

COVID-19: Differential Diagnosis and Co-infections

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Background

As COVID-19 has a variety of clinical manifestations, including fever, cough, headache, myalgia, fatigue, etc., it may be challenging to distinguish the infection from other diseases with similar presentations such as malaria, especially in endemic areas. Furthermore, there is always a potential of co-infections in the same patient. It is therefore important to understand the local epidemiology and presence of infectious diseases in your duty station and have increased vigilance so that the patient diagnosis/es can be made accurately and appropriate clinical management of potential co-infections be implemented.

This document will provide brief guidance on COVID-19 differential diagnosis and co-infections.

Clinical Presentations of Common Endemic Diseases vs COVID-19

The table below outlines the overlapping clinical presentations of some common endemic infectious disease vs that of COVID-19. This will help to prevent under-diagnosis and increase the index of suspicion when dealing with suspect / probable cases of COVID-19 in your health facility.

Infectious Disease	Typical Clinical presentation
COVID-19¹	Fever, cough, fatigue, anorexia, shortness of breath/dyspnea, myalgia. Others: sore throat, nasal congestion, headache, diarrhea, nausea, vomiting, anosmia, ageusia
Malaria²	Fever, headache, chills, fatigue. In severe malaria: altered sensorium (cerebral malaria), metabolic acidosis, respiratory distress, anemia
Dengue³	High fever, severe headache, pain behind the eyes (retro-orbital), muscle/joint pains, nausea, vomiting, rash, swollen glands. Severe: severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness, blood in vomit
Chikungunya⁴	Fever, joint pain, muscle pain, headache, fatigue, rash
Zika virus⁵	Usually mild – fever, rash, conjunctivitis, muscle and joint pain, headache and malaise
Influenza⁶	Fever, cough, headache, muscle and joint pain, severe malaise, sore throat, running nose
Meningitis (bacterial)⁷	Fever, headache, neck stiffness, altered consciousness, other meningeal signs
Sepsis⁸	Fever (or low temperature), altered sensorium, difficulty breathing/rapid breathing, increased heart rate, weak pulse, low urine output, cyanotic or mottled skin, extreme body pain and discomfort.
Other differential diagnosis as appropriate	

¹ <https://www.who.int/publications-detail/clinical-management-of-covid-19>

² <https://www.who.int/news-room/fact-sheets/detail/malaria>

³ <https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>

⁴ <https://www.who.int/news-room/fact-sheets/detail/chikungunya>

⁵ <https://www.who.int/news-room/fact-sheets/detail/zika-virus>

⁶ [https://www.who.int/en/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/en/news-room/fact-sheets/detail/influenza-(seasonal))

⁷ https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/sentinel/meningitis_surveillance/en/

⁸ <https://www.who.int/news-room/fact-sheets/detail/sepsis>

DHMOSH Recommendations:

- Always assume that all patients seen in your clinic are suspect COVID-19 cases until proven otherwise; always be ready to use appropriate PPE and practice universal precautions at all times with all patients.
- Do not forget that the patient can be co-infected with both COVID-19 and another disease.
 - Even if COVID-19 is lab confirmed, this does not rule out presence of another infection.
 - Even if another pathogen (e.g. malaria) has been confirmed, this does not rule out presence of COVID-19 co-infection.
- Depending on local epidemiology and clinical symptoms, for all suspect COVID-19 patients, make sure to perform diagnostic testing for other conditions such as malaria, dengue, typhoid etc. as appropriate.
 - Note that in **malaria**-endemic areas patients with fever should be tested for the presence of malaria using validated rapid diagnostic tests (RDTs) or microscopy with thin and thick films. If results are positive, they should be treated for malaria.
 - COVID-19 testing would also be warranted in patients where you suspect malaria and vice versa given overlapping signs and symptoms and irrespective of respiratory signs and symptoms. Neither diagnosis should be missed.
 - **Arboviruses such as dengue** are endemic and should be considered as part of the differential diagnosis in the context of an undifferentiated febrile illness particularly if there is thrombocytopenia. Leukopenia/lymphopenia can be seen with arboviruses as well as in COVID-19 therefore COVID-19 testing would also be warranted when you suspect arboviruses and vice-versa where you suspect arboviruses irrespective of respiratory signs and symptoms.
 - In COVID-19 patients with severe or critical disease, blood cultures should be collected ideally prior to initiation of antimicrobial therapy.
 - Do not forget **other clinical syndromes** such as meningitis – COVID-19 is also known to cause delirium, stroke, encephalopathy which can be confounded with other causes of meningitis. If meningitis is suspected this could be due to viruses, bacteria and also cerebral malaria.
 - Note that symptoms such as dyspnea, fever, headache, gastrointestinal symptoms or fatigue can also be seen with COVID-19 as they can be seen in malaria (and other infectious diseases).