Original Research

Post-COVID-19 avascular necrosis of the femoral head in Southeastern Europe

Ardit Zanaj[1], Qamil Dika[2]

[1] University Hospital of Trauma, Tirana, Albania.
[2] Department of Public Health, Faculty of Medicine, University or Medicine, Tirana, Albania.

Recommended citation:
Zanaj A, Dika Q. Post-COVID-19 avascular necrosis of the femoral head in Southeastern Europe. JGPOH 2026. DOI: 10.61034/JGPOH-2026-03.

Corresponding author: Ardit Zanaj, MD
University Hospital of Trauma, Tirana, Albania
Address: Rr. "Lord Bajron", Tirana 1000, Albania
Email: arditzanaj@ymail.com

Abstract

Aim: While acute outcomes of COVID-19 pandemic have been extensively documented, attention has recently shifted toward long-term sequelae, including musculoskeletal complications such as avascular necrosis (AVN) of the femoral head. Our aim was to analyze the burden of musculoskeletal disorders in Southeastern European (SEE) countries, with emphasis on the "other musculoskeletal disorders" category that encompasses AVN, and to contextualize these findings against COVID-19 mortality and disability trends.
Methods: We carried out a comparative analysis across Albania, Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia using Global Burden of Disease (GBD) estimates. Age-standardized mortality rates and disability-adjusted life years (DALYs) were extracted for COVID-19 (for the period 2020-2023) and musculoskeletal disorders (for 2020 and 2023).
Results: COVID-19 mortality and DALYs peaked in 2021 across all SEE countries, followed by sharp declines in 2022 and 2023. Montenegro and North Macedonia consistently reported the highest values, whereas Croatia and Slovenia had comparatively lower burdens. In contrast, musculoskeletal disorders exhibited stable mortality and DALY rates between 2020 and 2023, with "other musculoskeletal disorders" contributing modest but persistent morbidity. AVN accounts for 8%-12% of primary hip arthroplasties in Europe, predominantly affecting adults aged 30-50 years, with case reports also from SEE region linking post-COVID corticosteroid use to AVN onset.
Conclusion: Musculoskeletal disorders remain a substantial contributor to morbidity in SEE countries. AVN, though relatively rare, carries disproportionate disability and surgical burden. Pandemic-related exposures may have amplified AVN risk in the SEE region, underscoring the need for improved surveillance, early diagnosis, and cautious corticosteroid management.

Keywords*: avascular necrosis (AVN), avascular necrosis of femoral head, musculoskeletal disorders, orthopedy, other musculoskeletal disorders, post COVID-19, Southeastern Europe.*

Conflict of interests: None.
Funding: None.
Ethics statement: Not applicable.
Data availability: All data are publicly available at: https://vizhub.healthdata.org/gbd-results/.
Authors contributions: Both authors contributed to the study conceptualization and design, analysis and interpretation of the data and writing of the article.

Introduction

Post-COVID-19 musculoskeletal disorders

The COVID-19 pandemic imposed a profound burden on health systems worldwide, with Southeastern European (SEE) countries experiencing particularly high mortality and disability rates during autumn-winter 2020 and subsequently throughout 2021 (1). Vaccination campaigns in SEE region started around the same time as Western European nations (1,2); however, vaccination coverage in the SEE region remained comparatively lower (1,2).

While the acute impact of COVID-19 has been extensively documented, attention has increasingly shifted toward its long-term sequelae, including musculoskeletal complications (3-5). A fairly recent systematic review (13) has highlighted musculoskeletal complications as part of post-COVID syndrome, defined as a chronic condition that develops following the acute phase of infection and is typically characterized symptoms such as by pain, weakness, and fatigue, which can substantially impair quality of life (3,6,7). Another very recent systematic review including meta-analysis reports a high prevalence of musculoskeletal symptoms in individuals with post-acute COVID-19 sequela, with muscle pain being the most common symptom (4). Furthermore, an earlier systematic review has documented musculoskeletal complications such as myopathy, chronic pain and avascular necrosis in long-COVID patients (5).

Within the broad category of "other musculoskeletal disorders", avascular necrosis (AVN) of the femoral head represents a clinically significant condition (8). AVN is characterized by compromised blood supply to the femoral head, leading to progressive bone necrosis, collapse, and eventual hip dysfunction (9,10). Although relatively rare in the general population, AVN carries a disproportionate burden due to its disabling nature and frequent requirement for surgical intervention (10). Indeed, a literature review has emphasized that AVN, despite being relatively uncommon, is a progressive condition that often culminates in femoral head collapse thereby necessitating total hip arthroplasty (10).

Emerging literature suggests that COVID-19 may have acted as a catalyst for new AVN cases, particularly through corticosteroid therapy, endothelial dysfunction, and microvascular injury (9-11). Especially the use of corticosteroids in patients with COVID-19 infection and respiratory insufficiency has been linked to occurrence of AVN (9-11). A recent study indicated that cumulative steroid dose is the main determinant of osteonecrosis of the femoral head severity in post-COVID-19 patients, and combined use of corticosteroids may accelerate the onset of this condition, thereby highlighting the need for cautious steroid management in COVID-19 patients (12).

In the SEE region, musculoskeletal disorders including AVN constitute a substantial contributor to morbidity (13,14). Thus, the World Health Organization reports that musculoskeletal disorders are highly prevalent across Europe and represent a major cause of disability, with significant rehabilitation needs, including SEE countries (13). Furthermore, a recent study emphasizes that musculoskeletal diseases are highly prevalent in Europe and place a significant burden on healthcare systems including SEE countries (14), underscoring the importance of these chronic conditions during and after the COVID-19 pandemic years.

As a matter of fact, the intersection of pandemic-related risk factors and persistent musculoskeletal morbidity provides a compelling rationale for examining musculoskeletal disorders and especially AVN in the SEE context.

Epidemiology of AVN in SEE region

Epidemiological data on AVN in SEE region remain limited, but available evidence highlights its importance as a non-arthritic cause of hip disability (10,15). Registry studies and orthopedic reports from the Western Balkan countries, albeit not well-documented, indicate that AVN accounts for approximately 10% of primary total hip arthroplasties, a proportion that is consistent with global estimates (10,16). The condition most commonly affects adults between 30 and 50 years of age, often leading to premature disability and surgical intervention in otherwise active populations (10,17). As a matter of fact, a review has indicated that AVN is a major non-arthritic indication for hip arthroplasty, particularly in younger adults, accounting for 8%-12% of cases in European orthopedic registries (10). Additionally, a more recent report states that AVN symptoms cause disability predominantly in young to middle-aged individuals, with surgical intervention often required to prevent collapse and secondary arthritis (17).

Risk factors prevalent in the SEE region – including high levels of corticosteroid use in rheumatology and oncology, alcohol consumption, and traumatic femoral neck fractures – contribute to AVN incidence (10,18). Case reports from North Macedonia and Turkey have documented AVN developing after COVID-19 infection, with onset typically occurring weeks to months after recovery (18,19). These cases highlight the potential role of pandemic-related exposures in amplifying AVN risk (18,19).

Study context

Although precise incidence and prevalence figures are lacking for SEE countries, the consistent identification of AVN in orthopedic registries and case series (10,18) underscores its clinical relevance. In SEE countries, where healthcare access and early diagnostic imaging may be limited, AVN cases may often present at advanced stages, necessitating hip arthroplasty rather than joint-preserving interventions. This pattern suggests that the true burden of AVN may be underestimated in SEE regional datasets, reinforcing the need for systematic surveillance and targeted research.

Given the scarcity of epidemiological data specifically addressing AVN in the SEE countries, we sought to contextualize its potential impact by analyzing the broader burden of musculoskeletal disorders in the region. Within this framework, we examined separately the category of “other musculoskeletal disorders”, which encompasses AVN of the femoral head. This approach may allow assessment of the contribution of musculoskeletal morbidity to overall disease burden, while acknowledging AVN as a clinically significant condition that may be underrecognized in regional datasets.

Methods

This analysis utilized publicly available estimates from the Global Burden of Disease (GBD) Study, as reported by the Institute for Health Metrics and Evaluation (IHME) (20,21). The GBD provides standardized, comparable metrics of mortality and disability across countries,

enabling cross-national and temporal analyses (20,21). Age-standardized rates were extracted to account for differences in population age structures between countries and over time.

The analysis focused on the following seven SEE countries: Albania, Bosnia and Herzegovina, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia. These countries were selected to represent the SEE region, notwithstanding country differences regarding epidemiological profile and, especially, health system characteristics.

Two primary outcomes were examined: i) mortality rates: age-standardized deaths per 100,000 population, with 95% confidence intervals (CIs); disease burden: age-standardized disability-adjusted life years (DALYs) per 100,000 population, with 95% CIs.

Both outcomes were assessed for: i) COVID-19 (communicable disease); ii) musculoskeletal disorders (noncommunicable diseases), including the subcategory of "other musculoskeletal disorders", which encompasses AVN of the femoral head.

A comparative analysis was conducted across countries and over time to identify temporal trends and geographic variation. Regarding the time frame, trends of mortality and burden (DALYs) of COVID-19 were analyzed annually for the years 2020, 2021, 2022, and 2023, covering respectively the onset, peak, and decline phases of the COVID-19 pandemic. Conversely, mortality rates and disease burden (DALYs) from musculoskeletal disorders and next separately for the category "other musculoskeletal disorders" were assessed for the years 2020 and 2023, allowing comparison between the start of the pandemic and the most recent available GBD estimates (20).

Point estimates and 95% CIs were reported directly from GBD data (20); no additional statistical modeling was applied. Results were presented in tabular format to facilitate cross-country comparison, with narrative synthesis highlighting key differences and patterns.

For musculoskeletal disorders, emphasis was placed on the "other musculoskeletal disorders" category to contextualize AVN within the broader burden of chronic musculoskeletal morbidity.

Regarding the ethical considerations, this analysis used secondary, aggregated, publicly available data from IHME (20). No individual-level data were accessed and, therefore, ethical approval was not required.

Results

Analysis of COVID-19 mortality and disease burden in Southeastern Europe between 2020 and 2023 revealed marked temporal and geographic variation.

COVID-19 mortality trends (Table 1)

Age-standardized mortality rates per 100,000 population peaked in 2021 across all SEE countries, followed by a sharp decline in 2022 and 2023. The highest mortality rates were consistently observed in Montenegro and North Macedonia, whereas Croatia and Slovenia reported comparatively lower values.

Albania recorded 122 deaths (per 100,000 population) in 2020, rising to 155 in 2021, before dropping to 35 in 2022 and to only nine deaths (per 100,000 population) in 2023. Similar declining patterns were observed in Montenegro (from 144 to only 11 deaths per 100,000 population in 2020 and 2023, respectively), North Macedonia (from 127 to 14 deaths per

100,000 population in 2020 and 2023, respectively), Bosnia and Herzegovina (from 92 to only six deaths per 100,000 population in 2020 and 2023, respectively), Serbia (from 96 to 23 deaths per 100,000 population in 2020 and 2023, respectively), Croatia (from 53 to six deaths per 100,000 population in 2020 and 2023, respectively), and Slovenia (from 69 to 16 deaths per 100,000 population in 2020 and 2023, respectively).

Table 1. Mortality rates from COVID-19 in SEE countries during 2020-2023 (20)

COUNTRY	Year: 2020	Year: 2021	Year: 2022	Year: 2023
Albania	122 (104-133)*	155 (132-169)	35 (28-40)	9 (7-11)
Montenegro	144 (130-155)	320 (295-339)	66 (58-73)	11 (9-12)
North Macedonia	127 (121-136)	265 (255-284)	70 (66-77)	14 (13-15)
Bosnia and Herzegovina	92 (87-101)	201 (190-219)	65 (61-74)	6 (5-7)
Serbia	96 (91-104)	237 (227-260)	78 (73-87)	23 (21-26)
Croatia	53 (50-55)	99 (94-103)	56 (52-58)	6 (5-6)
Slovenia	69 (63-73)	68 (62-71)	31 (28-34)	16 (14-17)

* Age-standardized deaths per 100,000 population and their respective 95% confidence intervals (in parentheses).

Trends in COVID-19 burden (Table 2)

COVID-19 burden, expressed as age-standardized DALYs per 100,000, also peaked in 2021 before declining in all SEE countries. Burden of COVID-19 in Albania increased from 2,688 (DALYs per 100,000) in 2020 to 3,925 in 2021, then fell to 1,320 in 2022 and 419 (DALYs per 100,000) in 2023.

Table 2. COVID-19 burden rates in SEE countries during 2020-2023 (20)

COUNTRY	Year: 2020	Year: 2021	Year: 2022	Year: 2023
Albania	2688 (2257-3172)*	3925 (3276-4849)	1320 (928-1976)	419 (251-697)
Montenegro	2958 (2700-3252)	7148 (6602-7873)	1733 (1398-2296)	408 (260-682)
North Macedonia	3549 (3239-4101)	6842 (6229-7817)	2246 (1827-2901)	610 (424-923)
Bosnia and Herzegovina	2339 (2135-2749)	4850 (4388-5605)	1825 (1465-2356)	372 (185-679)
Serbia	2277 (2106-2531)	5261 (4918-5842)	1781 (1517-2175)	653 (508-907)
Croatia	1277 (1136-1512)	2499 (2198-2988)	1376 (1113-1817)	334 (184-601)
Slovenia	1206 (1107-1343)	1389 (1237-1618)	744 (600-967)	389 (273-564)

* Age-standardized DALYs per 100,000 and their respective 95% confidence intervals (in parentheses).

Montenegro exhibited the highest burden in 2021 (7,148 DALYs per 100,000), followed by North Macedonia (6,842 DALYs per 100,000) and Serbia (5,261 DALYs per 100,000). Croatia and Slovenia consistently reported lower burdens, with Croatia peaking at 2,499 DALYs per 100,000 in 2021 and Slovenia at only 1,389 DALYs per 100,000.

By 2023, all SEE countries demonstrated substantial reductions in COVID-19 burden, with values ranging between 334 DALYs per 100,000 (in Croatia) and 653 DALYs per 100,000 (in Serbia).

Musculoskeletal disorders (Table 3)

The analysis of musculoskeletal disorders in the SEE region for 2020 and 2023 exhibits relatively stable patterns in both mortality and disease burden, with only minor fluctuations across countries.

Table 3. Mortality rates and burden of musculoskeletal disorders in SEE countries in 2020 and in 2023 (20)

Upper panel: All musculoskeletal disorders				
COUNTRY	**Mortality***		**Disease burden***	
	Year: 2020	**Year: 2023**	**Year: 2020**	**Year: 2023**
Albania	0.76 (0.48-1.21)	0.73 (0.46-1.18)	2104 (1555-2853)	2085 (1540-2822)
Montenegro	0.63 (0.46-0.87)	0.63 (0.46-0.85)	2122 (1565-2887)	2096 (1541-2861)
North Macedonia	0.27 (0.19-0.36)	0.25 (0.17-0.34)	1981 (1468-2729)	1967 (1451-2692)
Bosnia and Herzegovina	0.53 (0.38-0.72)	0.51 (0.36-0.73)	2056 (1513-2785)	2032 (1493-2786)
Serbia	0.86 (0.63-1.10)	0.82 (0.61-1.08)	2152 (1577-2969)	2121 (1556-2910)
Croatia	0.93 (0.83-1.06)	0.87 (0.76-1.01)	2061 (1516-2826)	2033 (1497-2772)
Slovenia	1.12 (0.99-1.27)	1.15 (1.00-1.34)	2010 (1468-2769)	1990 (1458-2752)
Lower panel: Other musculoskeletal disorders†				
COUNTRY	**Mortality***		**Disease burden***	
	Year: 2020	**Year: 2023**	**Year: 2020**	**Year: 2023**
Albania	0.58 (0.35-0.98)	0.55 (0.32-0.95)	173 (119-240)	168 (114-237)
Montenegro	0.42 (0.28-0.61)	0.42 (0.29-0.60)	186 (128-265)	181 (125-250)
North Macedonia	0.24 (0.15-0.34)	0.22 (0.14-0.31)	187 (129-265)	180 (122-262)
Bosnia and Herzegovina	0.31 (0.20-0.47)	0.30 (0.20-0.46)	178 (120-257)	171 (155-244)
Serbia	0.63 (0.44-0.83)	0.61 (0.43-0.82)	202 (140-282)	193 (134-276)
Croatia	0.65 (0.57-0.73)	0.61 (0.52-0.72)	190 (133-266)	184 (125-258)
Slovenia	0.74 (0.64-0.84)	0.76 (0.65-0.89)	170 (119-238)	166 (115-232)

* Age-standardized rates and their respective 95% confidence intervals (in parentheses).

† "Other musculoskeletal disorders" category includes AVN.

All musculoskeletal disorders (upper panel)

Age-standardized mortality rates were consistently low, ranging between 0.25 and 1.15 deaths per 100,000 population. Slovenia reported the highest mortality (1.12 in 2020 and 1.15 in 2023), whereas North Macedonia had the lowest (0.27 in 2020 and 0.25 in 2023). Across all

countries, mortality rates remained essentially unchanged between 2020 and 2023, with only slight decreases observed in Albania, Serbia, and Croatia.
On the other hand, disease burden, expressed as DALYs per 100,000, was substantial but stable over time. Values ranged from approximately 1,981 DALYs per 100,000 in North Macedonia (in 2020) to 2,152 DALYs per 100,000 in Serbia (in 2020). By 2023, these figures showed minimal reductions, with Serbia reporting 2,121 DALYs per 100,000 and Slovenia 1,990 DALYs per 100,000. Overall, the burden of musculoskeletal disorders remained high and relatively constant across the SEE region.

Other musculoskeletal disorders (lower panel)
Mortality rates from "other musculoskeletal disorders" were slightly lower than for the broader category (of musculoskeletal disorders), ranging between 0.22 and 0.76 deaths per 100,000 population. Slovenia again reported the highest values (0.74 in 2020 and 0.76 in 2023 – deaths per 100,000 population), whereas North Macedonia had the lowest mortality rates (0.24 in 2020 and 0.22 in 2023 – deaths per 100,000 population). The temporal changes were minimal, with most SEE countries showing stable or marginally reduced mortality rates.
Conversely, disease burden for "other musculoskeletal disorders" was considerably smaller than for the overall musculoskeletal disorders category, ranging from 170 to 202 DALYs per 100,000 in 2020, and from 166 to 193 in 2023. Serbia and Croatia reported the highest burdens, whereas Slovenia and Albania had the lowest. Again, the changes between 2020 and 2023 were minor, suggesting a persistent but relatively modest contribution of these conditions to overall musculoskeletal morbidity.

Discussion
This analysis provides specific insights into the burden of musculoskeletal disorders in SEE countries during the COVID-19 pandemic, with particular attention to AVN of the femoral head. In the SEE region, COVID-19 mortality and disability peaked in 2021, followed by a sharp decline in 2022 and 2023, consistent with vaccination rollout and improved clinical management in all SEE countries (2). In contrast, musculoskeletal disorders – including the "other musculoskeletal disorders" category that encompasses AVN – remained stable across the study period, highlighting their persistent contribution to morbidity in the SEE region.
Although AVN is relatively rare, its disproportionate impact is evident. Registry data suggest that AVN accounts for 8%-12% of primary hip arthroplasties in Europe, including SEE countries (10,16), and predominantly affects adults aged 30-50 years (10,17). Case reports from North Macedonia and Turkey further highlight AVN onset after COVID-19, often linked to corticosteroid therapy (18,19). These observations support the premise that pandemic-related exposures may have amplified AVN risk in SEE populations too.
The stability of musculoskeletal burden in GBD estimates may mask under-recognition of AVN, particularly in SEE settings with limited access to early diagnostic imaging. Consequently, in SEE countries such as Albania, Bosnia-Herzegovina, Kosovo or North Macedonia, AVN cases may present at advanced stages, necessitating surgical intervention rather than joint-preserving therapies. This underlines the need for systematic surveillance,

improved diagnostic pathways, and cautious use of corticosteroids in COVID-19 management, as convincingly indicated in the international literature (11,12).

Musculoskeletal disorders include more than 150 different conditions affecting the spine, joints, muscles, bones, ligaments, and tendons (22). The GBD database includes a residual musculoskeletal category for conditions other than osteoarthritis, rheumatoid arthritis, gout, low back pain, and neck pain (20,22). This category referred to as "other musculoskeletal disorders" includes also AVN (20,22). A systematic analysis of GBD Study 2021 has reported on the prevalence of other musculoskeletal disorders based on estimates from 204 countries and territories from 1990 to 2020 (22). According to this comprehensive report, 494 million individuals worldwide had other musculoskeletal disorders in 2020, representing an increase of more than 120% compared to 1990 (22). Furthermore, the number of cases with other musculoskeletal disorders is projected to increase by 115% from 2020 to 2050 (22). In 2020, the worldwide age-standardized prevalence of other musculoskeletal disorders was about 47% higher in females than in males (22). For the same year, globally, other musculoskeletal disorders ranked as the sixth cause of morbidity (22).

A recent study from Romania reported that a significant proportion of patients diagnosed with avascular necrosis had previously been confirmed with COVID-19 (23). Furthermore, there was evidence of a high prevalence of bilateral necrosis among COVID-19-positive patients in this study conducted in Romania, indicating a potential systemic impact of the virus on vascular homeostasis and bone metabolism (23). Also, notwithstanding the fact that patients with COVID-19 were more likely to receive corticosteroid therapy and to show pulmonary involvement than those without infection, intriguingly, COVID-19 itself was not an independent risk factor for developing AVN in logistic regression analysis (23). Instead, steroid treatment emerged as the key predictor, underscoring the central role of medication-related effects in the pathogenesis of this condition (23).

On another aspect, it should be noted that SEE countries have undergone rapid demographic and socioeconomic transformations in the past few decades, associated with considerable changes in disease patterns and population risk profiles (24). Notwithstanding these tremendous changes, a recent analysis has nonetheless documented notable improvements in reducing premature mortality and disease burden across the SEE region, largely attributable to declines in environmental and occupational risk exposures (25). However, the persistence, and in some cases increase, of metabolic risk factors presents a growing public health challenge that threatens to offset these gains (25). This pattern reflects the broader global epidemiological transition toward noncommunicable diseases (25). Overall, the available evidence from the SEE region highlights the dual imperative of sustaining progress in mitigating environmental and behavioral risks, while simultaneously prioritizing prevention, policy action, and health system innovation to address metabolic determinants of health (25).

Conclusion

Acute COVID-19 imposed a substantial but time-limited burden in SEE countries, whereas its sequela such as musculoskeletal disorders (including AVN) remained a stable and significant contributor to morbidity. AVN of the femoral head, though uncommon, represents a major

non-arthritic cause of hip disability and surgical intervention. Pandemic-related risk factors, especially corticosteroid use, may have increased AVN incidence in the SEE region.
Therefore, in conclusion, strengthening surveillance, ensuring timely diagnosis, and promoting judicious corticosteroid management are essential to mitigate the long-term musculoskeletal consequences of COVID-19 in SEE populations.

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