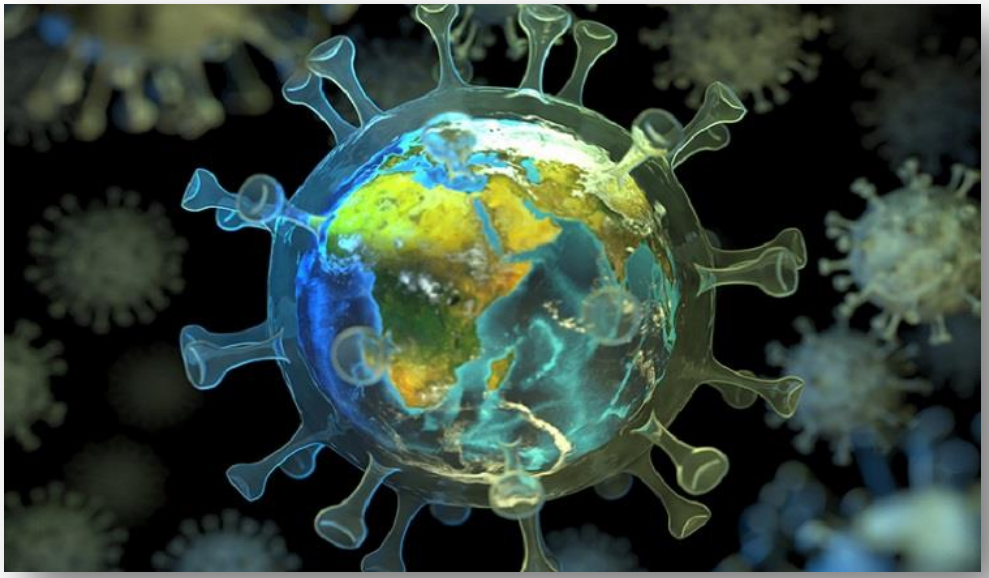
بسم الله الرحمن الرحیم

MANAGMENT

Elaheh seidaie MD

Assictant professor of SH.K university of medicine

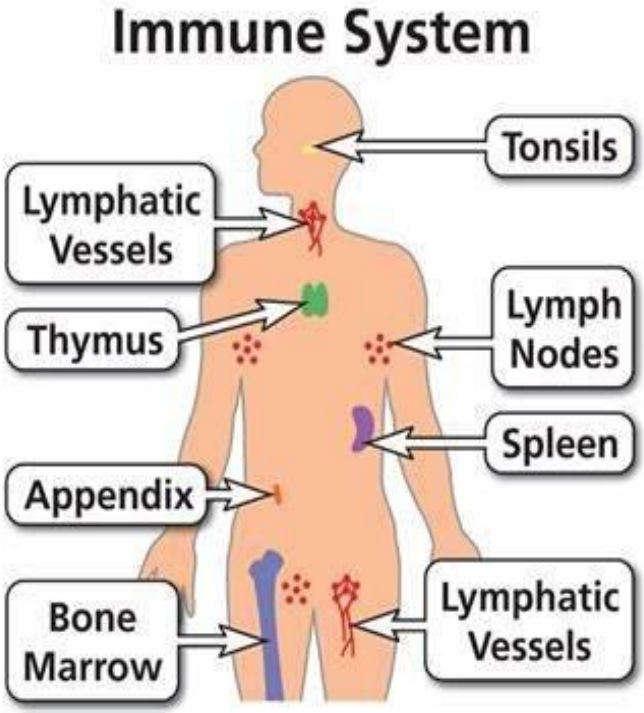
- Omicron multiplies faster in airways , slower in lungs.



- Compared to the r Delta variant, Omicron multiplies itself 70 times more quickly in tissues that line airway passages, which may facilitate person-to-person spread.

- In lung tissues, Omicron replicates 10 times more slowly than the original version of the coronavirus.

- severity of disease in humans is not determined only by virus replication" but also by each person's immune response to the infection.

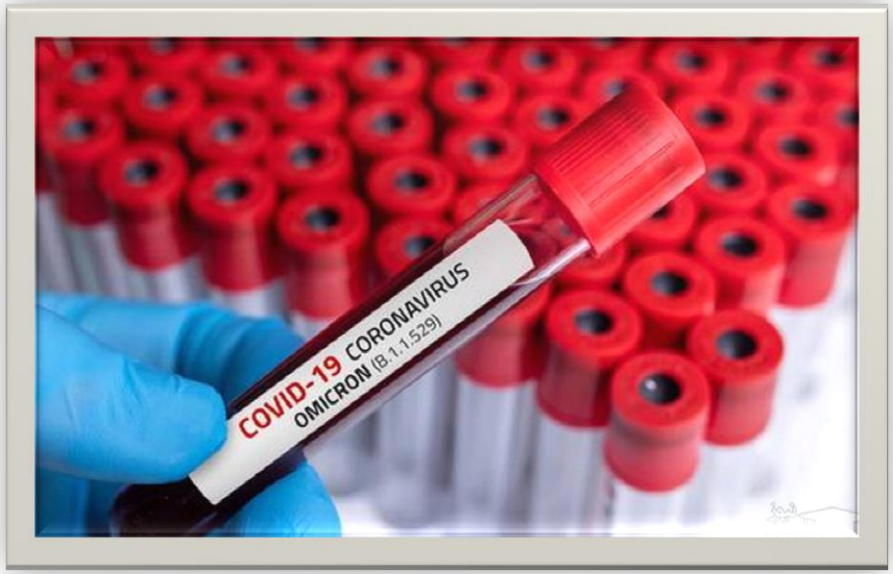


- By infecting many more people, a very infectious virus may cause more severe disease and death even though the virus itself may be less pathogenic.

- The pooled percentage of asymptomatic infections was about 46% in North America, 44% in Europe and 28% in Asia.

- "The high percentage of asymptomatic infections highlights the potential transmission risk of asymptomatic infections in communities.

- This analysis found no clear difference in the symptom profile of Delta and Omicron.



Clinical Spectrum of SARS-CoV-2 Infection

- ***Asymptomatic or Presymptomatic Infection:***

- Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., [NAAT] or an antigen test).
- who have no symptoms that are consistent with COVID-19.

❑*Mild Illness:*

- Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, malaise, headache, muscle pain, nausea, vomiting, diarrhea;runny nose; fatigue; sneezing; sore throat, seen loss of smell and taste become much less.

- No imaging or specific laboratory evaluations are routinely indicated in otherwise healthy patients with mild COVID-19.

- Older patients and those with underlying comorbidities are at higher risk of disease progression;

- Therapeutic Management of Nonhospitalized Adults With COVID-19 for recommendations regarding SARS-CoV-2-specific therapy.

❑*Moderate Illness*:

- Individuals who show evidence of lower respiratory disease during clinical assessment or imaging.

- Who have an oxygen saturation (SpO_2) ≥ 94% on room air at sea level.

- Therapeutic Management of Nonhospitalized Adults With COVID-19 for recommendations regarding SARS-CoV-2-specific therapy.

❑*Severe Illness:*

- Individuals who have SpO_2 <94% on room air
- A respiratory rate >30 breaths/min
- Lung infiltrates >50%

❑ *Critical Illness:*

- Individuals who have respiratory failure
- Septic shock, and/or multiple organ dysfunction

❑These comorbidities :

aged ≥65 years; cardiovascular disease, chronic lung disease, sickle cell disease, diabetes, cancer, obesity, or chronic kidney disease; pregnancy; smoker; transplant recipient; immunosuppressive therapy

- Oxygen supplementation is recommended for pregnant patients when SpO_2 falls below 95% on room air.

Infectious Complications

- The use of immunomodulators such as dexamethasone, tocilizumab, sarilumab, or., baricitinib, tofacitinibto treat COVID-19 may also be a risk factor for infectious complications.

- ***Coinfections at Presentation With COVID-19:***

including influenza and other respiratory viruses

- ***Community-acquired bacterial pneumonia***:
  Antibacterial therapy is not recommended unless additional evidence for bacterial pneumonia is present

❑ *Reactivation of Latent Infections:*

- underlying chronic hepatitis B virus
- latent tuberculosis infections
- herpes simplex virus infections
- varicella zoster virus infections

❑Nosocomial Infections:

- hospital-acquired pneumonia (including ventilator-associated pneumonia)
- catheter-associated urinary tract infection
- Clostridioides difficile-associated diarrhea

- **Opportunistic Fungal Infections:**
  - fungal infections, including aspergillosis and mucormycosis.

- **SARS-CoV-2 Reinfection**
- **Fatigue**
- **Cardiopulmonary**
- **Neuropsychiatric**

Treatment for High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19

- Multiple therapeutic agents are now available for nonhospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression.

- **Ritonavir-Boosted Nirmatrelvir (Paxlovid)**
- **Sotrovimab**
- **Remdesivir**
- **Molnupiravir**

Ritonavir-Boosted Nirmatrelvir (Paxlovid)

- Nirmatrelvir (PF-07321332) is an orally bioavailable protease inhibitor.

- Ritonavir is required to increase nirmatrelvir concentrations

Paxlovid

- Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid) orally twice daily for 5 days

- initiated as soon as possible Rand within 5 days of symptom onset in those aged ≥12 years and weighing ≥40)

- (Paxlovid) is not recommended in patients with an eGFR of <30 mL/min until more data are available .
- (Paxlovid) is not recommended in patients with severe hepatic impairment (i.e., Child-Pugh Class C.
- The most common adverse effects of (Paxlovid) are dysgeusia, diarrhea, hypertension, and myalgia.

Molnupiravir

- Molnupiravir is the oral prodrug of beta-D-N4-hydroxycytidine (NHC), a ribonucleoside that has broad antiviral activity against RNA viruses.

Molnupiravir

- As a mutagenic ribonucleoside antiviral agent, there is a theoretical risk that molnupiravir will be metabolized by the human host cell and incorporated into the host DNA, leading to mutations. The FDA concluded that, based on the available genotoxicity data and the 5-day duration of treatment.

Molnupiravir

- Molnupiravir 800 mg orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥18 years ONLY when none of the above options can be used.

Molnupiravir

- molnupiravir is not recommended for use in pregnant patients due to concerns about the instances of fetal toxicity observed during animal studies.

Molnupiravir

- Molnupiravir is expected to be active against the Omicron VOC, although in vitro and in vivo data are currently limited.

Molnupiravir

- Patients should complete the 5-day treatment course of molnupiravir.

- It is unknown whether a shorter course is less effective or associated with the emergence of molnupiravir-resistant mutations.

Molnupiravir

- Patients of childbearing potential should be counseled about abstaining from sex or using reliable contraception for the duration of therapy and for up to 4 days after receiving molnupiravir.

Molnupiravir

- Men of reproductive potential who are sexually active with individuals of childbearing potential should abstain from sex or use a reliable method of contraception for the duration of treatment and for at least 3 months after the last dose of molnupiravir.

Molnupiravir

- Recommendation is to avoid feeding an infant breast milk during molnupiravir treatment and for 4 days after the final dose.

- Pumping and discarding breast milk to maintain supply during this time is recommended.

Molnupiravir

- Molnupiravir is not for use in children aged <18 years due to potential effects on bone and cartilage growth.

- The most common adverse effects of molnupiravir are diarrhea, nausea, and dizziness.

Molnupiravir

- These anti-SARS-CoV-2 therapeutics, which were evaluated initially in unvaccinated individuals, provide the greatest benefit for nonhospitalized patients who have risk factors for progression to severe COVID-19.

Molnupiravir

- The risks for progression are substantially higher for those who are not vaccinated or those who are vaccinated but who are not expected to mount an adequate immune response to the vaccine.

monoclonal antibodies

- Prior to mid-December 2021, the anti-SARS-CoV-2 monoclonal antibodies (mAbs) bamlanivimab plus etesevimab, casirivimab plus imdevimab, and sotrovimab were the only therapies recommended by the Panel for nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe diseas.

- The Omicron VOC has become the dominant variant in the United States and is predicted to have markedly reduced susceptibility to bamlanivimab plus etesevimab and casirivimab plus imdevimab.

- In vitro studies indicate that sotrovimab remains active against the Omicron VOC.

Sotrovimab

- Sotrovimab 500 mg as a single IV infusion, administered within 10 days of symptom onset in those aged ≥12 years and weighing ≥40 kg.

- Sotrovimab should be administered in a setting where severe hypersensitivity reactions, such as anaphylaxis, can be managed.

Remdesivir

- Remdesivir 200 mg IV on Day 1, followed by remdesivir 100 mg IV daily on Days 2 and 3.

- Initiated as soon as possible and within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg.

- The Panel favors the use of ritonavir-boosted nirmatrelvir (Paxlovid) in most high-risk, nonhospitalized patients with mild to moderate COVID-19.

- If ritonavir-boosted nirmatrelvir (Paxlovid) is not available or cannot be used because of drug interactions, then the Panel recommends using sotrovimab.

- If sotrovimab is not available, then the Panel recommends using remdesivir.

- Molnupiravir should only be administered when the other 3 options are either not available or cannot be used.

Therapeutic Management of Hospitalized Adults With COVID-19

Remdesivir

- RDV 200 mg IV once, then RDV 100 mg IV once daily for 4 days or until hospital discharge.

Dexamethasone

- 6 mg IV or PO once daily for up to 10 days or until hospital discharge.

Baricitinib

- eGFR ≥60: Baricitinib 4 mg PO once daily for up to 14 days or until hospital discharge
- eGFR 30 to <60: Baricitinib 2 mg PO once daily
- eGFR 15 to <30: Baricitinib 1 mg PO once daily
- eGFR <15: is not recommended

Tofacitinib

- Tofacitinib 10 mg PO twice daily for up to 14 days or until hospital discharge.

- Use as an alternative immunomodulatory drug if baricitinib is not available or not feasible to use

- eGFR <60 : Tofacitinib 5 mg PO twice daily

Tocilizumab

- Tocilizumab 8 mg/kg actual body weight (up to 800 mg) administered as a single IV dose.

- In clinical trials, a third of the participants received a second dose of tocilizumab 8 hours after the first dose if no clinical improvement was observed.

Sarilumab

- Use the single-dose for SQ injection.
- Reconstitute sarilumab 400 mg in 100 cc 0.9% NaCl and administer as an IV infusion over 1h.
- Use as an alternative immunomodulatory drug if tocilizumab is not available or not feasible to use.

Patients Who Do Not Require Supplemental O2

- Recommends against the use of corticosteroids for the treatment.

- Remdesivir for the treatment of COVID-19 in hospitalized patients who do not require supplemental oxygen, may be appropriate in patients at high risk of disease progression.

Patients who require supplemental oxygen, but not high-flow oxygen, noninvasive ventilation (NIV), or mechanical ventilation

- Remdesivir
- Dexamethasone plus remdesivir
- Dexamethasone; for patients on dexamethasone who have rapidly increasing oxygen needs and systemic inflammation, add a second immunomodulatory drug (e.g., tocilizumab or baricitinib

- this clinical benefit of remdesivir was most evident in those who had symptoms for ≤10 d.

- The Panel recommends remdesivir (without dexamethasone) in the early course of the disease.

- Rationale for the use of Remdesivir Plus Dexamethasone

- The potent anti-inflammatory effects of corticosteroids might prevent or mitigate these hyperinflammatory effects.

- Some experts prefer not to use dexamethasone monotherapy in patients who require supplemental oxygen because that corticosteroids might slow viral clearance when administered without an antiviral drug.

- Randomized trials evaluating the use of IL-6 inhibitors or JAK inhibitors in patients have included patients who required only low-flow O2 such as baricitinib or tocilizumab, to dexamethasone treatment with rapidly increasing oxygen requirements and elevated markers of systemic .

- Baricitinib or tocilizumab should only be given in combination with corticosteroid.

- If baricitinib and tocilizumab are not available, tofacitinib can be used instead of baricitinib and sarilumab can be used instead of tocilizumab.

- The Panel recommends against the use of baricitinib in combination with tocilizumab.

Patients Who Require Oxygen Through a High-Flow Device or Noninvasive Ventilation

- Dexamethasone
- Dexamethasone plus remdesivir

- Patients who have rapidly increasing oxygen needs and have increased markers of inflammation, add either baricitinib or tocilizumab

- Patients who start remdesivir monotherapy and then progress to requiring oxygen through a high-flow device or NIV, recommends continuing remdesivir until the treatment course is completed.

- The evidence of efficacy for tocilizumab is more extensive than for sarilumab.

Patients Who Require Mechanical Ventilation or Extracorporeal Membrane Oxygenation

- Dexamethasone
- Dexamethasone plus tocilizumab for patients with COVID-19 who are within 24 hours of admission to the ICU
- Against the initiation of remdesivir monotherapy
- If tocilizumab are not available sarilumab can be used instead of tocilizumab

- Recommending the Use of Tocilizumab Plus Dexamethasone in Patients Within 24 Hours of Admission to the Intensive Care Unit

- it is unclear whether there is a clinical benefit for tocilizumab in patients who received mechanical ventilation for >24 hours.

Thanks for your attention