Oral Antibiotics in Hospitalized COVID-19 Patients

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National Protocol

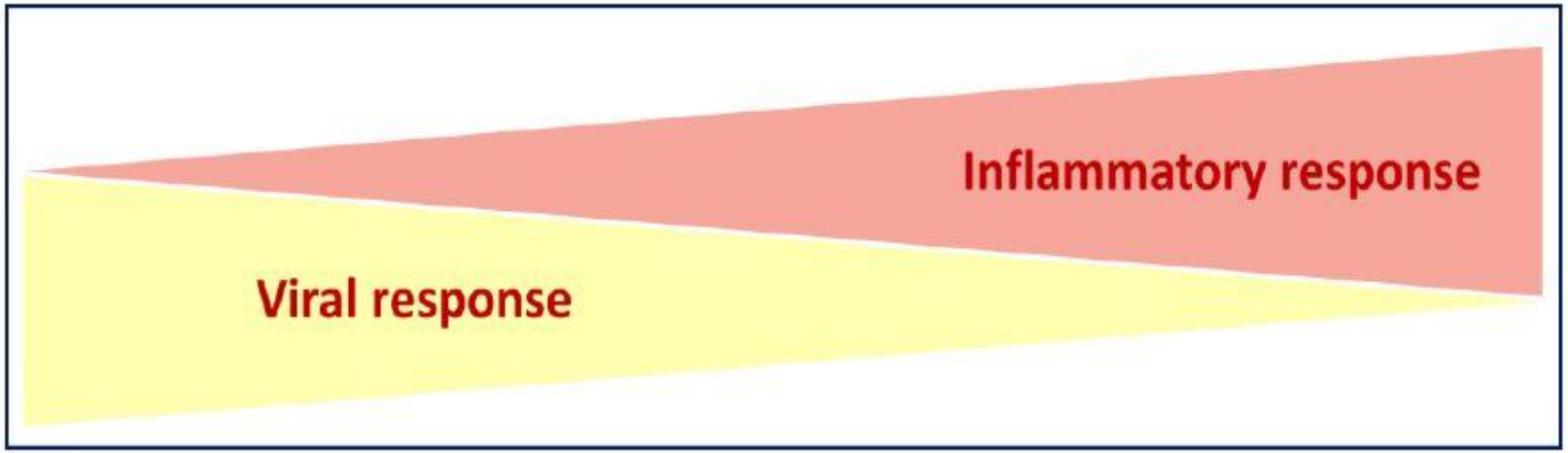
Disease course:

0 stage:
Asymptomatic or before the symptom onset

First stage:
Early infection

Second Stage:
Respiratory phase

Third stage:
Hyper inflammation



National Protocol

- **0 stage**
  - Diagnosis only with RT-PCR
  - Possible symptom development in future
- **First stage**
  - Mild symptoms
  - Various symptoms
  - Stable vital sign
  - Spo2≥93%

National Protocol

- **Second stage:** Respiratory phase

Moderate respiratory phase → Chest tightness, shortness of breath, ± Fever ≥38° c

Spo2≥90-93%

Severe respiratory phase → Chest symptoms exacerbation

Tachypnea, shortness of breath

PaO2/FiO2≤300mmhg, SpO2 <90%

CT scan More than 50% lung involvement

National Protocol

- **Third stage: Hyper inflammation**

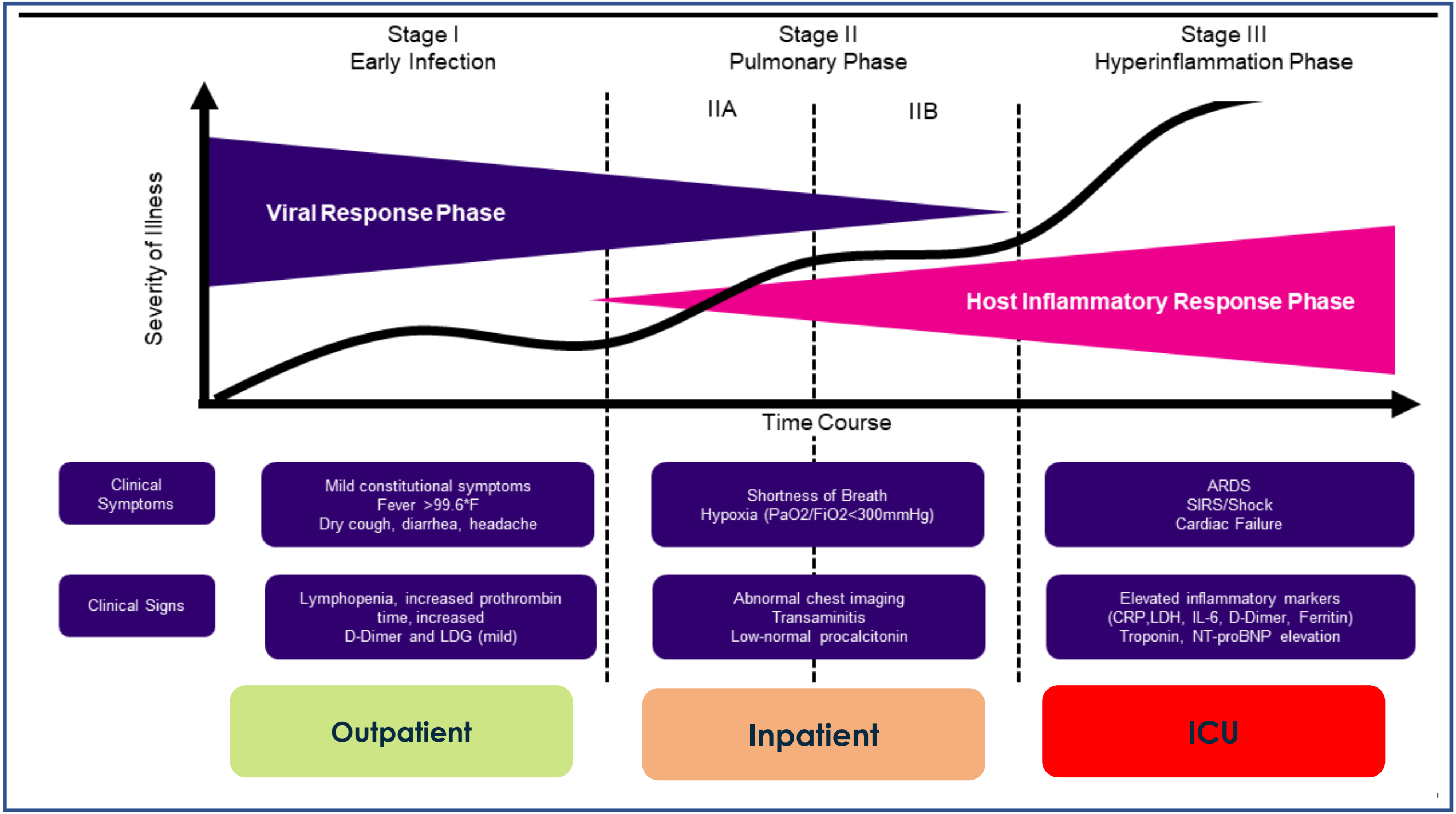
  Patient need ICU

  Symptoms of respiratory failure, $SpO_2 \leq 88\%$ despite Oxygen therapy

  Shock symptoms

  Need for mechanical ventilation

  Multi-organ Failure


Stage I
Early Infection
Stage II
Pulmonary Phase
Stage III
Hyperinflammation Phase
IIA
IIB
Severity of Illness
Viral Response Phase
Host Inflammatory Response Phase
Time Course
Clinical Symptoms
Mild constitutional symptoms
Fever >99.6*F
Dry cough, diarrhea, headache
Shortness of Breath
Hypoxia (PaO2/FiO2<300mmHg)
ARDS
SIRS/Shock
Cardiac Failure
Clinical Signs
Lymphopenia, increased prothrombin time, increased
D-Dimer and LDG (mild)
Abnormal chest imaging
Transaminitis
Low-normal procalcitonin
Elevated inflammatory markers
(CRP,LDH, IL-6, D-Dimer, Ferritin)
Troponin, NT-proBNP elevation
Outpatient
Inpatient
ICU

National Protocol

- **Criteria for inpatient treatment**
  - Shortness of breath
  - SpO2 < 93%
  - RR > 30 ± Fever

} Might be SARI

National Protocol

- **Criteria for inpatient treatment**

High risk patient with immunodeficiency

transplant, malignancies or under chemotherapy and Corticosteroids

- No Shortness of breath
- Clinical suspicion for COVID-19
- Even if the patient has no fever

✓**Chest imaging should be performed.**

National Protocol

- **Criteria for inpatient treatment**

High risk patient with comorbidities

HTN, Uncontrolled Diabetes, Cardiovascular disease, BMI > 40, underlying Chronic Respiratory disease, CKD

- Fever ≥ 37.8◦ C

✓ **Chest imaging should be performed.**

National Protocol

- Antibiotic therapy
  - Based on patient clinical condition
  - Possibility of superinfection
  - Based on Antibiogram and culture results
  - And **Resistance Pattern** of the region

Azithromycin is omitted from the national protocol of COVID-19

Management in hospitalized adults

- **Empiric treatment for bacterial pneumonia**
  - Do not routinely administer empiric therapy for bacterial pneumonia
  - **bacterial superinfection** does not appear to be a prominent feature of COVID-19
  - The clinical features of COVID-19 may be difficult to distinguish from bacterial pneumonia, empiric treatment for community-acquired pneumonia is **reasonable** when the diagnosis is uncertain.
  - Empiric treatment for **bacterial pneumonia** may also be reasonable in patients with documented COVID-19 if there is **clinical suspicion** for it (eg, new fever after defervescence with new consolidation on chest imaging).

Management in hospitalized adults

- **If empiric antibiotic therapy is initiated:**
  - Try to make a microbial diagnosis (e.g., through sputum Gram stain and culture, urinary antigen testing)
  - Reevaluate the need to continue antibiotic therapy daily
  - A low procalcitonin may be helpful to suggest against a bacterial pneumonia;
  - However, elevated procalcitonin has been described in COVID-19, particularly late in the course of illness, and does not necessarily indicate bacterial infection

Common etiology of Community-acquired Pneumonia

Patient type	Etiology
Outpatient	S.pneumoniae Mycoplasma Pneumonia H. Influenzae Clamydophila Pneumonia Respiratory Viruses
Inpatient (non-ICU)	S. pneumoniae M. pneumoniae C. pneumoniae H. Influenzae Legionella Species Aspiration Respiratory Viruses
Inpatient (ICU)	S. pneumoniae Staphylococcus aureus Legionella Species Gram-negative bacilli H. Influenzae

Recommended Antibiotic treatment for Community-acquired pneumonia

Outpatient			Inpatient (non-ICU)	Inpatient (ICU)
1.Previously healthy and no use of AB within 3 months	2.presence of comorbidities or use of antimicrobials within the previous 3 months.	3. in regions with high rate (>25%) with high level (MIC≥16mcg/mL) macrolide-resistant S.pneumoniae for patients without comorbidities		
Macrolide	Respiratory fluoroquinolones	Respiratory fluoroquinolones	**Respiratory fluoroquinolones**	a β-lactam + a azithromycin a β-lactam + a Respiratory flouroquinolones
doxycycline	a β-lactam + a macrolide	a β-lactam + a macrolide	a β-lactam + a macrolide	

Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19

- Published in 23 July 2020
- a multicenter, randomized, open-label, three-group, controlled trial
- 504 confirmed cases of COVID-19 were included
- Group A: standard care plus HCQ at a dose of 400 mg twice daily

  Group B: standard care plus HCQ at a dose of 400 mg twice daily plus AZT at a dose of 500 mg once daily for 7 days
- Among patients hospitalized **with mild-to-moderate Covid-19**, the use of hydroxychloroquine, alone or with azithromycin, **did not improve clinical status** at 15 days as compared with standard care.

Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19

- Multi-center retrospective observational study.
- Consecutive patients hospitalized with a COVID-related admission in the health system from March 10, 2020 to May 2, 2020 were included.
- Receipt of
  - Hydroxychloroquine alone,
  - Hydroxychloroquine in combination with azithromycin
  - Azithromycin alone
  - Neither of the treatment

Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19

Characteristics	Total	Neither Medication	HCQ alone	AZM alone	HCQ + AZM
Mortality %	18.1%	26.4%	13.5%	22.4%	20.1

Azithromycin alone vs. neither medication **dose not reduce mortality**. P =0.825

COVID-19 rapid NICE guideline: antibiotics for pneumonia in adults in hospital

- When choosing antibiotics, also take account of **local antimicrobial resistance data** and other factors such as their availability.
- Give oral antibiotics if the patient can take **oral medicines** and their condition is not severe enough to need intravenous antibiotics.
- Stop antibiotics if the pneumonia is due to COVID-19 and there is no evidence of bacterial infection.

COVID-19 rapid NICE guideline: antibiotics for pneumonia in adults in hospital

Table 1 Antibiotics for people 18 and older with suspected community-acquired pneumonia

Empirical treatment	Antibiotics and dosage (oral doses are for immediate-release medicines)
Oral antibiotics for moderate or severe pneumonia	**Options include:** **Doxycycline**: 200 mg on first day, then 100 mg once a day **Co-amoxiclav**: 500 mg/125 mg three times a day **with** **Clarithromycin**: 500 mg twice a day **In severe pneumonia, and if the other options are unsuitable:** **Levofloxacin**: 500 mg once or twice a day (consider the safety issues with fluoroquinolones)
Intravenous antibiotics for moderate or severe pneumonia	**Options include:** **Co-amoxiclav**: 1.2 g three times a day **with** **Clarithromycin**: 500 mg twice a day **Cefuroxime**: 750 mg three or four times a day (increased to 1.5 g three times a day if infection is severe) **with** **Clarithromycin**: 500 mg twice a day **In severe pneumonia, and if the other options are unsuitable:** **Levofloxacin**: 500 mg once or twice a day (consider the safety issues with fluoroquinolones)

Antimicrobial resistance in *Streptococcus pneumoniae* isolates from invasive pneumococcal infections in **Iran**

- From June 2012 to September 2016 in Milad hospital among patients with suspected invasive pneumococcal disease (IPD).
- In conclusion our study revealed a high rate of resistance among S. pneumoniae isolate to commonly used Antibiotic such as Penicillin and Erythromycin
- The most effective Antibiotic for treatment of invasive Pneumococcal infection were Levofloxacin and Vancomycin respectively.

Antibiotic	Breakpoint (µg/ml)	N	Susceptible (%)	Intermediate (%)	Resistant (%)	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)
Penicillin (meningitis)	S≤ 0.06, R ≥ 0.12	7	0	0	100	1	2
Levofloxacin	S ≤ 2, I = 4, R ≥ 8	50	98	0	2	0.75	1.5
Trimethoprim/ Sulfamethoxazole	S≤ 0.5/9.5, I = 1.19-2/38, R ≥ 4/76	50	2	34	64	2	8
Clindamycin	S≤ 0.25, I = 0.5, R ≥ 1	50	46	2	52	0.125	3
Azithromycin	S ≤ 0.5, I = 1, R ≥ 2	50	26	4	70	0.75	16
Erythromycin	S ≤ 0.25, I = 0.5, R ≥ 1	50	28	0	72	0.19	6
Vancomycin	S ≤ 1	50	88	0	0	0.75	1.5
Chloramphenicol	S ≤ 4, R ≥ 8	50	74	0	26	3	24
Tetracycline	S ≤ 1, I = 2, R ≥ 4	50	44	0	56	12	32