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Review Article
Infectious Diseases

Severe COVID-19 in the Republic of Korea: Epidemiology, Risk Factors, Therapeutics, and Prognostic Models From Nationwide Data

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ABSTRACT

Severe coronavirus disease 2019 (COVID-19) has posed ongoing clinical and public health challenges worldwide, with Korea providing a unique perspective due to its comprehensive surveillance system and extensive real-world data. This review summarizes evidence from nationwide registries, cohort studies, and clinical trials in Korea, alongside global findings, to describe the epidemiology, risk factors, therapeutic interventions, and prognostic models for severe COVID-19. Between January 2020 and August 2023, Korea reported more than 34 million confirmed cases, with 38,112 classified as severe and 35,608 deaths, yielding one of the lowest case fatality rates among member countries comprising the Organisation for Economic Co-operation and Development. Severity was strongly associated with advanced age and comorbidities such as cardiovascular disease, diabetes mellitus, cancer, psychiatric disorders, and immunocompromised states, including solid organ transplantation and hematologic malignancies. Other risk modifiers included obesity, chronic kidney disease, asthma, and prolonged glucocorticoid therapy. Protective factors included vaccination, regular physical activity, and, in some studies, specific pharmacologic agents. The effectiveness of vaccines was consistently demonstrated, with booster doses markedly reducing hospitalization and mortality, including in high-risk groups such as pregnant women, patients with cancer, and transplant recipients. Antiviral therapies, notably nirmatrelvir/ritonavir and molnupiravir, significantly reduced severe outcomes, while immunomodulators such as dexamethasone and tocilizumab improved recovery in patients with severe disease. Advanced interventions, including extracorporeal membrane oxygenation and lung transplantation, were used for refractory respiratory failure, with favorable survival observed in selected patients. Prognostic models integrating clinical, radiological, and machine learning approaches have been developed to predict disease progression, supporting early risk stratification and resource allocation. The rapid generation of evidence on predicting, preventing, and treating severe disease is a critical element of pandemic preparedness. Although COVID-19 has transitioned to an endemic disease, sustaining and advancing the research expertise and infrastructure developed during the pandemic remains essential for responding to future emerging infectious disease outbreaks.

Keywords: COVID-19; Severe Disease; Risk Factors; Prognosis; Antiviral; Korea

INTRODUCTION

Coronavirus disease 2019 (COVID-19), which emerged in late 2019, has infected more than 700 million people globally and caused over 7 million deaths by the end of 2024.[1] The World Health Organization declared it a Public Health Emergency of International Concern (PHEIC) on January 30, 2020, and lifted the declaration on May 5, 2023, meaning the PHEIC lasted for approximately three years and three months.[2,3]

Clinically, COVID-19 is classified into mild, moderate, severe, and critical categories. "Severe" refers to cases with pneumonia requiring supplemental oxygen, while "critical" refers to illnesses requiring intensive interventions such as mechanical ventilation or extracorporeal membrane oxygenation (ECMO).

The proportion of mild cases has varied since the early pandemic, with the emergence of variants such as alpha, beta, delta, and omicron.[4] Even during periods when the rate of severe disease was relatively high, only about 14% of patients with COVID-19 were classified as severe, and about 5% as critical, indicating that the majority of cases remained mild.[5] However, when the number of severe cases exceeds the healthcare system capacity or when mortality among severe cases rises, a major societal crisis results. For this reason, from the early stages of the pandemic, numerous studies focused on risk factors, clinical characteristics, and treatments for severe COVID-19.

Although the clinical features of severe COVID-19 were initially unclear, they became more clearly defined through a large body of research conducted over time. In this review, we focus on studies conducted in the Republic of Korea that investigate the epidemiology, risk factors, and treatment outcomes of severe COVID-19.

EPIDEMIOLOGY AND CHANGES ACROSS VARIANT-DOMINANT PERIODS

In Korea, after the first confirmed COVID-19 case was identified on January 20, 2020, the disease was designated as a Class 1 notifiable infectious disease until April 25, 2022, and nationwide surveillance was maintained until August 30, 2023. According to reports from the Korea Disease Control and Prevention Agency (KDCA), during the surveillance period (January 20, 2020 to August 30, 2023), a total of 34,572,554 confirmed cases were reported, representing approximately 67.3% of the national population. Within this period, 38,112 patients were classified as severe cases, defined as requiring at least one of the following interventions: high-flow oxygen therapy, noninvasive mechanical ventilation, invasive mechanical ventilation, ECMO, or continuous renal replacement therapy. A total of 35,608 deaths were documented.[5,6] The overall severity rate and case fatality rate (CFR) were 0.19% and 0.10%, respectively.

In 2022, the year with the highest number of confirmed cases, 26,363 deaths occurred, accounting for 74.0% of all COVID-19-related deaths. The mean age of the deceased was 79.8 years. The sex distribution was 18,018 women (50.6%) and 17,587 men (49.4%).

The overall CFR during the surveillance period was 0.10%, which ranked as the second lowest among the 38 member countries of the Organisation for Economic Co-operation and

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Development (OECD). Year-specific CFRs declined progressively as the pandemic evolved: 2.16% in 2020, 0.91% in 2021, 0.09% in 2022, and 0.06% in 2023. The overall mortality rate was 69 per 100,000 population: 2 per 100,000 in 2020, 9 in 2021, 51 in 2022, and 7 in 2023. As observed globally, Korea experienced a sharp decline in CFR following the emergence of the omicron variant.

A study evaluating risk factors for severe COVID-19 during delta- and omicron-predominant periods in Korea, using the Korea Disease Control and Prevention Agency-COVID-19-National Health Insurance Service (K-COV-N) cohort dataset,[7] reported a severity rate of 1.9% during the delta period (September 20–December 4, 2021), which decreased to 0.1% during the omicron period (February 20–March 31, 2022). However, another study that examined COVID-19 clusters in long-term care facilities found that mortality during the omicron wave remained similar to that observed during the delta wave.[8]

RISK FACTORS

Demographic factors

The most important demographic factor influencing the progression of COVID-19 to severe disease is age. According to statistics from the KDCA, individuals aged ≥ 60 years accounted for 33,415 cases (93.9%) of all deaths during the nationwide surveillance period.[5] Among the deceased, those aged ≥ 80 years represented 55.5% of deaths in 2020, 50.0% in 2021, and more than 60.0% from 2022 onward. In contrast, only 62 deaths occurred among individuals aged ≤ 19 years, comprising 0.2% of the total. The highest CFR was observed in the ≥ 80-year age group (1.75%), followed by those in their 70s (0.40%), 60s (0.11%), and 50s (0.03%). As the pandemic progressed, CFRs decreased across all age groups.

Between January 20, 2020 and October 7, 2021, of 39,146 pediatric COVID-19 cases, only eight (0.02%) were classified as severe. Severe disease was defined as requiring high-flow oxygen therapy, positive-pressure ventilation, mechanical ventilation, ECMO, or continuous renal replacement therapy.[9] A meta-analysis further identified neonates, premature infants, obese children, and those with diabetes, cardiovascular disease, epilepsy, chronic lung disease, or an immunocompromised status as high-risk groups for severe outcomes.[10]

To monitor multisystem inflammatory syndrome in children (MIS-C), a Kawasaki disease-like condition associated with severe COVID-19, the KDCA implemented prospective surveillance between June 2020 and April 2023. Nationwide pediatricians reported 180 suspected cases, of which 146 were confirmed as MIS-C after expert review. No deaths were reported. During the omicron-predominant period, the incidence of MIS-C declined, although the absolute number of cases increased, and the clinical manifestations became milder.[11] A retrospective analysis of 17 pediatric patients with severe neurological complications during the omicron surge (January–April 2022) showed that 11 (64.7%) had preexisting neurological disorders (e.g., intellectual disability, cerebral palsy, epilepsy), and nine (53%) presented with MIS-C.[12]

With respect to sex, the KDCA reported similar mortality rates between men and women. However, in a multicenter study of 64 patients who required mechanical ventilation for severe COVID-19 pneumonia, male sex was identified as an independent risk factor for pulmonary fibrosis (hazard ratio [HR], 3.14; 95% confidence interval [CI], 1.08–9.14;

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$P = 0.036$).[13] Another study evaluated the influence of body mass index (BMI), fasting plasma glucose, blood pressure, and estimated glomerular filtration rate on COVID-19 severity and mortality by sex. The authors reported that hyperglycemia, mild renal impairment, and overweight status (BMI, 25–29.9) were significantly associated with greater disease severity, particularly among women.[14]

A cohort of 410 pregnant women hospitalized with COVID-19 in two Korean hospitals between August 2020 and February 2022 reported that one in four required oxygen therapy. Late pregnancy, hyperinflammatory status, and lack of vaccination were identified as major risk factors for hypoxemia.[15]

Obesity has consistently been confirmed as a risk factor for severe outcomes and mortality in COVID-19. A nationwide cohort study of 2,119,460 individuals who underwent two health screenings between 2017 and 2020 categorized weight by BMI as underweight (< 18.5), normal (18.5–22.9), overweight (23–24.9), and obese (≥ 25) and assessed the effect of weight changes on outcomes. Weight gain was associated with an increased risk of severe COVID-19, whereas weight loss was protective (adjusted odds ratio [aOR] for severe outcomes: normal to overweight 1.30, normal to obese 1.53, overweight to obese 1.25).[16]

The impact of smoking on COVID-19 outcomes has yielded inconsistent findings. In one nationwide study assessing combustible cigarettes (CCs), noncombustible tobacco products (e-cigarettes, heated tobacco), and overall tobacco product use. Current CC smokers (relative risk [RR], 0.51) and all current tobacco users (RR, 0.53) demonstrated a lower risk of hospitalization, with no significant association between smoking and COVID-19-related mortality.[17]

Physical activity also demonstrated a protective effect. A nationwide cohort study using health screening data found that individuals who engaged in both aerobic and strength training had lower risks of infection (adjusted relative risk [aRR], 0.85), severe disease (aRR, 0.42; 58% reduction), and COVID-19-related mortality (aRR, 0.24; 76% reduction) compared with those with insufficient physical activity.[18]

Socioeconomic disparities were also explored. Medicaid beneficiaries had a 22% higher risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection compared with National Health Insurance (NHI) enrollees, although no significant differences were observed in severe outcomes such as mortality, intensive care unit (ICU) admission, or need for mechanical ventilation.[19]

Comorbidities

Comorbidities, alongside age, represent the most influential factors associated with the risk of severe COVID-19. A study using NHI claims data demonstrated that the age-adjusted Charlson Comorbidity Index was highly predictive of mortality, with a score ≥ 3.5 showing strong predictive performance (area under the receiver operating characteristic curve, 0.92; sensitivity 86.8%, specificity 84.1%).[20]

During the nationwide surveillance period, approximately 96.0% of individuals who died had at least one underlying condition. The most common comorbidities were cardiovascular diseases such as hypertension (53.5%), neurological diseases such as dementia (45.0%), and endocrine or metabolic diseases such as diabetes mellitus (33.4%). The KDCA registry,

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linked with National Health Insurance Service (NHIS) data to establish the K-COV-N cohort, enabled comprehensive analyses of the impact of underlying diseases on clinical outcomes.

A nationwide case-control study of 219,961 adults who underwent COVID-19 testing by May 15, 2020, revealed that diabetes mellitus (odds ratio [OR], 1.009–1.543), hypertension (OR, 1.245–1.317), chronic lower respiratory disease (OR, 1.216–1.233), and chronic renal failure or end-stage renal disease (OR, 2.052–2.178) were significantly associated with severe outcomes, including the need for oxygen therapy, mechanical ventilation, ECMO, or cardiopulmonary resuscitation.[21]

An analysis of 5,307 patients aged 30 years or older confirmed that diabetes independently increased the risks of requiring oxygen therapy (aOR, 1.35; 95% CI, 1.10–1.66), mechanical ventilation (aOR, 1.93; 95% CI, 1.28–2.92), and mortality (aOR, 2.66; 95% CI, 1.90–3.73).[22]

A multinational cohort study involving eight countries and 2,851,035 COVID-19 cases (including 563,708 hospitalized patients) identified hypertension as a major risk factor for severe complications, hospitalization, and death in both outpatient and inpatient populations.[23] Similarly, heart failure and atrial fibrillation significantly increased the risk of severe disease.[24,25]

Between January 2020 and March 2022, a propensity-matched analysis of 397,050 patients with cancer and an equal number of noncancer controls demonstrated increased risks of hospitalization (OR, 1.09), severe hospitalization (OR, 1.17), and death (OR, 1.94). Risks were highest among those with recent cancer diagnoses, with hematologic malignancies carrying greater risks than solid tumors.[26]

Psychiatric illness was also associated with adverse outcomes. A nationwide study classified mental illness into severe categories (e.g., psychotic disorders, schizophrenia) and other categories (e.g., anxiety disorders, mood disorders, eating disorders). Severe mental illness was associated with a substantially higher risk of severe COVID-19 outcomes (OR, 2.27; 95% CI, 1.50–3.41).[27] Although Alzheimer's disease did not increase susceptibility to infection, it significantly elevated the risks of severe complications and mortality once infection occurred.[28]

A study analyzing 8,070 COVID-19 cases and 121,050 non-infected controls (including 7,261 individuals with disabilities) between January and May 2020 found that people with disabilities had significantly higher risk of infection (OR, 1.36; 95% CI, 1.24–1.48) and, once infected, greater risk of severe outcomes (OR, 1.43; 95% CI, 1.11–1.86), particularly among those with severe disabilities (grade 1).[29] Follow-up research confirmed that younger individuals with disabilities, those with internal organ dysfunction, and those with intellectual disabilities were at especially high risk.[30]

Allergic diseases such as asthma and allergic rhinitis were associated with an increased risk of infection and severe outcomes, including ICU admission, invasive mechanical ventilation, and death. Asthma increased the risk of severe outcomes (aOR, 1.62; 95% CI, 1.01–2.67), and allergic rhinitis also conferred elevated risk (aOR, 1.27; 95% CI, 1.00–1.64). Non-allergic asthma demonstrated the strongest effect on both infection and severity (aOR, 4.09; 95% CI, 1.69–10.52).[31] Another study reported that uncontrolled asthma, particularly in older men with recent exacerbations, was associated with higher mortality, underscoring the clinical importance of asthma control.[32]

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Several studies have also investigated the association between comorbidities and COVID-19 severity. Even mild renal impairment was linked to an increased risk of severe disease,[33] and nonalcoholic fatty liver disease independently heightened risks of infection, severe outcomes, and mortality.[34] In patients with osteoporosis, those with severe disease and fractures experienced worse outcomes, whereas fracture-free patients—particularly those receiving consistent medical care—paradoxically exhibited lower mortality.[35] Age-related macular degeneration (AMD), specifically the exudative form, was associated with a significantly higher risk of severe COVID-19.[36] Chronic rhinosinusitis (CRS) was also associated with higher SARS-CoV-2 positivity and greater risk of severe COVID-19. The risk was particularly elevated in patients without nasal polyps, those with non-atopic CRS, and individuals with a history of intranasal corticosteroid use.[37]

Immunocompromised conditions

Several studies have examined the impact of immunocompromised status on COVID-19 outcomes.

Solid organ transplant recipients (SOTRs), who require long-term immunosuppressive therapy, are considered particularly vulnerable to COVID-19 and may experience unfavorable clinical outcomes.[38,39] In a propensity score-matched (1:2) study of 85 SOTRs and 160 nontransplant controls drawn from 7,327 patients hospitalized with COVID-19 at two tertiary hospitals between February 2021 and August 2022, SOTRs had significantly higher rates of high-flow nasal cannula use, mechanical ventilation, acute kidney injury, and composite severe outcomes compared with non-SOTRs.[40] A nationwide analysis of SOTRs further confirmed elevated risks of severe COVID-19 compared with nontransplant patients (aOR, 4.30–18.14), with lung transplant recipients showing the highest risk (aOR, 18.14). Vaccination provided significant protection, with vaccine effectiveness against severe disease estimated at 47% (95% CI, 18–65%) after two doses and 64% (95% CI, 49–75%) after three doses.[41] Using linked KDCA registry and NHIS claims data, a study of 206 pediatric SOTRs (transplanted between 2008 and 2022) compared with 803 matched nontransplant pediatric COVID-19 patients demonstrated that pediatric transplant recipients were at significantly higher risk for severe disease.[42]

In a single-center study of 117 adult lymphoma patients who developed SARS-CoV-2 infection between January 2020 and April 2022, patients with lymphoma were at increased risk of developing COVID-19 pneumonia and exhibited delayed recovery. Risk was particularly high among those receiving rituximab maintenance therapy, patients with follicular lymphoma, and those who were unvaccinated.[43,44]

A study conducted during the omicron variant wave compared outcomes in 93 patients receiving B-cell depletion therapy (BCDT) with 145 matched non-BCDT patients who had similar comorbidities.[45] Severe-to-critical COVID-19 occurred in 41.9% of patients in the BCDT group compared with 28.3% of controls ($P = 0.030$). COVID-19–related mortality was 11.8% versus 2.8% ($P = 0.005$), indicating that BCDT remained a significant risk factor for adverse outcomes even during the omicron wave. Another single-center study of patients with B-cell lymphoma receiving BCDT found that those treated with T-cell engagers had significantly higher disease severity and mortality compared with those receiving rituximab.[46]

Long-term glucocorticoid therapy (LTGT) was also associated with increased COVID-19 severity and mortality. In a nationwide cohort study of 509,216 confirmed cases,

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12,794 patients were identified as LTGT users and compared with 359,013 controls.[47] Hospital mortality (14.0% vs. 2.3%), 30-day mortality (5.9% vs. 1.1%), and 90-day mortality (9.9% vs. 1.8%) were all significantly higher in the LTGT group. LTGT was confirmed as an independent risk factor for mortality (OR, 1.82; 95% CI, 1.67–2.00).

Medications

Because many individuals take medications such as antihypertensive drugs, antidiabetic agents, and lipid-lowering therapies for chronic disease management, several studies have examined whether these drugs influence the severity of COVID-19. Research has focused in particular on angiotensin-converting enzyme inhibitors (ACEIs), statins, and metformin.

In a study of 1,865 patients with type 2 diabetes and confirmed COVID-19, metformin use did not affect survival rates and showed no significant association with heart failure, mortality, or indicators of intensive care treatment.[48]

Initial concerns were raised that ACEIs and angiotensin II receptor blockers (ARBs) might worsen the severity and mortality of COVID-19. However, an analysis of Korean nationwide health insurance claims data found that prior use of renin-angiotensin-aldosterone system (RAAS) inhibitors was not independently associated with mortality or severe outcomes in patients with COVID-19.[49] A meta-analysis of 20 observational studies further demonstrated that ACEI/ARB use did not increase mortality and, in fact, was significantly associated with reduced mortality (OR, 0.52; 95% CI, 0.37–0.72). ACEI/ARB use was also not significantly associated with severe disease (OR, 0.68; 95% CI, 0.44–1.07).[50]

Another study using NHIS claims data assessed the effects of dipeptidyl peptidase-4 (DPP-4) inhibitors and RAAS inhibitors among patients with diabetes and COVID-19. While RAAS inhibitors did not significantly affect outcomes, use of DPP-4 inhibitors was associated with a lower risk of severe disease—defined as ICU admission or death—compared with non-users (aOR, 0.362; 95% CI, 0.135–0.971).[51]

Proton pump inhibitors (PPIs) have also been evaluated in relation to COVID-19 outcomes using nationwide Korean data. PPI use did not affect susceptibility to SARS-CoV-2 infection itself, but current use was associated with increased risk of severe clinical outcomes in COVID-19.[52] This effect was particularly pronounced with high-dose, short-term use and with continued use after hospitalization.[53]

The potential anti-inflammatory effects of statins have been investigated as well. A systematic review and meta-analysis of 13 cohort studies (110,078 patients; published between January 2019 and December 2020) examined the association between statin use and adverse COVID-19 outcomes.[54] Pre-hospital statin use was associated with a non-significant trend toward reduced mortality. In contrast, in-hospital statin use was significantly associated with reduced mortality (HR, 0.53; OR, 0.57), with stronger effects observed in non-ICU patients than in ICU patients. However, because many patients newly initiated on statins during hospitalization may have had underlying cardiovascular events, the protective effect may have been either underestimated or overestimated.

Antidepressant use has also been studied in relation to COVID-19 severity using K-COV-N data. Effects varied by drug class. Selective serotonin reuptake inhibitors were associated with a 34% reduced risk of severe COVID-19, tricyclic antidepressants were

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associated with a 48% increased risk, while serotonin–norepinephrine reuptake inhibitors and other antidepressants showed no significant associations.[55]

A study assessing the impact of prior anticoagulant use on COVID-19 clinical outcomes found no significant difference in severe outcomes between anticoagulant users and non-users.[56]

IMPACT OF THERAPEUTICS AND VACCINES

Vaccines

The effectiveness of COVID-19 vaccines has been evaluated across multiple studies, demonstrating not only preventive effects against SARS-CoV-2 infection but also a significant reduction in hospitalization and risk of severe disease in Korea. Although effectiveness against symptomatic infection varies depending on the circulating variant, vaccines have consistently shown strong protection against severe disease and death.[57-59]

During the nationwide surveillance period, 14,705 deaths (41.3% of total COVID-19-related deaths) occurred among unvaccinated individuals, while 6,785 deaths (19.1%) occurred among those who had received a primary series, and 14,115 deaths (39.6%) occurred among those who had received three or more doses.

A study analyzing data from 530,827 confirmed COVID-19 cases during the delta and omicron variant waves (July 2021–January 2022) found that mortality risk was lower during the omicron-dominant period compared with the delta period (aOR, 0.75).[60] Across all periods, receipt of a third vaccine dose markedly reduced the risk of severe disease (aOR, 0.05–0.08), with the lowest mortality observed in patients who received a third dose of a messenger ribonucleic acid (mRNA) vaccine (aOR, 0.02). Although vaccine-induced protection against severe disease waned over time, protection against death was maintained across all vaccine types and dose regimens. An additional study evaluated the effectiveness of a second mRNA booster (fourth dose) compared with the first booster in immunocompromised individuals and residents of long-term care facilities (n = 972,449).[61] The second booster conferred 22.3% effectiveness against infection (95% CI, 19.4–25.1%), 56.9% effectiveness against severe infection (95% CI, 30.0–73.5%), and 63.0% effectiveness against death (95% CI, 34.2–79.2).

Among patients with cancer, who often experience diminished vaccine efficacy due to immunosuppression, one study assessed breakthrough infection risk and protection against severe outcomes. In a cohort of 14,448 cancer patients with COVID-19, vaccination significantly reduced the risk of death (HR, 0.28; 95% CI, 0.22–0.35) and severe outcomes requiring ICU admission or mechanical ventilation (HR, 0.52).[62] Another study investigated the clinical course of COVID-19 in pregnant women before and after the emergence of the omicron variant, stratified by vaccination status.[63] Among 224 hospitalized pregnant women between November 2020 and March 2022, disease severity declined significantly during the omicron period. Vaccination reduced progression to severe disease, oxygen requirement, and pneumonia (moderate-to-severe COVID-19: unvaccinated 25.4% vs. vaccinated 4.1%; oxygen therapy: unvaccinated 16.2% vs. vaccinated 2.6%; pneumonia: unvaccinated 21.6% vs. vaccinated 2.6%).

The Korean Society of Infectious Diseases periodically updates national vaccination recommendations. The 2024–2025 guidelines prioritize high-risk groups, including

adults aged ≥ 65 years, individuals with comorbidities, residents of facilities vulnerable to outbreaks, pregnant women, and healthcare workers, for updated vaccination. COVID-19 vaccination is also recommended for all individuals aged ≥ 6 months.[64]

Therapeutics

Clinical trials have demonstrated that antiviral agents such as nirmatrelvir/ritonavir, molnupiravir, and remdesivir prevent progression to severe disease in more than 80% of patients with mild COVID-19. Real-world data from Korea have corroborated these findings.

Nirmatrelvir/ritonavir received emergency use authorization in Korea on January 14, 2022. Concerns regarding its effectiveness against the omicron BA.5 variant were addressed in a nationwide study that analyzed 1,936,925 patients (420,966 treated vs. 1,515,959 untreated) between July 1 and November 30, 2022. Nirmatrelvir/ritonavir reduced the risk of severe disease or death by 43.2% and lowered mortality by 31.1%.[65]

For molnupiravir, a Korean study compared 190,692 users with a propensity score-matched control group at a 1:4 ratio. Molnupiravir use reduced hospitalization by 29% and mortality by 25%, with stronger protective effects observed in older adults (≥ 70 years: hospitalization reduced by 39%, mortality by 32%; ≥ 80 years: hospitalization reduced by 44%, mortality by 38%).[66]

The monoclonal antibody regdanvimab, developed in Korea, was evaluated in high-risk patients with mild COVID-19 who were admitted within seven days of symptom onset (December 2020–May 2021).[67] In this cohort, 234 patients received regdanvimab and 544 received standard care. Regdanvimab significantly reduced oxygen requirement (8.1% vs. 18.4%, $P < 0.001$), disease progression (2.1% vs. 9.6%, $P < 0.001$), and length of hospital stay (median 11 days vs. 12 days, $P < 0.001$). However, with the emergence of novel variants, regdanvimab is no longer widely used.

PREDICTIVE MODELS FOR SEVERE DISEASE

Multiple studies have sought to develop models that predict severe outcomes in patients with COVID-19.

A retrospective study of 110 adult patients admitted to a hospital in Daegu from February 19 to March 26, 2020, compared the prognostic accuracy of National Early Warning Score (NEWS), the quick Sequential Organ Failure Assessment (qSOFA), and the Systemic Inflammatory Response Syndrome (SIRS) score in predicting 28-day mortality and severe outcomes (ICU admission or death).[68] The study demonstrated that the NEWS score at admission was useful in predicting poor outcomes and outperformed both SIRS and qSOFA.

Radiological findings have also been evaluated as prognostic markers. In a nationwide cohort of 271 adult patients hospitalized between February and May 2020, chest computed tomography scans obtained within 10 days of diagnosis were categorized into organizing pneumonia, diffuse alveolar damage (DAD), and bronchopneumonia patterns.[69] Extensive lung involvement and DAD patterns were significantly associated with poor prognosis. Another study combined deep learning with traditional machine learning models to develop a severity prediction tool capable of differentiating COVID-19 pneumonia from

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influenza pneumonia. The hybrid model demonstrated improved predictive performance in viral pneumonias, although it was less accurate in bacterial pneumonias due to differing radiographic patterns.[70]

Additionally, a machine learning model to predict maximum COVID-19 severity based on initial hospitalization records was developed using data from 2,263 patients admitted to 10 hospitals in Daegu between February 18 and May 19, 2020. The model was subsequently implemented as a web-based nomogram.[71] Other machine learning–based prediction models have also been developed.[72,73]

TREATMENT

Standard treatments (including dexamethasone, tocilizumab, baricitinib, and remdesivir) were widely used in Korea in accordance with clinical guidelines. Several domestic studies have evaluated their effectiveness.

In severe cases, dexamethasone combined with immunomodulators improved recovery rates without increasing infectious complications or impairing antiviral immune responses.[74] While dexamethasone 6 mg/day remains the standard of care, a nationwide matched cohort study using health insurance data (January 2020–June 2021) compared high-dose versus standard-dose corticosteroids in adults with severe-to-critical COVID-19 requiring supplemental oxygen.[75] High-dose therapy was associated with higher 28- and 90-day mortality, as well as a trend toward increased COVID-19–associated pulmonary aspergillosis (aHR, 2.97; 95% CI, 0.94–9.43).

The use of ECMO has also been reported. A multicenter study of 19 critically ill patients treated with ECMO in six hospitals in Daegu (February–April 2020) demonstrated a mortality rate of 58%, with many survivors requiring prolonged mechanical ventilation because of delayed lung recovery.[76] Another multicenter registry analysis compared 72 patients treated with ECMO to 390 patients managed with mechanical ventilation alone.[77] Among those with arterial partial pressure of oxygen/fraction of inspired oxygen < 80 or arterial partial pressure of carbon dioxide ≥ 60 mmHg, ECMO initiated within seven days of mechanical ventilation significantly reduced mortality (HR, 0.56; 95% CI, 0.36–0.96) and risk of pulmonary fibrosis (HR, 0.30; 95% CI, 0.11–0.70). The greatest benefit was observed in patients younger than 70 years, with fewer comorbidities, prior prone positioning, and driving pressure ≥ 15 cmH_2O.

In cases of irreversible COVID-19–induced lung damage and fibrosis, lung transplantation has been performed. A single-center study reported outcomes for 10 patients transplanted between May 2020 and February 2022, with a mean waiting period of 76 days, an average pre-transplant ECMO duration of 48.5 days, and a one-year survival rate of 70%.[78] A multicenter report of 11 transplant recipients noted that, aside from one early death at four days, the remaining patients survived during a median follow-up of 322 days.[79] Case reports have also described successful lung transplantation using grafts from donors who had recovered from COVID-19 pneumonia, highlighting both donor safety and post-transplant graft function.[80]

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CONCLUSIONS

In Korea, there has been extensive research on risk factors for severe COVID-19, effectiveness of vaccines and therapeutics, predictive models, and treatment outcomes. The rapid generation of scientific evidence played a pivotal role in shaping the national pandemic response. In particular, research capacity directed toward predicting, preventing, and treating severe disease proved to be a critical component of preparedness. Although COVID-19 has transitioned into an endemic infection, sustaining and further advancing the research expertise and infrastructure established during the pandemic remain essential to confronting future outbreaks of emerging infectious diseases.

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