (23). The capacity of PA is impaired due to the coupling effect between Mg and energy metabolism efficiency. Studies evaluating the relationship between Mg status or supplementation and exercise performance Have indicated the requirements of Mg to increase proportionally with PA status (63).

Mg deficiency is closely related to brain fog, fatigue, post-exertional malaise, headache, dizziness, myalgia (22) and asthma of Long Covid or Post Acute Coronavirus Syndrome (PACS) also known as Post Acute Sequelae of COVID-19 (PASC) (36). Muscle cramps and headaches, which are often seen with Mg deficiency, are caused due to dehydration (31). Sodium ions (Na^+) and water are reabsorbed by the kidneys when aldosterone is present, but potassium (K^+) and Mg^{2+} ions, are expelled to maintain electrical neutrality. Stress is also a major contributor. The hormone cortisol from the adrenal cortex exerts aldosterone-like activity (36). Another major factor disturbed by Mg deficiency is sleep. Sleep functions as a homeostatic regulator of the immune system that plays a specific role in innate immune memory. Sleep disturbances and deprivation are therefore likely to have adverse effects on immune system (64), including dysregulation of natural killer cells (NK), pro-inflammatory and anti-inflammatory cytokines (62) (65).

An overview on the potential mechanisms implicated in low Mg-induced inflammation

Mg is an anti-inflammatory nutrient that plays a key role in immune functioning. Mg is essential for more than 300 physiological functions, which include enzymatic reactions within the cells, including those involved in the immune response, specifically the promotion and activation of T cells and NK cells. Whereas deficiency of Mg can interfere with the activation of these cells, which increases inflammation and triggers a cytokine storm (32). In monocytes, it was shown that Mg supplementation reduced cytokine production and toll-like receptor (TLR) stimulation (23). Mg is involved in the regulation of all metabolic pathways and in redox balance; its deficiency generates metabolic and energetic stress and is associated with the accumulation of free radicals. Consequently, cells undergo adaptive changes, altering their functional roles and potentially exacerbating the inflammatory response (49).

Evidence from *in vitro* studies showed that Mg deficiency leads to increased production of (IL)-β, and (TNF)-α factors. Mg deficiency also results in increased aggregation of platelets, which had an impact on microvascular function (66). Corresponding to these findings, a recent meta-analysis proved that Mg supplementation reduces serum levels of CRP (45). However, more clinical studies need to be carried out in a larger population.

Mg is crucial for nerve and muscle impulse transmission. Mg deficiency in smooth muscles is characterized by constipation, bronchial asthma, and vasospasms. The regulation of bronchial smooth muscle requires further consideration in COVID-19 (27). In skeletal muscles, these are known as fasciculations. It causes palpitations (premature atrial contractions) and atrial fibrillation in the heart muscle. Any of these symptoms are indicative of a Mg deficiency (46). Therefore, a reduced Mg status, which is frequently underdiagnosed, increases the reactivity to various immune challenges and is implicated in the pathogenesis of numerous common chronic diseases (49).

Regular activities require not only an adequate skeletal muscle mass to produce force and power but also an optimal metabolic capacity to sustain its function. As fatigue and exercise intolerance are common clinical symptoms in patients with COVID-19 and PASC, it is possible that metabolic functions of the skeletal muscle is impaired (20) (67).

Zhang et al (63) showed that gerbils/rats given 90 mg/kg body weight of Mg sulfate 30 minutes prior to engaging in exercise experienced a rapid influx of glucose and delayed accumulation of lactate in the brain compared to the control group. Since the brain regulates all physiological functions and metabolic activities during exercise, such enhanced glucose utilization may benefit performance. Furthermore, gerbils/rats receiving the pre-workout Mg treatment demonstrated an ability to swim much longer than those in the control group(63) . A similar inference was observed in another animal study (68). All test animals followed protocols of forced exercise designed to closely simulate approximate human physical training.

Mechanisms of Mg against COVID-19 in relation to sports and performance

Myalgia and fatigue are frequently observed in 4470% of patients with COVID-19 (22). Athletes with COVID-19 infection reported fatigue, myalgia, and headache. It was also reported that fatigue and myalgia were the most frequently experienced (69) symptom in patients with COVID-19 (16). This could be explained through the activation of angiotensin-converting enzyme 2 (ACE2),and a membrane-attached protein that mediates the entry of SARS-CoV-2 (32). In this context, studies performed in animal models show that activation of ACE2 induces skeletal muscle alterations and reduces exercise capacity, with mitochondrial dysfunction and decreased oxidative fiber number, resulting in subsequent muscle atrophy. This uncontrolled immune response produces the “cytokine storm” with a large release of inflammation-stimulating cytokines by hyperinflammatory cells (70). It can be hypothesized that the “cytokine storm” induced by SARS-CoV-2 could be a possible mechanism underlying the persistent myalgia and fatigue (45), but this statement needs further research.

Mg Deficiency Contributes to Increased Inflammation and Oxidative Stress in COVID-19

Mg is an essential mineral that plays a vital role in numerous physiological processes. Mg deficiency can result in immunodeficiency, inflammation, decreased antioxidant response, and oxidative stress (71). Innate immune response to diverse immunological challenges is boosted by Mg shortage. Thus, neutrophils and macrophages that have been isolated from Mg deficient mice are hypersensitive to a variety of stimuli (72). This over reactivity may be compounded by the fall of local Mg concentration in acutely inflamed tissues, which is a result of the IL33/ST2 signaling that stimulates inflammatory reactions in different organs (73).

The supplementation of Mg has been shown to alleviate symptoms and biomarkers associated with stress. In a clinical study, 46 healthy subjects aged between 60 and 75 years were administered 500 mg of Mg oxide tablets/day for eight weeks. The findings revealed a decrease in the subjects' subjective assessments of insomnia. Another study involving university students, concluded that Mg supplementation (500 mg/day in the form of a Mg oxide capsule) significantly decreased baseline blood cortisol levels, over the course of one month(74) (75). These findings together emphasize the significance of Mg's role in managing stress across different age groups.

Several studies have now demonstrated a correlation between Mg levels and COVID-19 disease outcomes, with Mg deficiency being more frequently found among those with COVID-19 and associated with a higher risk of COVID-19 mortality (29). In the context of infections, Mg plays a crucial role in the interaction between vitamin D metabolism and its co-factor Mg. Inadequate Mg levels can lead to reduced formation of vitamin D from its precursors. Although animal experiments provide more evidence on immunodepression and its association with Mg status, they have shown that Mg deficiency can disrupt the inflammatory response, potentially increasing the risk of infection (71) (76).

One of the most significant causes of hypomagnesemia is inadequate dietary intake. Several studies suggests that a large proportion of the population in North America and Europe fail to meet the RDA of Mg (approximately 420 mg for adult males and 320 for adult females) (28) (30). Studies indicate that increased consumption of processed and ultra-processed food, filtered/deionized drinking water, and crops cultivated on Mg-deficient soil has led to a significantly low intake of Mg (32). Under hypomagnesemia, low serum (i.e., extracellular) Mg^{2+} levels can activate Mg transporters such as TRPM7 and SLC41A1 to induce Mg efflux from cells to increase serum Mg levels. This would be expected to decrease Mg free ionized intracellular Mg concentration and affect Mg/MgATP-dependent cellular signaling and functions. A decreased ionized Mg could trigger Mg stores such as in mitochondria (77) to release Mg through SLC41A3 (78). Decreased mitochondrial Mg levels could affect further Mg/MgATP-associated mitochondrial signaling and functions, which may explain the mitochondrial reactive oxygen species (ROS) overproduction and decreased ATP levels observed in Mg deficient mice (79). Another interesting issue that might be relevant in causing breathing difficulties in COVID-19 patients comes from the evidence that low Mg reduces diaphragm function in an experimental model of sepsis (80). Obviously, a deterioration of diaphragm contraction severely impairs breathing and might result in the need of assisted ventilation.

It was recently discovered that intracellular free Mg regulates the cytotoxic functions of NK and CD8+ T cells and that decreased intracellular free Mg causes defective expression of the

natural killer activating receptor NKG2D on NK and CD8+ T cells and impairs their cytolytic responses (81). Elevated levels of oxidative stress and inflammation are characteristics of COVID-19. If untreated can lead to a cytokine storm and multiple organ failure. In parallel with paroxysmal inflammation, CD8 + and CD4 + T-lymphocytes are impaired in COVID-19 (82) and this finding might again be attributed to a low Mg status, since Mg deficiency reduces both proliferation and activation of these cells (83). In conclusion, it is feasible to propose that correcting, maintaining Mg homeostasis and taking a higher dosage than recommended levels might tame cytokine storm and, therefore, prevent the transition from mild to severe forms of COVID-19 in general population and especially in athletes. Notably, a recent retrospective research conducted in Wuhan, Hubei, found that severe COVID-19 patients had considerably lower blood Mg levels than non-severe COVID-19 patients (84),

Evidence from clinical trials has shown that Mg supplementation reduces inflammation by decreasing levels of IL-6, nuclear factor kappa B (NF-κB), and TNF- α. Adequate T cell activity is necessary to regulate inflammation and control the infection (85) (17). However, a deficiency of Mg can impair T cell activation, increase inflammation, and trigger a cytokine storm. Furthermore, Mg supplementation improves mitochondrial function (77) and increases the antioxidant glutathione (GSH) content, reducing oxidative stress (81) (86). Therefore, Mg may have a therapeutic role in COVID-19, but further research is needed to establish its efficacy and optimal dosage (32).

Mg and its Anti -Inflammatory property to Reduce the Risk of COVID-19

Stress hormones such as catecholamines and corticosteroids induce a shift in Mg from the intracellular to the extracellular region, which decreases blood Mg concentrations under acute or chronic stress. Low blood Mg concentrations send signals to the receptors and it further increases the production of stress hormones including adrenocorticotrophic hormone and cortisol and interrupts brain access, causing a vicious cycle of lower stress resistance and greater Mg depletion (87).

According to data revealed by NHANES, 79% of US adults do not meet their Recommended Dietary Allowance of Mg (43). Increasing dietary Mg intake can help prevent diseases associated with Mg deficiency, including COVID-19. Mg supplements and Mg-rich foods such as nuts and seeds, legumes, whole grain cereals, leafy greens, vegetables, and dark chocolate are effective in increasing Mg levels. Monitoring Mg levels is important to ensure adequate intake (85).

Professional athletes' performance depends on their respiratory function, which can be hindered by various factors including exercise induced stress, environmental stress, and any underlying respiratory disorders. COVID-19 can cause lasting damage to the respiratory system of unvaccinated athletes, even in mild cases, which may lead to the premature end of their careers. Although over 50% of the general population has recovered from COVID-19, its impact on athletes still remains unclear (88) (89) (90). Micronutrient deficiencies are a recognized global public health issue, and poor nutritional status predisposes to certain infections. Immune functions may be improved by restoring deficient micronutrients to recommended levels, thereby increasing resistance to infection, and supporting faster recovery when infected. Diet alone may be insufficient therefore tailored micronutrient supplementation based on specific age-related needs are necessary (62).

A rapidly increasing body of research reports that higher intake of dietary Mg is inversely associated with COVID-19 severity and symptoms (91). A meta-analysis and systematic review indicate that dietary Mg intake is significantly and inversely associated with serum CRP levels. The potential beneficial effect of Mg intake on chronic diseases may be, at least in part, explained by inhibiting inflammation (92).

Mg supplementation seems to facilitate elevated levels of plasma glucose post-workout as well, suggesting that this trace element could assist in muscle tissue recovery (93) (77). The COVID-19 pandemic has had and will continue to have very considerable effects on the sporting world as well as on the physical and mental well-being of people around the world (44). Despite the end of pandemic, the world is still recovering from COVID-19, there will be significant issues to be addressed to ensure the safety of sporting events at all levels and the well-being of sporting organizations in present and future (13).

Benefits of Mg supplementation in reducing the risk of covid-19 symptoms

Mg plays a significant role in the general population, particularly in athletes, as it possesses the potential to mitigate inflammation, enhance the recovery period, and boost performance. Its involvement in cellular energy metabolism leads to an increase in energy production, facilitating brain-muscle signaling. This signaling pathway upregulates glucose homeostasis, creating an environment conducive to the proliferation of beneficial microbes, thereby preventing inflammation. Moreover, Mg activates other essential nutrients, such as Vitamin D, which further contributes to improved sleep quality and facilitates optimal recovery. These factors collectively play a crucial role in promoting overall well-being and elevating performance levels.

Summary of Different studies on Mg and Covid 19 in athletes

Mg supplementation protects organs and tissues from damage through multiple mechanisms including anti-inflammation, anti-oxidation, and immune regulation. Despite its importance in energy metabolism, the general population and especially athletes often neglect its importance. Suboptimal Mg status may impair overall metabolism in the general population, and it can have a negative impact on strength, power, and overall performance in athletes. Mg consumption reduces oxygen requirements and improves cardiorespiratory performance during extended aerobic exercise.

Mg is a key mineral that plays a significant role in numerous physiological processes in the body, includes energy metabolism, muscle contraction, and nerve function. While the recommended dietary intake of Mg for adults is between 310-420 mg, recent studies have suggested that higher levels of Mg intake could have additional health benefits, especially in athletes' population. Moreover, National Institute of Health, 2022 has shown that Mg supplementation may have potential benefits in reducing the severity of COVID-19 symptoms and other health outcomes (94) (63).

Table 1: Benefits of Mg Supplementation in Athletes: Recent studies have demonstrated that higher levels of Mg intake than the recommended dietary allowance could enhance the performance of athletes. By increasing endurance, reducing inflammation, and enhancing recovery after exercise. Additionally, it has been associated with improved bone health,

Table 1 : Benefits of higher Mg status for athletes

Reference	Study Design	Participants	Gender/ Age	Mg Dosage	Duration	Outcomes
(95)	Double-blind, placebo-controlled, cross-over study	9 Recreational runners	Male Age: 27 ± 4 years	Experimental group supplemented with 500 mg/day of Mg (Mg oxide, Mg stearate, microcrystalline cellulose)	7 days	Mg supplementation reduced IL-6 response, enhanced recovery of blood glucose, and muscle soreness.
(96)	Randomized Controlled Trial	12 elite Basketball players	Male Age: 25.3 ± 4.4 years	400 mg/day of Mg, in the form of Mg lactate	6 Months	Mg supplementation during the season of competition prevented associated tissue damage.
(97)	Double Blind Randomized controlled	22 college students	Male and female Age : NA	350 mg/day of Mg	10 days	Significant decrease in muscle soreness, session rating of perceived exertion, acute rating of perceived exertion, and improved perceived recovery was observed after Mg supplementation
(98)	Randomized Controlled Trial	18 professional cyclists	Male Age: 26.2 ± 1.8 years	400 mg/day of Mg oxide	3 weeks	Mg supplementation showed a protective effect on muscle damage.
(99)	Pre -post trial without control	55 elite athletes	Male and female Age : NA	370mg Mg oxide	3 months	Significant improvement in muscularity metabolism for each 0.1 mmol/l increase in whole blood Mg, the pyruvate improved significantly by 0,06 mg/dl.
(100)	Randomized Controlled Trial	25 professional volleyball players	Male Age : NA	350 mg/day Mg oxide	4 weeks	Mg supplementation improved lactic anaerobic metabolism, even though the players were not Mg deficient.

immune function, and cardiovascular health in athletes.

Table 2: Mg status and COVID-19 Outcomes: COVID-19 patients with low levels of serum Mg had higher risk of severity of COVID-19 symptoms and increased rate of mortality compared to patients with optimal to higher levels of serum Mg. Evidence from RCTs showed Mg supplementation in COVID-19 patients helped in faster recovery, reducing inflammation and oxidative stress. The precise mechanism of Mg in COVID-19 infection remains unclear.

Table 3: Mg supplementation and other health outcomes: In addition to the beneficial role of Mg in athletes and COVID-19 patients. Results from various studies indicated the vital role of Mg in improved insulin sensitivity, sleep quality, and blood pressure. According to different studies it was also shown that Mg supplementation helped in treating migraine, depression, headaches, and anxiety.

In summary, maintaining optimal to above optimal levels of Mg through supplementation have numerous health benefits, particularly for athletes. Moreover, with the recent available information and findings it can be now suggested that Mg supplementation may be beneficial in reducing the severity of COVID-19 symptoms, improving performance and other health outcomes. Therefore, athletes with a history of COVID-19 or those at risk of contracting the disease may benefit from Mg supplementation. However, more research is needed to fully understand the mechanisms and effectiveness of Mg supplementation in gender specific health outcomes.

While these studies provide some initial evidence of a potential role for Mg in COVID-19. It is important to review the importance of Mg in athletes during COVID-19 infection to reduce the risk of severity and post COVID-19 infection to improve the performance. More studies are required to fully

Table 2 : Evidence for Mg Levels for Covid outcomes

Reference	Study Design	Participants	Component Assessed/ Tool used	Evidence of Mg levels	Odds of severity of symptoms
(91)	Retrospective cross-sectional study	250 COVID-19 subjects Age: 44.1 ± 12.1 years	Dietary Mg intake Tool – FFQ	Increased levels of Mg intake (332 ± 11 (382 ± 24 mg/day)	Higher intake of dietary Mg was inversely associated with COVID-19 severity and symptoms.
(37)	Cross-sectional study	260 COVID-19 subjects Age: 65.4 ± 15.4, years	Serum Mg	Decreased Mg ≤ 1.96 mg/dL	Decreased levels of serum Mg associated with higher odds of mortality, length of hospital stay, and onset of long COVID symptoms compared to those with serum Mg > 1.96.
(101)	Retrospective study	118 T2D and non-diabetic COVID-19 subjects	Serum Mg Renal function	Decreased	Reduced GFR and Mg levels were associated with increased mortality in T2D.
(102)	Retrospective cohort study	83 Covid-19 subjects Age: 62.9 ± 14.4 years	Serum Mg Lymphocyte count, CRP	Decreased (0.72 ± 0.15 mmol/L)	Hypomagnesemia might be associated with increased mortality in COVID-19 by affecting enzyme activity and activating the inflammatory response
(103)	single-center, observational retrospective study	629 COVID 19 - subjects Age : 64.5 years	Serum Mg levels cardiac troponin I (cTnI) myocardial damage	Increased or Above 1.94 mg/dL and decreased cTnI	Although serum Mg level was not a predictor for in-hospital mortality, there was a significant negative correlation between Magnesemia and myocardial damage.
(104)	Cross-sectional study	60 COVID 19 - subjects Age : 53.5 years	Serum levels micronutrients Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) score erythrocyte sedimentation rate and CRP	Decreased	Lower serum levels of vitamin D, zinc, and Mg were related to increased severity COVID-19.

Table 3 : Evidence for beneficial effects of Mg for other outcomes.

Reference	Study Design	Total Participants Analyzed, Age, and Gender	Component assessed and tool used/ Duration	Dosage	Outcomes
(105)	Cross-Sectional Study	2570 healthy subjects Age : 48.3 ± (12.7) years	Dietary Mg using FFQ. CRP levels and muscle Mass	NA	Significant positive associations between a higher Mg and indices of skeletal muscle mass and Leg Explosive Power Dietary Mg may aid conservation of age-related loss of skeletal muscle mass, power in women of all ages and reduce the serum C Reactive protein levels
(106)	Double-blind randomized-controlled clinical study	49 COPD subjects Age : 72.6 ± 9.9 years	180 days	300 mg/day of Mg citrate	Oral Mg supplementation may have a potential anti-inflammatory role.
(107)	Randomized Controlled study	83 healthy subjects Age : 45 years	8 Weeks	Co -Supplementation 50,000-IU vitamin D soft gel (weekly) + 250-mg Mg oxide tablet (daily)	A significant difference was observed in handgrip strength. The serum level of hs-CRP decreased significantly in the intervention group. Co-supplementation of vitamin D and Mg →In presences of vitamin D deficiency have beneficial impacts on muscle strength, muscle function, and ↓ inflammation.
(108)	Single-arm non-blinded intervention study	28 subjects with Hypertension Age: 47.4 ± 11.3 years	1 month	300 mg of oral Mg oxide	Systolic and diastolic pressures were significantly decreased. The observed hemodynamic changes may explain lowering blood pressure after Mg supplementation.
(93)	Randomized, double-blind, placebo-controlled trial.	60 subjects with GDM, Age: 30.0±4.5 years	6 weeks	100 mg Mg oxide 4 mg zinc, 400 mg calcium plus 200 IU vitamin D supplements Twice a day	Intervention group had significant reduction on fasting plasma glucose, serum insulin, triglycerides, and markers of cardiometabolic risk.
(109)	A randomized, double-blind, placebo-controlled multicenter study	175 Subjects Age: 52.3 ±10.7 years	60 days	266 mg Mg oxide monohydrate (MOMH) day	Mg supplementation showed reduction in Nocturnal Leg Cramp (NLC) episodes. ($p = 0.01$) MOMH → greater reduction in NLC duration ($p < 0.007$) and greater improvement in sleep quality ($p < 0.001$) as compared to placebo.
(110)	Randomized clinical study	180 subjects Mean Age 35.9 years.	6 Months Follow-up	2 ml Mg sulfate	Injection of Mg sulfate is an effective treatment measure for myofascial trigger points. Quality of life → significantly higher in the Mg sulfate group compared to the placebo group ($p < 0.001$).
(111)	Randomized controlled study	264 subjects Age: 31.6 ± 8.5 years	8 weeks	300 & 30 mg of Mg Mg lactate dihydrate & B6 or 300 Mg lactate dihydrate alone	Mg supplementation, with or without vitamin B6 → clinical benefit in daily life for individuals with stress and low Magnesemia.
(112)	RCT	60 open-heart surgery subjects	5 days	500 mg Mg oxide	Mean level of anxiety and depression was significantly lower in the intervention group than the control group ($p = 0.007$) Mean sleep quality improved in the intervention group (8.3 ± 2.1) compared to the control group (10.5 ± 2.0) ($p < 0.001$).
(113)	Randomized Double-Blind Placebo-Controlled Clinical Trial	198 subjects with MetS and hypomagnesemia Age : 30 to 60 years	16 weeks	Mg chloride 382 mg/ day	Mg supplementation improves MetS by reducing blood pressure, hyperglycemia, and hypertriglyceridemia.
(114)	RCT	52 healthy postmenopausal subjects Age: 59.7 ± 9.1 years	8 weeks	500 mg/day	Mg supplementation→ significantly increased vitamin D levels in the intervention group

understand the effects of Mg in these contexts. As always, athletes and individuals with COVID-19 should consult with their healthcare providers before starting any new supplement.

CONCLUSION

Certain athletic settings, characterized by group training, contact sports, shared equipment, inadequate personal hygiene, and common facilities, increases the risk of COVID-19 transmission. Despite being younger and healthier, athletes remain susceptible, with 10% experiencing prolonged COVID-19 symptoms.(115). Limited studies exist on Mg supplementation's benefits for athletes, including its potential to reduce COVID-19 risk and severity. Globally recognized guidelines and bioavailability of Mg supplements for different sports are lacking. Further research, particularly randomized controlled trials, is necessary to understand Mg supplementation's role in athletic performance and its impact on COVID-19.

FUTURE IMPLICATIONS

Further research is needed to examine the bioavailability of different Mg supplements for diverse sports. Understanding the varying effectiveness of Mg supplementation based on the type of PA performed can guide the selection of optimal Mg forms for athletes. Studying the relationship between Mg and gut microbiome could be another interesting area in human research. According to recent trends gut microbes play a vital role in reducing inflammation and over all well-being. This can bring interesting insights that can be incorporated in different population like athletes.

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