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Review Article

COVID-19: Diagnostic Methods and Recent Advances in Treatment

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The emergence of SARS-CoV-2 stimulated rapid development of molecular diagnostics, rapid antigen tests, serological assays, imaging approaches and emerging point-of-care technologies. Accurate diagnosis supports clinical management, infection-control decisions, surveillance and timely identification of patients who may benefit from antiviral therapy. Nucleic-acid amplification tests, particularly reverse transcription polymerase chain reaction (RT-PCR), remain important laboratory methods for detecting viral RNA, while rapid antigen tests provide faster results and are useful for point-of-care and self-testing. Serological assays detect host antibodies and have more limited roles in early diagnosis. Newer approaches include reverse transcription loop-mediated isothermal amplification (RT-LAMP), CRISPR-based detection, biosensors, microfluidic platforms and multiplex respiratory pathogen assays. Treatment has evolved from predominantly supportive care toward risk- and severity-based management. Antiviral therapy is most relevant during the early viral-replication phase in patients at increased risk of progression, while corticosteroids and selected immunomodulators are used mainly in appropriately selected patients with severe or critical disease. Nirmatrelvir/ritonavir and remdesivir are important antiviral options in current clinical guidance, whereas molnupiravir has a more restricted role. Supportive respiratory care, oxygen therapy and management of complications remain essential. This review summarizes established and emerging diagnostic methods, current therapeutic strategies, limitations, and future directions in COVID-19 management.

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INTRODUCTION

COVID-19 is caused by SARS-CoV-2, an enveloped, positive-sense single-stranded RNA virus belonging to the family Coronaviridae. The infection primarily involves the respiratory tract but may affect multiple organ systems. Clinical presentation ranges from asymptomatic infection and mild upper-respiratory symptoms to pneumonia, hypoxemic respiratory failure, thrombo-inflammatory complications and multi-organ dysfunction.

The COVID-19 pandemic accelerated diagnostic innovation. Early diagnosis depended largely on molecular detection of viral RNA. Subsequently, rapid antigen tests, antibody assays, isothermal amplification, CRISPR-based detection, biosensors and integrated point-of-care platforms expanded the available diagnostic landscape. The appropriate test depends on the clinical question, timing of illness, specimen quality, test performance and availability.

Therapeutic strategies have also changed with accumulating clinical evidence. Early treatment of selected high-risk patients focuses on inhibiting viral replication, while severe disease may require oxygen, corticosteroids and selected immunomodulatory therapy. Therefore, diagnosis and treatment should be integrated with assessment of disease severity and risk of progression.

SARS-CoV-2: Structure and Important Components

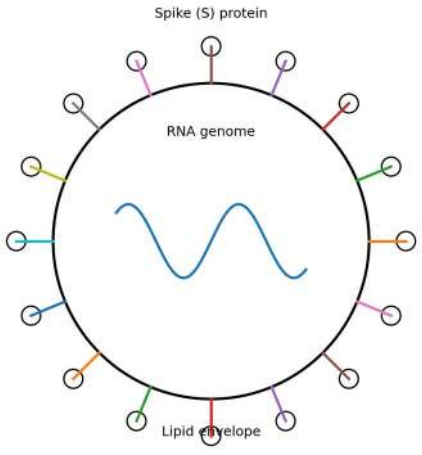


Figure 1: ***Schematic structure of SARS-CoV-2***

SARS-CoV-2 is an enveloped RNA virus. Its structural proteins include spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins. The spike protein is involved in attachment and entry into host cells. The nucleocapsid protein associates with the viral RNA genome. These structural components are also important targets for diagnostic assays and research.

Pathogenesis of COVID-19

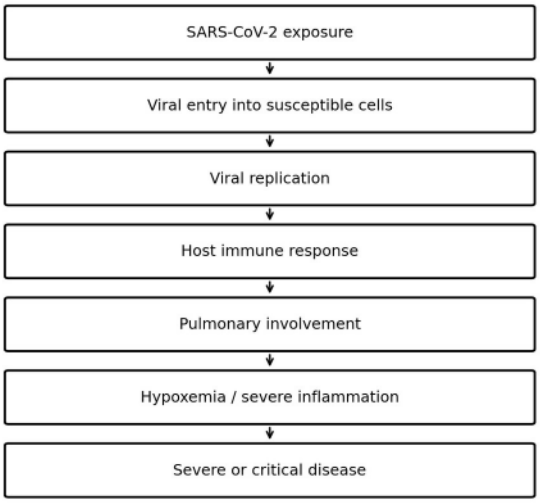


Figure 2: ***Pathogenesis of COVID-19***

After exposure, SARS-CoV-2 reaches susceptible respiratory cells and initiates viral entry and replication. The host immune response contributes to viral clearance, but excessive inflammation in some patients can produce pulmonary injury and systemic complications. Disease severity is heterogeneous and is influenced by host factors, underlying conditions, immune status and other clinical variables.

Clinical Manifestations

Common clinical manifestations include fever, cough, sore throat, fatigue, headache, myalgia, nasal symptoms and altered smell or taste. More severe disease may involve pneumonia, hypoxemia, acute respiratory distress syndrome, thrombo-inflammatory complications, acute kidney injury and cardiovascular or multi-organ complications.

- Mild or asymptomatic infection
- Upper respiratory tract symptoms
- Lower respiratory tract infection and pneumonia

- Hypoxemia and respiratory failure
- Systemic or multiorgan complications

Diagnostic Methods

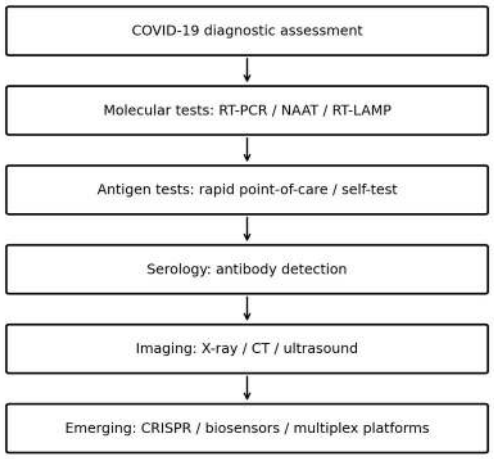


Figure 3: ***Classification of Covid-19 Diagnostic method***

COVID-19 diagnostic methods can be broadly classified into direct detection of viral components, detection of host immune responses, and clinical/imaging assessment. Direct viral detection includes nucleic-acid amplification tests and antigen tests. Serology detects antibodies generated after infection or vaccination. Imaging assists assessment of pulmonary involvement but is not a specific replacement for laboratory confirmation.

Molecular Diagnostic Methods

1. Reverse Transcription Polymerase Chain Reaction (RT-PCR)

RT-PCR is a nucleic-acid amplification method widely used for laboratory detection of SARS-CoV-2 RNA. Because the viral genome is RNA, reverse transcription first generates complementary DNA, followed by amplification of selected target sequences. Fluorescence generated during amplification is measured by the instrument and interpreted according to the validated assay algorithm.

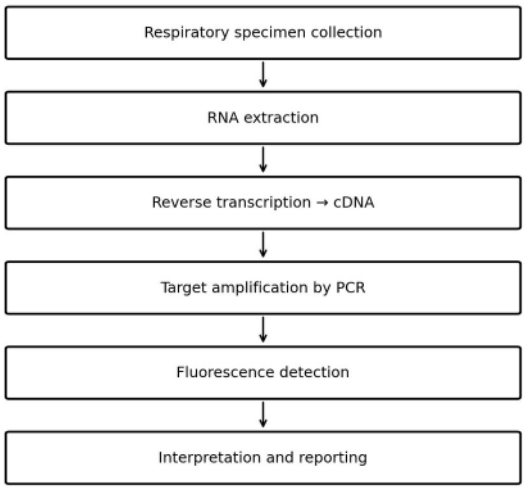


Figure 4: ***General RT-PCR Diagnostic workflow***

Advantages

- High analytical sensitivity and specificity when appropriately designed and validated
- Useful for laboratory confirmation and surveillance
- Can detect viral RNA when viral antigen levels are relatively low

Limitations

- Requires appropriate laboratory equipment and trained personnel
- Turnaround time may be longer than rapid antigen testing
- Results can be affected by specimen quality, timing and assay design

2. RT-LAMP

Reverse transcription loop-mediated isothermal amplification (RT-LAMP) amplifies nucleic acid under near-constant temperature conditions and therefore does not require conventional thermal cycling. The method has been investigated for rapid and decentralized SARS-CoV-2 detection. Depending on assay design, amplification can be monitored by fluorescence, turbidity or color change.

- Rapid amplification
- Potential for portable and point-of-care platforms

- Reduced dependence on conventional thermocyclers
- Requires careful primer design and assay validation

Rapid Antigen Testing

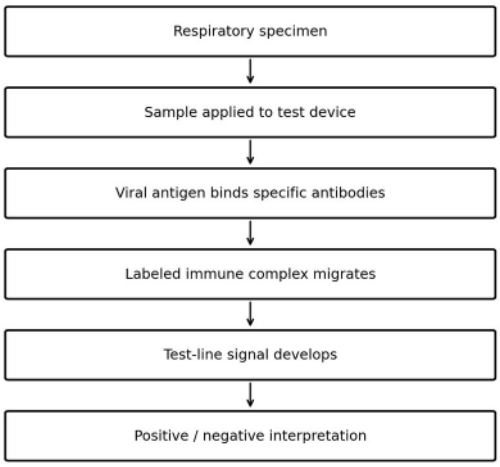


Figure 5: ***Principal of rapid antigen testing***

Rapid antigen tests detect viral proteins, commonly nucleocapsid antigen, in respiratory specimens. They can provide results quickly and are useful for point-of-care testing and self-testing. Compared with molecular assays, antigen tests generally have lower analytical sensitivity, particularly when viral antigen concentration is low. A negative result should therefore be interpreted in the context of symptoms, exposure, timing and applicable testing guidance.

Advantages

- Rapid results
- Simple workflow
- Useful in community and point-of-care settings
- Can support repeated testing strategies

Limitations

- Lower sensitivity than many molecular tests
- Performance depends on specimen quality and timing
- A negative result may not exclude infection when clinical suspicion remains high

Serological / Antibody Testing

Serological tests detect antibodies generated by the host following infection or vaccination. Common targets include IgG, IgM or total antibody responses. Because antibody production takes time, serology is generally not the preferred method for detecting very early acute infection. It can be useful in selected epidemiological studies, seroprevalence investigations and other defined clinical or research questions.

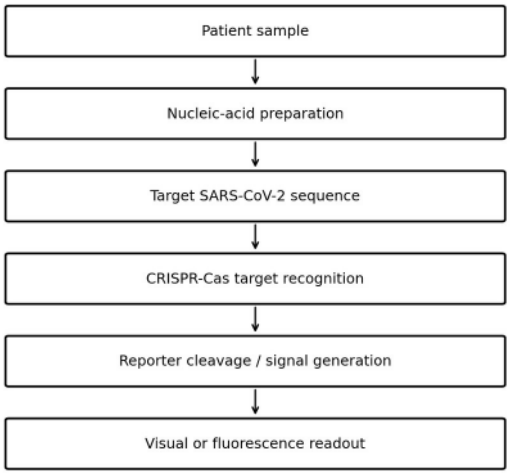
- Antibody detection after immune response develops
- Useful for epidemiological and seroprevalence studies
- Interpretation may be complicated by vaccination and previous infection

Imaging Methods

Chest radiography, computed tomography (CT) and lung ultrasound may support assessment of respiratory involvement in selected patients. Imaging findings are not specific to SARS-CoV-2 and should be interpreted together with clinical findings and laboratory testing.

- Chest X-ray: accessible assessment of pulmonary abnormalities
- CT: detailed evaluation of lung involvement in selected clinical situations
- Lung ultrasound: bedside assessment in appropriate settings

CRISPR-Based Diagnostic Methods



CRISPR-based diagnostic systems use sequence-specific recognition by CRISPR-associated enzymes to identify target nucleic-acid sequences. When a target is recognized, collateral reporter cleavage or another signal-generation mechanism can produce a detectable output. These approaches are being investigated for rapid, specific and portable molecular diagnostics.

Fig no 6 simplified CRISPR- based detection work-flow

Biosensors and Emerging Diagnostic Platforms

Biosensor-based approaches have been explored for detecting viral proteins or nucleic acids using optical, electrochemical and nanomaterial-assisted mechanisms. Microfluidic devices can combine sample preparation, amplification and detection in compact formats. Multiplex respiratory panels can detect SARS-CoV-2 together with other respiratory pathogens, which may be useful when clinical symptoms overlap.

- Electrochemical biosensors
- Optical biosensors
- Nanomaterial-assisted sensors
- Microfluidic diagnostic systems
- Multiplex respiratory pathogen assays
- Portable and smartphone-assisted platforms

Comparison of Major Diagnostic Methods

Method	Primary target	Speed	Major use	Important limitation
RT-PCR	Viral RNA	Moderate	Laboratory diagnosis	Laboratory infrastructure
RT-LAMP	Viral nucleic acid	Rapid	Point-of-care molecular testing	Assay optimization/validation
Rapid antigen	Viral protein	Very rapid	Point-of-care/self-testing	Lower sensitivity
Serology	Host antibodies	Rapid–moderate	Selected immune/epidemiological studies	Limited value in early acute infection
CT/X-ray	Pulmonary abnormalities	Rapid	Assessment of lung involvement	Not specific for COVID-19
CRPR	Viral nucleic acid	Rapid potential	Emerging molecular diagnostics	Platform validation and availability

Recent Advances in Treatment

COVID-19 treatment should be individualized according to disease severity, risk factors, timing of illness, contraindications, drug interactions and organ function. Current clinical guidance broadly separates early antiviral therapy for selected patients at increased risk of progression from anti-inflammatory treatment for appropriately selected patients with severe or critical disease.

Nirmatrelvir/Ritonavir



Figure 7: ***Nirmatrelvir/Ritonavir drug***

Nirmatrelvir inhibits the SARS-CoV-2 main protease, thereby interfering with processing of viral

polyproteins required for replication. Ritonavir inhibits CYP3A-mediated metabolism and increases nirmatrelvir exposure. It is an important oral antiviral option for selected nonhospitalized adults at increased risk of progression when started within the recommended treatment window. Drug–drug interactions are a major practical consideration.

- Oral administration
- Targets viral protease activity
- Most relevant early in disease in eligible high-risk patients
- Requires careful review of concomitant medicines and contraindications

Remdesivir

Remdesivir is a nucleotide analogue prodrug that is metabolized intracellularly to an active nucleotide analogue. It interferes with viral RNA synthesis through interaction with the SARS-CoV-2 RNA-dependent RNA polymerase. It is used in selected patients according to disease severity and current clinical guidance.

- Antiviral mechanism directed at viral RNA synthesis
- Intravenous administration
- Useful in selected early disease and selected hospitalized patients



Figure 8: ***Remdesivir Injection***

- *Requires clinical assessment and appropriate administration setting*

Molnupiravir



Figure 9: ***Molnupiravir tablet***

Molnupiravir is an oral nucleoside analogue that introduces replication errors into viral RNA. Its clinical role is more restricted than preferred antiviral options and depends on patient-specific circumstances, availability, contraindications and current guidelines. Reproductive and other safety ***considerations must be reviewed before use.***

Corticosteroids



Figure 10: ***Corticosteroids medication***

Corticosteroids, particularly dexamethasone in appropriate settings, reduce excessive inflammatory responses and are important in severe COVID-19 associated with oxygen requirement. They are not routinely beneficial for patients with mild disease who do not require supplemental oxygen, and inappropriate use may expose patients to unnecessary adverse effects.

Immunomodulatory Therapy

In selected patients with severe or critical disease, excessive inflammation may contribute to organ injury. Immunomodulatory agents such as interleukin-6 pathway inhibitors and Janus kinase inhibitors have been studied and are recommended in specific clinical

circumstances by contemporary guidelines. Their use depends on disease severity, inflammatory status, timing, concomitant corticosteroid treatment and contraindications.

- Tocilizumab
- Sarilumab
- Baricitinib
- Other selected immunomodulatory strategies under guideline-defined conditions

Oxygen and Supportive Management

Supportive care remains fundamental. Patients with hypoxemia may require supplemental oxygen and escalation to non-invasive or invasive respiratory support depending on clinical status. Additional management may include fluid and electrolyte care, fever control, nutritional support, monitoring for thrombotic and organ complications, and treatment of secondary complications when present.

Treatment by Disease Severity

Clinical category	General approach	Examples of treatment considerations
Asymptomatic / mild, low risk	Supportive care and monitoring	Symptom management; no routine antiviral for low-risk patients
Mild–moderate, increased risk	Early antiviral assessment	Nirmatrelvir/ritonavir or remdesivir when appropriate; alternatives in selected circumstances
Severe with hypoxemia	Respiratory and anti-inflammatory management	Oxygen; corticosteroid-based therapy; selected additional immunomodulation
Critical disease	Intensive supportive care	Advanced respiratory support and guideline-directed anti-inflammatory/ organ-supportive management

Vaccination and Prevention

Vaccination remains an important strategy for reducing the risk of severe COVID-19. Preventive measures can also include appropriate ventilation, respiratory hygiene, staying home while acutely ill, testing when indicated, and protecting individuals at increased risk. Recommendations vary according to age, risk group, vaccine availability and national guidance.

Recent Advances in Diagnostic Technology

- CRISPR-based point-of-care molecular detection
- Portable and microfluidic diagnostic platforms
- Multiplex respiratory pathogen assays
- Electrochemical and optical biosensors
- AI-assisted imaging and clinical decision support
- Improved home and decentralized testing technologies

Recent Advances in Therapeutic Research

- Broad-spectrum antiviral development
- New viral protease and polymerase inhibitors
- Combination antiviral strategies
- Long-acting antiviral formulations
- Host-directed therapies
- Improved immunomodulatory strategies
- Research into post-acute COVID-19 conditions
- Variant-resilient therapeutic targets

Challenges

- Continued viral evolution and emergence of new variants
- Differences in diagnostic sensitivity between platforms
- Specimen collection and timing effects
- Antiviral drug interactions and contraindications
- Potential antiviral resistance
- Unequal access to advanced diagnostics and treatment
- Need for continuous guideline updates
- Limited evidence for some emerging technologies

Future Perspectives

Future COVID-19 management is likely to emphasize rapid decentralized diagnostics, multiplex respiratory testing, broad-spectrum antivirals, precision risk assessment and integrated digital health technologies. CRISPR diagnostics, biosensors and microfluidics may shorten the time from sampling to result. Therapeutic research is increasingly directed toward targets that are conserved across viral variants and toward combinations that may reduce the risk of resistance.

- Rapid molecular point-of-care testing
- Variant-resilient and broad-spectrum antivirals
- Multiplex pathogen detection
- AI-supported clinical and imaging assessment
- Personalized risk-based treatment
- Long-acting and easier-to-administer therapies

CONCLUSION

COVID-19 has driven major advances in both diagnostic science and therapeutics. RT-PCR remains an important molecular method, while rapid antigen testing offers speed and convenience for point-of-care and self-testing. RT-LAMP, CRISPR-based methods, biosensors, microfluidic systems and multiplex assays represent important areas of continuing development. Treatment has progressed toward severity- and risk-based care, with early antiviral therapy for selected high-risk patients and anti-inflammatory or immunomodulatory treatment for appropriately selected severe disease. Continued surveillance, diagnostic innovation, evidence-based prescribing and regular updating of clinical guidance are essential for effective management of COVID-19.

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