

Bone mineral density and pandemic

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ABSTRACT

The COVID-19 pandemic has significantly impacted physical health, including bone mineral density (BMD). This review aims to explore the effects of various pandemic-related factors such as reduced physical activity, stress, depression, dietary changes, and SARS-CoV-2 infection on BMD. Methods involved analyzing studies that investigate the impact of these factors on bone health, including observational studies, systematic reviews, and meta-analyses. Results show that decreased physical activity, depression, and changes in diet lead to a reduction in BMD, particularly in the lumbar spine and femoral neck. SARS-CoV-2 infection and the use of corticosteroids are also associated with an increased risk of osteoporosis. Additionally, cytokine storms induced by the virus further exacerbate bone resorption. The review also highlights the complex interaction between obesity, sedentary behavior, and BMD, which may contribute to either increased BMD in certain areas or lead to a higher risk of fractures. The study suggests that the pandemic may have long-term effects on bone health, emphasizing the need for preventive strategies, including promoting physical activity, managing stress, and cautious use of medications like corticosteroids. Further research is needed to understand the long-term consequences and to develop therapeutic interventions aimed at mitigating the adverse skeletal effects of COVID-19 and its treatments. Understanding the lasting impact on bone health requires a comprehensive approach considering the multifactorial aspects of the pandemic's effect on human physiology.

KEY WORDS: osteoporosis, COVID-19, bone mineral density, pandemics, bone diseases

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INTRODUCTION

The end of 2019 was the time when the scientists first reported the COVID-19 pandemic. COVID-19 is contagious disease cause by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The rapid spread and the severity of the disease, as well as the strain on the global health care system, took a heavy toll.

In most cases it causes a mild or even asymptomatic infection. Headache, dry cough, dyspnea, loss of taste, tiredness and fever are the most common symptoms. Furthermore, an infection with COVID-19 can also cause a wide range of extra-pulmonary symptoms probably related to vascular pathology and long-term complications known as post-COVID-19 syndrome. Studies using RT-PCR have shown that in some patients the virus can persist in the body for up to 3-4 months [1].

Post-COVID syndrome is thought to be caused by prolonged tissue damage and pathological inflammation due

to prolonged viral presence. The most common symptoms of long COVID reported in many studies are fatigue and dyspnea, which persist for months after acute COVID-19 [2].

Post-COVID syndrome also affect to the musculoskeletal system, where known symptoms include: arthralgia, myalgia, muscle weakness, back pain. The commonly used corticosteroid therapy is thought to be the cause of the bone pathologies associated with COVID-19. Bone changes are influenced by the duration and intensity of this therapy. This is confirmed by the increase in bone resorption markers correlating with the duration of steroid therapy [3] Examination of Osteoprotegerin (OPG) levels, an important regulator of bone remodeling, also confirms the disruptive effect of COVID-19 on bone mineral density. Patients after COVID-19 had significantly different OPG levels compared to patients without COVID-19. In addition, bone mineral density (BMD) assessment showed significant differences between

these two groups. The OPG index may be important in the assessment of bone mineral density [4].

The mineral density and functionality of bones also depend on physical activity [5]. Significant reduction in physical activity can contribute to a deterioration in bone mineral density [2]. Various types of exercises, including aerobic, strength, and resistance training, have a positive impact on bones. The effects vary, and the most significant improvements among older adults have been observed in patients engaging in multifaceted exercises that combine the aforementioned types of training [6]. The nature of physical activity performed significantly influences bone mineral density (BMD). It has been observed that activities with lower biomechanical loading shift the balance towards bone resorption, resulting in a decrease in both bone mass and bone mineral density. Swimming, for example, falls into this category [7].

AIM

A reduction in the density of minerals in the bones results in a higher susceptibility to bone fractures [8]. Enhancing our comprehension of how SARS-CoV-2 triggers bone deterioration will enhance the management and preventive strategies amid the ongoing pandemic. In this review, we will focus on the impact of COVID-19 infection on bone density in patients and the consequences of the bone changes caused by the disease.

MATERIALS AND METHODS

A manual search was conducted in PubMed and Google Scholar to identify relevant studies and research related to bone mineral density (BMD), osteoporosis, osteopenia, the COVID-19 pandemic, post-COVID syndrome, COVID-19 cytokine storm, anorexia nervosa, fractures, hormones, corticosteroid effects, hypercortisolism, COVID-19 therapy.

REVIEW

POST-COVID SYNDROME AND BONES

The post-COVID syndrome, also referred to as long-term COVID-19, is a cluster of symptoms that co-occur in patients as a consequence of a previously experienced COVID-19 infection. The causes of this phenomenon are sought in the body's response, which, in reaction to the systemic inflammatory response syndrome (SIRS), activates counteracting processes, namely the Compensatory Anti-Inflammatory Response Syndrome (CARS). The goal is to restore systemic homeostasis. The heightened activity of pro-inflammatory factors and excessive release of cytokines such as Interleukins

1, 6, 8, 17, and 1β , as well as TNF α , is termed a cytokine storm [9]. Post-COVID syndrome is diagnosed at least 12 weeks after the onset of infection, but sometimes symptoms of acute infection persist long enough to progress smoothly to post-COVID syndrome [10].

The research conducted using computer tomography on patients post-acute phase of COVID-19 clearly illustrates the adverse impact of the infection on bone mineral density. This, in turn, significantly contributes to the heightened prevalence of osteoporosis among the examined patient cohort. Imaging studies carried out during follow-up visits have substantiated the observation that osteoporosis induced by COVID-19 infection can be discerned in patients [11]. Acute infection is not the only reason of BMD decreasing.

THE MEDICATIONS EMPLOYED IN THE TREATMENT OF COVID-19 INFECTION AND THEIR IMPACT ON BONES

During the pandemic, corticosteroids were frequently employed medications, primarily owing to their anti-inflammatory properties. This was largely attributed to the constraints in therapeutic alternatives available during that specific period of the pandemic [12]. Patients are administered corticosteroids in the treatment of numerous pathological conditions, resulting in a pronounced prevalence within the general population. The impact of corticosteroids on bones is contingent upon various factors, including gender, age, patient's body mass, as well as the route of drug administration (inhaled or oral) [13]. The efficacy and justification for the use of corticosteroids during the COVID-19 pandemic are not unequivocal. Arguments both in favor of and against this therapy in the context of COVID-19 infection can be discerned. The previous SARS-CoV pandemic (2003) demonstrated the effectiveness of these drugs in attenuating the cytokine storm, forming the basis for their utilization in the SARS-CoV-2 pandemic among patients experiencing severe COVID-19 with hypoxemic respiratory failure [14]. In the study conducted by Özer Balin Ş, et al. in 2022, the effectiveness of early methylprednisolone therapy in reducing the hospitalization duration of COVID-19 patients was confirmed. No statistically significant difference in mortality rates was observed between the group of patients receiving methylprednisolone and those receiving dexamethasone [15]. On the other hand, the study conducted by Xinsheng Zhang, et al. in 2008 on pigs infected with porcine respiratory coronavirus (PRCV) showed that corticosteroids in the form of dexamethasone may prove effective in early anti-inflammatory responses; however, with prolonged use, they may lead to increased viral replication in the lungs [16].

THE COVID-19 PANDEMIC AND EATING DISORDERS

During the COVID-19 pandemic, a significant increase was observed in cases of patients reporting issues related to nutrition, body image, weight, and the resultant feelings of loneliness. This was accompanied by restricted access to psychotherapists and general practitioners. For many patients, this situation led to the development of eating disorders.

ANOREXIA IN THE COVID-19 PANDEMIC: EXPLORING ITS IMPACT ON BONE STRUCTURE

A significant pathological entity within the realm of eating disorders is Anorexia nervosa [17]. In accordance with the study conducted by Agostino H, et al. (2020) during the initial wave of the pandemic, there was an increase in the number of newly diagnosed patients with anorexia nervosa and atypical anorexia, accompanied by a rise in the hospitalization rate among the newly diagnosed patients. This ascending trajectory was notably discernible among inhabitants of provinces exhibiting heightened rates of COVID-19 infections [17]. Anorexia nervosa constitutes a significant determinant of diminished bone mineral density (BMD) in both adult females and adolescents. Among adult patients with anorexia nervosa, the reduction in BMD is linked to the dysregulation of bone turnover markers, manifesting as heightened bone resorption and diminished bone formation markers. Conversely, adolescents present a generalized decrease in bone turnover. These alterations stem from diminished estrogen levels, hypogonadism, heightened cortisol levels, and decreased body mass—distinctive characteristics of anorexia nervosa [18]. The studies confirm that during the COVID-19 pandemic, the predominant gender affected by anorexia nervosa was female; however, the elevated rate of newly diagnosed patients was observed across both genders [19]. Considering the accompanying pandemic-induced upward trend in newly diagnosed eating disorders in recent years, one can anticipate that the issue of low bone density will become even more prevalent in the general population.

THE IMPACT OF THE COVID-19 PANDEMIC ON OBESITY: EXPLORING THE INTERRELATIONSHIP AND ITS SKELETAL RAMIFICATIONS

Throughout the pandemic, the reduction in physical activity has been implicated in the dynamic escalation of the obesity problem [20]. This was also contributed by the accompanying pandemic-induced depression,

loneliness, and nervousness, which led to binge eating, emotional eating as a coping mechanism for mental health issues, and snacking between meals [21]. Furthermore, individuals grappling with obesity prior to the onset of the COVID-19 pandemic were in a high-risk category for severe infection. It has been demonstrated that obesity correlates with heightened infection severity, an increased risk of hospitalization, and an extended duration of hospital stay [22]. Obesity constitutes one of the most frequently observed comorbidities in patients with COVID-19 [23]. However, obesity accompanying the infection may act as a protective factor for the skeletal system. The reasons for this phenomenon include obesity-related: increased mechanical load on bones, heightened estrogen production, increased activity of osteocytes, and hyperinsulinemia. It was observed that bone mineral density was higher among the examined group in obese participants, even despite their older age and the predominance of females among them [24].

THE IMPACT OF DEPRESSION ON BONE MINERAL DENSITY DURING THE COVID-19 PANDEMIC

Throughout the ongoing COVID-19 pandemic, a notable surge in psychological issues such as anxiety and depression has been noted. The age group exhibiting the highest vulnerability to the emergence of these psychological problems, as observed in China, encompasses individuals aged 21 to 40 years [25].

Even at the stage of stabilizing the SARS-CoV-2 infection rate in China, the prevalence of depressive symptoms among surveyed adolescents remained at a high level [26]. This indicates that the impact of the COVID-19 pandemic on mental health may be observed even after the conclusion of the pandemic.

The prevalence of depression during the pandemic varies across different social classes. Among the surveyed Nigerians, the middle class exhibited the highest percentage of individuals grappling with depression [27].

PHYSICAL ACTIVITY AND BONE MINERAL DENSITY

The ongoing COVID-19 pandemic has significantly restricted physical activity within the population. This limitation can be attributed to various factors, including quarantine measures imposed to curb the spread of the virus. Additionally, the closure of gyms, fitness clubs, sports halls, fields, and other venues designated for sports further contributes to the decline in physical activity. For a subset of individuals, infection has led to hospitalization or compelled bed rest, resulting in a

substantial reduction in even minimal physical activity [28]. A study conducted by Jeannet M. Delbressine, et al. has demonstrated that some patients maintain reduced physical activity relative to before the onset of infection symptoms, even up to 6 months after the onset of COVID-19 symptoms [29]. Other studies suggest that women represent a group for whom repeated exposure to sitting adversely affects bone mineral density. This phenomenon is not observed in the male population, where sitting exposure does not increase the risk of decreased BMD; A protective effects have been demonstrated for moderate and vigorous physical activity [30]. The correlation between reduced physical activity and the COVID-19 pandemic is complex and multifactorial. Lockdowns, closure of recreational facilities, and psychological factors like increased stress contribute to a sedentary lifestyle. Changes in daily routines and concerns about virus transmission limit opportunities for regular exercise, emphasizing the need for targeted interventions to promote physical activity and overall health during and after the pandemic.

RISKS OF LOW BMD CAUSED BY PANDEMIC

The aforementioned factors associated with the COVID-19 pandemic, manifesting both direct and indirect effects on bone mineral density, operate on a multifaceted level, rendering the cumulative end result difficult to ascertain. The considerable majority of these factors exert adverse effects on bone health, precipitating a decline in mineral density. Consequently, this phenomenon may contribute to skeletal fractures.

The studies reveal a substantial correlation between bone mineral density levels and the incidence of fractures in patients, emphasizing that, beyond BMD, a multitude of other factors exert an influence on fracture frequency [31].

In addition to this, the study showed a significant correlation between low bone mineral density levels and the frequency of intensive care unit hospitalization and mortality in patients with COVID-19 infection [32].

DISCUSSION

This review highlights the multifaceted effects of the COVID-19 pandemic on bone mineral density (BMD) and related skeletal health outcomes. The findings align with existing literature, reinforcing the detrimental impact of reduced physical activity, corticosteroid use, and systemic inflammatory responses during and after SARS-CoV-2 infection.

F. Alghamdi, et. al (2024) demonstrate in their work that BMD decreased in COVID-19 patients during the

acute infection phase. Additionally, the percentage of patients who had osteoporosis doubled within an average of three months [33]. Another study included evaluation of different methods of mobility between COVID-19, and non-COVID-19 patients. Results found that patients diagnosed with SARS-CoV-2 within a period of 30 days reported lower scores in tasks to assess movement. In the same study, DEXA examinations revealed significantly lower values of BMD and more than double the percentage of osteoporosis within the patients with a recent COVID-19 diagnosis, as compared to the group with no recent respiratory symptoms [34].

A scoping review (2023) revealed that the number of hospitalizations among young people with anorexia increased during the pandemic, with poorer overall behavioral and mental health being reported as a symptom [35]. Taylor, et al. reported that anorexia nervosa does not increase the risk of a severe COVID-19 infection [36].

As the pandemic was a stressful time for many, patients suffering from obesity experienced high levels of stress which increased vulnerability to overeating, combined with a sedentary lifestyle encouraged by quarantine rules [37]. Obesity is a risk factor for COVID-19, and a sedentary lifestyle and unhealthy diet are contributors to obesity [38].

A meta-analysis on the relationship between COVID-19 and depressive symptoms (2022) revealed a considerable rate of clinically relevant depressive symptoms among COVID-19 survivors. Female patients were found to have a higher likelihood of experiencing depressive symptoms. There was a higher frequency of depressive symptoms in patients who had been hospitalized compared to those who were treated as outpatients [39]. Fang et al found significantly lower BMD in the spine, total hip, and femoral necks of patients with major depressive disorder (MDD). There was no difference in BMD found in the forearm bones, or femoral trochanters between patients with MDD and the control group [40].

One significant limitation of this review is the reliance on studies with varying methodologies and sample sizes, which may introduce bias or limit generalizability. For instance, the referenced mouse model study by Awosanya, et al. (2022) provides valuable mechanistic insights but may not fully translate to human physiology. Another limitation of this review is the reliance on articles exclusively from PubMed and Google Scholar. While these databases are widely regarded for their high-quality, peer-reviewed content, this approach may have inadvertently excluded relevant studies published in other databases or less conventional sources. As a result, findings from emerging research

in preprint repositories or niche journals not indexed in these databases may not have been incorporated. This limitation could introduce a degree of publication bias, particularly as rapidly evolving topics such as COVID-19 often generate a significant volume of preliminary or region-specific research that may not yet be formally indexed. Additionally, this review predominantly focuses on short- to medium-term effects, leaving the long-term implications of pandemic-induced BMD changes underexplored.

Despite these limitations, this work provides crucial insights into the pandemic's impact on skeletal health. The findings underscore the importance of preventive measures, including early interventions for high-risk populations, promotion of physical activity, and careful consideration of corticosteroid use. Future studies should also investigate targeted therapeutic approaches, such as anabolic treatments or novel anti-resorptive therapies, to mitigate the adverse skeletal effects of COVID-19 and its treatments.

CONCLUSIONS

During the COVID-19 pandemic, many factors influenced changes in bone mineral density in individuals. The impact of these factors is complex and multifaceted. Some elements studied, such as patient-appropriate physical activity or weight control, acted synergisti-

cally to have a protective effect on the skeletal system. On the other hand, health issues, such as eating disorders and depression, are intricately linked, and their manifestation in a patient serves as a risk factor for low bone mineral density. In contrast, other factors acted in direct opposition to each other. Still others, such as the aforementioned obesity, affect bone mineral density in such an extensive way that the final effect of the changes taking place is difficult to predict. The vast majority of observed physiological changes in the human body in response to pandemic-induced changes, including isolation, reduced physical activity and the direct impact of COVID-19 infection, manifested as a reduction in bone mineral density. The cumulative effect of the changes discussed, the complex physiological processes and the interrelationships will be observed in the coming years. Understanding the lasting impact on bone health requires a comprehensive study of these multifaceted interactions in the context of the multifaceted impact of the pandemic on human physiology.

In conclusion, this review corroborates prior evidence linking the COVID-19 pandemic to a decline in BMD while highlighting gaps in current knowledge. Comprehensive, multidisciplinary strategies are essential to address the complex interplay of factors influencing bone health and to mitigate long-term skeletal complications stemming from the pandemic.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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