JOSTIR Publication 2025 | ISSN: 1118-3896

Special Issue December 2025 | 430-439

Journal of Science, Technology and Innovation Research
Volume 1 Special Issue | December 2025

COVID-19 in Immunocompromised Hosts: A Systematic Review of Disease Severity, Immune Response, and Clinical Management Strategies

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ABSTRACT

This study presents findings from a systematic review of Coronavirus Disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which has had negative impact on health, social life and economy. Extant literature show that immunocompetent patients have been infected with COVID-19. However, reports rather reveal much impact on the immunocompromised patients who have elevated risk of severe outcomes of morbidity, resulting in increased hospitalization and death. This review gives an overview of the diagnoses, immunocompromised conditions, impacts and clinical management strategies of immunocompromised patients. A qualitative research design is adopted to collate and analyze the impacts of COVID-19 on immunocompromised patients from literature between 2019 and 2025. The number of studies reviewed within these periods are: 2019 (1), 2020 (5), 2021 (8), 2022 (7), 2023 (4), 2024 (3) and 2025 (2). The selected articles were generated from databases such as PubMed, Google Scholar, Web of Science and Embase. Results revealed that defect in innate immunity, antibody deficiencies, T and B lymphocytes deficiencies, autoinflammatory disorders among others, have been identified as the cause of Primary Immunocompromised Disorders. Meanwhile, major medical conditions and treatments such as cancer, HIV, solid-organ transplantation and immunosuppressive drugs caused Secondary immunocompromised Disorders. Clinical therapies identified were the use of pre-exposure prophylaxis, monoclonal antibodies, lymphocyte infusion, antiviral drugs and immunoglobulin maintenance. However, immunocompromised conditions vary from persons to persons, therefore, specific clinical therapeutic measures should be used by health care providers, and, should be strictly based on identified conditions, for proper management of COVID-19 infection.

Keywords: COVID-19; immunocompromised patients; immunocompetent patients; Primary Immunocompromised Disorders (PIDs); Secondary Immunocompromised Disorders (SIDs)

Introduction

COVID-19 which is caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has had a global negative effect for the past 4 years (Begum *et al.,* 2024). Historically, this started late December 2019 in Wuhan, China where there was an information about the circulation of a frightening case of pneumonia of unidentified cause (Biancolella, *et al.,* 2022). Coronaviruses are enveloped, positive-sense single-stranded RNA viruses that belong to the family Coronaviridae. Nigeria recorded 266,463,000 confirmed cases of COVID-19 infection and 3,155 deaths (World Health Organization WHO, 2023). Globally, by the end of June, 2022, there was an exponential growth of data that rose from 527,971,809

doi.org/10.51459/jostir.2025.1.Special-Issue.0126

cases of infection and 6,284,871 deaths (Biancolella, *et al.,* 2022). However, as at May, 2025, number of cases of infection rose to over 777, 950,273 million with over 7,096,650 million deaths globally (WHO, 2025).

Centre for Disease Control and Prevention, CDC (2019), described immunocompromised patients as patients with weakened immune system, who can easily contract COVID-19 and get sick for a longer period. This is due to underlying medical conditions or treatments. The general underlying medical conditions such as Sickle cell disease, Tuberculosis, Chronic kidney disease, liver disease and lung disease, Cystic fibrosis, Disabilities, Heart diseases, Cancer, Dementia, HIV infection, Solid organ transplantation and Stroke among others. Fung and Babik (2021) identified the immunocompromised patients as persons with HIV, cancer, solid organ transplantation, primary immunodeficiency, and patients on autoimmune and inflammatory treatment. Those with viral loads <200 copies/mL have increased outcome of hospitalization, ICU and death. Dutta (2021) highlighted three diagnoses that can be used to detect immunocompromised conditions. Antibody Test which is carried out to identify the level of IgA, IgG and IgM antibodies in the serum. T cell Test which is carried out to detect reduction in T cells and neutrophil counts for identifying neutrophil system counts. The rationale for this systematic review sprouts from the clinical heterogeneity observed among immunocompromised patients with COVID-19.

Research carried out by Beak *et al.,* (2021) revealed that immunocompromised patients had higher chance of acute COVID-19. This could originate from the level of the management therapy that includes the use of mechanical ventilation, renal replacement and the use of corticosteroids. There are two types of immunocompromised conditions; According to Shields and Patel (2021), Primary Immunocompromised Disorders (PIDs) are such with different symptoms across varied patients which are caused as a result of defect in the immune system. Meanwhile, Secondary Immunocompromised Disorders (SIDs) on the other hand, occurs due to immune system suppression, chronic infection, malnutrition and immune-inhibiting drugs (Tuano, *et al*., 2021).

The validation for this study lies in the crucial need to describe the clinical course and immune responses in immunocompromised patients. Apart from being hospitalized, immunocompromised patients who contract COVID-19 are more possible to be hospitalized in Intensive Care Unit (ICU) and may likely die. University of Utah Health, (2022) confirmed that immunocompromised patients experienced a higher rate of breakthrough symptomatic infection. They may not generate a good immune response to vaccine due to immune deficiency as active immunity is needed for immune response. An important gap this review seeks to fill is the mechanistic understanding of immune responses in various immunocompromised subpopulations. Ultimately, this review helps evaluate the effectiveness and safety of existing clinical interventions, inform clinical guidelines, support individualized treatment approaches, and shape future research priorities in this high-risk population.

Materials and Methods

This systematic review uses a qualitative research design of databased search such as PubMed, Google Scholar, Web of Science and Embase for appropriate English Language Articles. This was conducted using peer-reviewed articles published between 2019 and 2025. Disease severity, immune response and clinical management of COVID-19 in immunocompromised hosts were collated from the selected articles and analyzed. This review focused on both primary and secondary immunocompromised conditions. The number of studies reviewed within this period are 2019 (1), 2020 (5), 2021 (8), 2022 (7), 2023 (4), 2024 (3) and 2025 (2). Total of 30 articles were reviewed in all. Suitable populations involved individuals with primary immunocompromised conditions, Human Immunodeficiency Virus (HIV)

patients, solid organ transplant (SOT) recipients and patients with cancer. The abstracts were scrutinized for appropriate articles. Full texts relevant articles were reviewed and included. Articles that do not focus on immunocompromised patients and deficient of primary data were not included.

Results

All the items discussed on Table 1 are generated from Bousfiha *et al* (2020), Table 2-3 from the study by Fung and Babik (2021), Table 4 from Osibogun *et al* (2021) and Table 5 from Goldman *et al* (2021)

HIV Patients

SARS-COV-2 has diverse effects on people living with HIV in contrast to those free from HIV (Muhammed *et al*., 2020). They have higher risk of SARS-CoV-2 reinfection (Teran *et al*., 2023). World Health Organization (WHO) global registry data estimated Death Threat Rate (MHR) of 1.29 (95% CL, 1.23-1.35) in persons with HIV. They experience great reduction in CD4+ cell counts (Jakharia, *et al.* 2022). Additionally, Cheng *et al*., (2024), identified CD4+ cell counts and HIV viral load as the major cause of SARS-CoV-2 infection and hospitalization. Fredericks, *et al., (*2025) reported that, the virus can be prolonged in patients with HIV as a result of prolonged viral shedding with uncontrolled HIV viral counts. This resulted in continuous disease thereby permitting the buildup of immune escape mutation in the viral genome (Jakharia, *et al.* 2022). Meanwhile, Payette and Terry (2022), reported that coinfection of HIV and COVID-19 makes it difficult to know the immune status of COVID-19 in HIV patients. Effective management of HIV includes sustained viral suppression, immune system monitoring, and prevention of opportunistic infections.

Cancer Patients

Patients with cancer often have impaired immune response that resulted from treatments such as chemotherapy, radiation, and immunotherapy (Reeg, *et al*., 2023). This increases their susceptibility to infections and complications like severe pneumonia and severe respiratory injury (Al-Quteimat and Amer, 2020). Blood cancers like leukemia and lymphoma directly affect immune cells, while treatments for other cancers reduce white blood cell counts, making patients more vulnerable to infections (Ballet *et al*., 2022). Cancer patients have a dual chance of being infected with COVID-19 in relation to the general population (Payette and Terry, 2022). Study shows that SARS-CoV-2 promote cancer cells which inhibit tumor suppressor genes and pathways (Jaiswal., *et al*., 2024). Cancer patients with COVID-19 comorbidities such as hypertension, chronic heart conditions, diabetes and chronic kidney diseases have an increased risk of severe outcomes. The use of prophylactic antibiotics, antifungals, and antivirals, especially during periods of neutropenia, helps to reduce infection rates (Klastersky *et al*., 2020). Administration of granulocyte colony-stimulating factors (G-CSF) helps to stimulate white blood cell production and shorten neutropenia duration (Adamo *et al*., 2022).

Solid-Organ Transplantation Patients (SOT)

COVID-19 pandemic had great effect on SOT recipients, brought about decreased and delayed in solid organ transplantation. Although, report has it that, there is a general reduced risk of SARS-COV-2 infection among SOT recipients but more in patients with lung transplants (Bartelt., 2022). Factors such as abnormal chest imaging on presentation, lymphopenia on presentation, obesity, age >65, chronic lung disease and congestive heart failure were seen to be associated with SOT recipients with COVID-19 infection (Jaffar., *et al.* 2020). This is as a result of weak immune response develop towards SARS-COV-2 infection arising from immunosuppressive drugs (Reeg., *et al*., 2023; Grossi., *et al.* 2025). Management of solid organ transplant recipients centers around immunosuppressive therapy, infection prevention, and graft function monitoring (Dashti-Khavidaki *et al*., 2021).

Discussion

Primary Immunocompromised Disorders

Table 1, represents classification of primary immunocompromised disorders. This comprises of immunodeficiencies, causes and diseases. The deficiencies were caused by mutations of several genes. These genetic defects weaken the immune system leading to recurrent infections, impaired antibody response, autoimmune and inflammatory disease, low IgA, IgG and IgM. This validates the work of Shields and Patel (2021) which state that primary immunocompromised patients have different deficiencies that causes defect in their immune system.

HIV Patients

Table 2 show studies of laboratory confirmed HIV patients with COVID-19. The study of Goldman *et al.*, (2021), identified population, study design and the primary findings. 286 United State HIV-COVID-19 patients on antiviral therapy with <200 CD4/mL showed risk factors for hospitalization, ICU and even death. Likewise, 2410 HIV-COVID-19 patients at the department of Health, New York City who were hospitalized with HIV viral loads <200 copies/mL also showed higher risk of hospitalization, ICU and death. 22,308 Western Cape and South Africa HIV-COVID-19 Patients with >1000 copies/mL or <200 CD4/mL experienced severe outcome of COVID-19 death. This study corroborated the work of Fung and Babik, (2021) that stated that HIV patients with viral loads <200 copies/mL have severe outcome of hospitalization, ICU and death.

Cancer Patients

In Table 3, the review highlights that cancer patients, mainly those with blood cancer or on active treatment, experience higher COVID-19 severity and mortality. Hospitalization rates were consistently high, with ICU admissions and intubation more common in severely immunocompromised groups. This supports the work of Al-Quteimat and Amer (2020), noting that cancer patients have higher risk of COVID-19 infection, as a

Table 1. Classification of Primary Immunocompromised Disorders

S/N	Deficiencies In	Causes	Infections/Diseases
1	Complement Protein Deficiencies (CD 19, CD 20 and CD 21)	Mutations in the MS4A1 gene	Recurrent infection and low IgG
2	Transmembrane Activator and CAML Interactor (TACI) Deficiency	Mutations in the TNFRSF13B gene	Impaired antibody response to vaccines
3	B-cell Activating Factor (BAFF Deficiency	Mutations in the TNFRSF13C gene	Variable clinical expression, low IgG and IgM
4	Tumor Necrosis Factor–Like Weak Inducer of Apoptosis (TWAEK) Deficiency	Loss-of-function mutations in the TNFSF12 *gene*	Pneumonia, bacteria infection, low IgA and IgM
5	Interferon Regulatory Factor 2 Binding Protein 2 (IRF2BP2) Deficiency	mutations in the IRF2BP2 gene	Low IgA, recurrent infection, and autoimmune and inflammatory disease.
6	X- Linked Agammaglobulinemia (XLA) Deficiency	Mutation in the BTK gene (Bruton's Tyrosine Kinase)	Antibody deficiency

Source: Bousfiha. *et al.* (2020).

Table 2. Studies of Laboratory Confirmed HIV Patients with COVID-19

S/N	Population	Study Design	Primary findings
1	• United State HIV-COVID-19 Consortium • 286 cases • On Antiretroviral Therapy 93% <200 CD4/mL 15%	Multicenter Registry of HIV and COVID-19	• 55% required hospitalization based on O_2 saturation <94% or elevated qSOFA score. • 29% received ICU level care. • Mortality is 9.4%. • <200 CD4/mL at risk factors for hospitalization as well as severe outcomes (ICU or death).
	• Public sector Western Cape, South Africa • 22,308 COVID-19 cases • 18% of cases in HIV 60% of HIV and COVID-19 with HIV viral load <1000 copies/Ml	Population cohort study	• HIV was associated with standardized mortality ratio 2.39 (95% CI 1.96 to 2.86). • Case fatality in HIV 3.2%. • Increased death in HIV and HIV viral loads >1000 copies/mL and/or <200 CD4 cells/mL. COVID-19 death associated with current or prior tuberculosis.
	• New York City Department of Health • 204,583 cases COVID-19 • 2410 in HIV 88% of HIV hospitalized with HIV viral loads <200 copies/Ml	COVID-19 HIV Registry Match	• 59% of HIV and COVID-19 had ≥1 other comorbidity. • HIV had higher rates of hospitalization, ICU admission and/or death. • Increased ICU admission and death

(Goldman *et al*., 2021)

result of weakened immune system that brought about several complications. Additionally, cancer treatment was observed to have increased their risk of infection. This was seen in 33% of patient with COVID-19. These findings emphasize the susceptibility of cancer patients to severe COVID-19 and the essence of targeted clinical management strategies.

SOT Patients

In Table 4, Solid Organ Transplant (SOT) recipients with COVID-19 exhibited high rates of hospitalization, ICU admission, and mortality, especially among kidney and heart transplant patients. This result, is in accordance with Bartelt., (2022). COVID-19 had great effect on SOT patients. Clinical

Table 3. Summary of Studies of COVID-19 in Patients with Cancer

S/N	Patient Population	Study Design	Active cancer treatment %	Clincal Severity %	COVID-19 Treatment %	Outcome %
1	1524 cancer patients, 12 with COVID-19	Retrospective cohort	42	Hospitalized (100) ICU (8)	Not available	Recovered (50) Died (25)
2.	928 cancer patients with CO VID-19	Registry/ Retrospective cohort	39	Hospitalized (100) ICU (8) Intubated (13)	Antiviral (30)	Died (13)
3	25Hematologic Malignancy with COVID-19	Case series	56	Intubated (24)	Antiviral (20) Immunomodulators (16) Steroids (16)	Died (40)
4	13,077 patients with COVID-19,232 with cancer.	Retrospective cohort	Not available	Hospitalized (10) Intubated (9)	Antiviral (79) Immunomodulators (37)	Died (20)
5	7 Multiple Myeloma patients with COVID-19	Retrospective cohort	Not available	Hospitalized (71) ICU (57) Intubated (14)	Antivirals (43) Tocilizumab (0)	Recovered (43) Died (57)

(Goldman *et al*., 2021)

severity correlated with the need for intubation and intensive care. Antiviral use was common, along with immunosuppressive (IS) reduction and steroids. Mortality rates ranged from 7% to 67%, with worse outcomes in smaller cohorts. These findings underscore the increased predisposition of SOT patients to severe COVID-19 and the importance of individualized clinical management strategies in immunocompromised populations.

COVID-19 Comorbidities

Table 5 shows analysis of COVID-19 Comorbidities with risk factors for death at ten (10) Isolation Centers in Lagos, Nigeria. This study involves 492 patients which have comorbidities such as hypertension, diabetes, renal disease, cancer. Asthma, cardiovascular disease, hepatitis B and HIV. Five major predictors of COVID-19 death with the highest scores and percentage were hypertension (7.36; 95%CL: 4.55=11.89), diabetes (10.67; 95%CL: 6.31-18.07), renal disease 33.28 (33.28; 95%CL: 7.31-15.56), cancer (9.69; 95%CL: 1.85-50.81) and HIV (9.69; 95%CL: 1.85-50.81). Cancer been one of the five predictors as researched by Osibogun, (2022) corroborates the study of Payette and Terry, (2022) that patients with cancer have a twofold higher chance of being infected with COVID-19 compared to the general population. Likewise, HIV patients, who

Table 4. Summary of Studies of COVID-19 in Patients with Solid-Organ Transplant Recipients

S/N	Patient Population	Study Design	Clincal Severity %	COVID-19 Treatment %	Outcome %
1	36 Kidney transplant recipients with COVID-19	case series	Hospitalized (76) Intubated (36)	Antiviral (87) Tocilizumab (7) Reduction (93)	Recovered (53) Died (7)
2.	13 heart transplant recipients with COV ID-19	case series	Hospitalized (100) ICU (46) Intubated (38)	Antiviral (62) Tocilizumab (23) Steroids (62)	Recovered (69) Died (15)
3	13 SOT recipients with COVID-19, 54% liver, 31% kidney and 15% dual.	case series	Intubated (8)	Antiviral (92) Tocilizumab (15) Steroids (23) IS reduction (62)	Died (20)
4	3581 SOT recipients, 23 with COVID-19, 65% kidney, 13% heart, 13 % lung, 4% liver and 4% dual.	Retrospective cohort	Hospitalized (83) ICU (9) Intubated (9)	Antiviral (13) Immunosuppressive medication reduction (43)	Recovered (61) Died (22)
5	2 kidney transplants recipients with COVID-19	Case series	Hospitalized (100) ICU (83) Intubated (75)	Antiviral (100) Steroids (100) IS reduction (100)	Recovered (33) Died (67)

(Goldman *et al*., 2021)

constantly experience CD4+ cell counts that makes them vulnerable to COVID-19 infection according to Jakharia, *et al*. (2022).

Acknowledgements

The authors wish to acknowledge Dr. Josiah U.G for the critical review of the manuscript and for technical assistance.

Conclusion and Recommendations

As of June 11 2025, immunocompromised individuals continue to face significant challenges related to COVID-19, particularly concerning long-term complications, immune system recovery, and the risk of reinfection (Annalisa *et al*., 2023; CDC, 2025). Recent studies indicate that immunocompromised individuals are at an elevated risk for developing long COVID. A multicentric Italian study found a high prevalence of persistent symptoms such as fatigue, cognitive impairment, and respiratory issues among patients with primary immunodeficiency, negatively impacting their quality of life (Muhammed et al., 2020; Annalisa *et al*., 2023). Monitoring strategies include early identification, close follow-up, and administration of additional vaccine doses (CDC, 2025). The Centers for Disease Control and Prevention

Table 5: Analysis of COVID-19 comorbidities as risk factors for death

S/N	Variable/ Comorbidities	Died N= 73	Discharged N=1725	OR (95%CL)	P-Value
1.	Hypertension	40 (14.08%)	244 (85.92%)	7.36 (4.55=11.89)	< 0.001
2	Diabetes	26 (23.42%)	85(76.58%)	10.67 (6.31-18.07)	<0.001
3	Asthma	3 (6.67%)	42(93.33%)	1.72 (0.52-5.68)	0.375
4	Renal disease	4 (57.14%)	3 (42.86%)	33.28 (7.31-15.56)	<0.001
5	Cancer	2 (28.57%)	5 (71.43%)	9.69 (1.85-50.81)	0.007
6	Cardiovascular disease	2 (22.22%)	12(77.78%)	6.91(1.41-33.88)	0.017
7	Hepatitis B	1 (14.29%)	6 (85.71%)	3.98 (0.47-33.49)	0.204
8	HIV	2 (28.57%)	5 (71.43%)	9.69 (1.85-50.81)	0.007

(Osibogun *et al*., 2021)

(CDC) specifically recommends that individuals with moderate to severe immunocompromise receive additional COVID-19 vaccine doses to boost protection (CDC, 2025). This review recommends the following for immunocompromised patients; additional fourth dose and a booster aside the initial three doses of vaccines series. Health care providers are to prioritized immunocompromised patients for quick preventive and therapeutics interventions. COVID-19 protocols should be regularly observed among immunocompromised patients especially when the rules and regulations are being relaxed in some part of the world. Donors as well as possible recipients must be tested for COVID-19 before transplant and the use of Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) should be used to identify active infection as it is the main assay for screening.

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