



- Human **Coronaviruses** (HCoVs) have long been considered inconsequential pathogens, causing the “common cold” in otherwise healthy people.
- In China, where most cases have occurred so far, people with diabetes had much higher rates of serious complications and death than people without diabetes.
- The problem people with diabetes face is primarily a problem of worse outcomes, not greater chance of contracting the virus. People who already have diabetes-related health problems are likely to have worse outcomes if they contract **COVID-19**.
- People with diabetes do face an increased risk of DKA (**diabetic ketoacidosis**) and or Hypoglycaemia. DKA is commonly experienced by people with type 1 diabetes
- The only approved treatment as of today is **‘Social Distancing, Quarantine’ and in affected cases symptomatic treatment only.**
- Symptoms of **COVID-19**:
 - a) Fever (98%)
 - b) Cough (76%)
 - c) Fatigue (44%)
 - d) Sputum production (28%)
 - e) Diarrhoea (3%).
- More than half of the patients developed shortness of breath roughly eight days from the onset of illness.
- Ibuprofen should be avoided during the COVID-19.
- **“With 334,981 cases confirmed and more than 14,652 deaths worldwide in 190 countries, concerns over the latest coronavirus outbreak continue to escalate. In India we have 446 cases and 9 deaths as on 24th Mar 2020”**



• **H**uman coronaviruses (HCoVs) have long been considered inconsequential pathogens, causing the “common cold” in otherwise healthy people. However, in the 21st century, 2 highly pathogenic HCoVs - severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)—emerged from animal reservoirs to cause global epidemics with alarming morbidity and mortality.

• **I**n December 2019, yet another pathogenic HCoV, 2019 novel coronavirus (2019-nCoV), was recognized in Wuhan, China, and has spread currently to almost 130 countries resulting in pandemic and has caused serious illness and death. The ultimate scope and effect of this outbreak is unclear at present as the situation is rapidly evolving.

• **F**our HCoVs (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10% to 30% of upper respiratory tract infections in adults.

• **W**hile the trajectory of this outbreak is impossible to predict, effective response requires prompt action from the standpoint of classic public health strategies to the timely development and implementation of effective countermeasures.

• **I**n China, where most cases have occurred so far, people with diabetes had much higher rates of serious complications and death than people without diabetes—and generally we believe that the more health conditions someone has (for example, diabetes and heart disease), the higher their chance of getting serious complications from COVID-19.

• **T**he problem, people with diabetes, face is primarily a problem of worse outcomes, not greater chance of contracting the virus.

Introduction

The coronavirus has derived its name because of resemblance of its shape to a crown or solar corona when imaged using an electron microscope.

The three deadly human respiratory coronaviruses so far:

- Severe acute respiratory syndrome coronavirus [sars-cov].
- Middle East respiratory syndrome coronavirus [mers-cov].
- 2019-ncov: the virus is 75 to 80% identical to the sars-cov.



People with diabetes do face a higher chance of experiencing serious complications from COVID-19:

In general, people with diabetes are more likely to experience severe symptoms and complications when infected with a virus. If diabetes is well-managed, the risk of getting severely sick from COVID-19 is about the same as the general population.

When people with diabetes do not manage their diabetes well and experience fluctuating blood sugars, they are generally at risk for a number of diabetes-related complications. Having heart disease or other complications in addition to diabetes could worsen the chance of getting seriously ill from COVID-19, like other viral infections, because your body's ability to fight off an infection is compromised. But if glucose control is poor, severity of viral illness and risk of complications will increase because of impairment of immunity.

Viral infections can also increase inflammation, or tissue oedema in people with diabetes. This is also caused by above-target blood sugars, and both could contribute to more severe complications.

People with diabetes do face an increased risk of DKA (diabetic ketoacidosis) and or Hypoglycemia. DKA is commonly experienced by people with type 1 diabetes.

COVID-19 risk for people with type 1 versus type 2 diabetes:

- In general, we don't know of any reason to think COVID-19 will pose a difference in risk between type 1 and type 2 diabetes.
- More important is that people with either type of diabetes vary in their age, complications and how well they have been managing their diabetes.
- People who already have diabetes-related health problems are likely to have worse outcomes if they contract COVID-19 than people with diabetes who are otherwise healthy, whichever type of diabetes they have.



Terms

Definitions

SARI	An ARI with history of fever or measured temperature $\geq 38\text{ C}^\circ$ and cough; onset within the last ~10 days; and requiring hospitalization.
Surveillance case definitions for SARI	<p>1. SARI in a person, with history of fever and cough requiring admission to hospital, with no other etiology that fully explains the clinical presentation¹ (clinicians should also be alert to the possibility of atypical presentations in patients who are immune-compromised); and any of the following:</p> <p>a) A history of international travel in 14 days prior to symptom onset; or b) the disease occurs in a health care worker who has been working in an environment where patients with severe acute respiratory infections are being cared for, without regard to place of residence or history of travel; or c) the person develops an unusual or unexpected clinical course, especially sudden deterioration despite appropriate treatment, without regard to place of residence or history of travel, even if another etiology has been identified that fully explains the clinical presentation</p> <p>2. A person with acute respiratory illness of any degree of severity who, within 14 days before onset of illness, had any of the following exposures:</p> <p>a) close physical contact with a confirmed case of COVID - 19 infection, while that patient was symptomatic; or b) a healthcare facility in a country where hospital-associated COVID - 19 infections have been reported</p>
Uncomplicated illness	Patients with uncomplicated upper respiratory tract viral infection, may have non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache. The elderly and immunosuppressed may present with atypical symptoms. These patients do not have any signs of dehydration, sepsis or shortness of breath.
Mild pneumonia	Patient with pneumonia and no signs of severe pneumonia. Child with non-severe pneumonia has cough or difficulty in breathing/ fast breathing: (fast breathing - in breaths/min):

When should a Diabetologist suspect COVID-19?

	Cold	Flu	Corona Virus
Time between catching the virus and beginning to show symptoms	1-3 days	1-4 days	2-14 days
Symptom onset	Gradual	Abrupt	Gradual
How long do symptoms last	7-12 days	3-7 days	Mild cases: approx 2 weeks. Severe or critical disease: 3-6 weeks
Fever	Sometimes	Common	Common
Runny nose	Common	Sometimes	Less Common
Sore throat	Common Sometimes Less Common	Sometimes	Less Common
Cough	Common	Sometimes	Common
Body Ache	Rare; if occurs mild	Common	Less Common
Difficulty breathing	Rare	Rare	Common



In adults, emergency warning signs include:

- Difficulty breathing or shortness of breath
- Persistent pain or pressure in the chest
- New confusion or inability to arouse
- Bluish lips or face

How to implement infection prevention and control measures for patients with suspected or confirmed COVID - 19 infection:

1) At triage:

- a) Give suspect patient a triple layer surgical mask and
- b) Direct patient to separate area, an isolation room if available.
- c) Keep at least 1 meter distance between suspected patients and other patients.
- d) Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others.
- e) Perform hand hygiene after contact with respiratory secretions.

2) Apply droplet precautions:

- a) Droplet precautions prevent large droplet transmission of respiratory viruses.
- b) Use a triple layer surgical mask if working within 1-2 metres of the patient.
- c) Place patients in single rooms, or group together those with the same etiological diagnosis.
- d) If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers). If equipment needs to be shared among patients, clean and disinfect between each patient use.
- e) Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). Ensure adequate room ventilation.

Precautions to be taken in diabetics:

- Advise patients to drink lots of fluids. If patient is having trouble or pain in swallowing, advise them to have small sips every 15 minutes or so throughout the day to avoid dehydration.
- Patients should be advised for frequent self-monitoring of blood glucose to prevent hypoglycaemia as well as to identify glycaemic excursions. Specific instructions should be given about hypoglycaemia management e.g. to eat 15 grams of simple carbohydrates (like honey, jaggery, jam or hard candy) and about modification in their drug or insulin dose according to physician advice if hypoglycaemia occurs.
- Patients, particularly type 1 diabetes patients, should be advised to check urine ketones when there is sustained Hyperglycemia with two readings of random blood sugar above 250mg/dl. If urine ketones are trace or small, they should be advised for adequate hydration and rechecking ketones in few hours. If urine ketones are moderate or large or persistently small or there are symptoms of DKA (abdominal pain, nausea, vomiting), they should immediately consult physician or emergency department of nearby hospital.



- Patients should be instructed about personal hygiene like regularly washing hands, avoid touching face and cleaning injection/infusion sites & finger-stick sites with soap and water or rubbing alcohol.
- Patients with diabetes, particularly those with poor glycaemic control, as they are at increased risk of complications, they should be instructed about warning symptoms and need for hospitalization if they develop such symptoms.
- Apart from these, patients should be instructed to follow social isolation to prevent spread of infection to others.
- **Always to be in touch with your personal doctor in such situations.**

Investigations:

Laboratory Markers In COVID-19 Patients:

Most Frequent:

- Decrease lymphocyte count
- Decrease albumin
- Decrease haemoglobin levels
- Increase C-reactive protein (CRP)
- Increase Erythrocyte Sedimentation Rate (ESR)
- Increase Lactate Dehydrogenase (LDH)
- Increase D-dimer

In SEVERE COVID-19:

- Decrease lymphocyte count
- Decrease albumin
- Decrease haemoglobin levels
- Increase C-reactive protein (CRP)
- Increase Erythrocyte Sedimentation Rate (ESR)
- Increase Lactate Dehydrogenase (LDH)
- Increase D-dimer
- Increase Neutrophil count
- Increase Alanine Aminotransferase (ALT)
- Increase Aspartate Aminotransferase (AST)
- Increase Cardiac biomarkers (e.g. cardiac troponins)
- Increase Procalcitonin



Specimen collection:

Responsibilities:

- The clinician should decide necessity for collection of clinical specimens for laboratory testing of 2019-nCoV only after following the case definition as given by the health authorities, Government of India.
- Appropriate clinical sample need to be collected by laboratory personnel/ health care worker trained in specimen collection in presence of a clinician.
- By following all biosafety precautions and using personal protective equipment (PPEs), clinical samples need to be sent to the designated laboratories as approved by Government of India, by following standard triple packaging.

Selection of patient:

- The ICMR have revised the strategy for testing of COVID-19 on 21/03/2020. According to this recommendation, the following have been included for testing
 - a) All asymptomatic individuals who have undertaken International travel in the last 14 days
 - b) All symptomatic contacts of laboratory confirmed cases
 - c) All symptomatic healthcare workers
 - d) All hospitalized patients with Severe Acute Respiratory illness (Fever and cough and/or shortness of breath)
 - e) Asymptomatic direct and high risk contacts of a confirmed case should be tested between day 5 and day 14 coming in/her contact

Specimen labelling and processing:

- Personal protective equipment (apron, hand gloves, face shield, N95 Masks etc.) need to be used and all biosafety precautions should be followed so as to protect individuals and the environment.
- Proper labelling (name/age/gender/specimen ID) need to be done on specimen container and other details of sender (name/address/phone number) on the outer container by mentioning "To be tested for 2019-nCoV".
- Diagnosis by PCR is available from imported kits and now we have Indian kit available for diagnosis (ICMR recommended and approved by DCGI)

Research Society for the Study of Diabetes in India (RSSDI)

Guidance for People with Diabetes on COVID - 19 for Healthcare Professionals



Specimen type	Collection materials	Transport to laboratory	Storage till testing	Comment
Nasopharyngeal and oropharyngeal	swab Dacron or polyester flocked swabs*	4 °C	≤5 days: 4 °C >5 days: -70 °C	The nasopharyngeal and oropharyngeal swabs should be placed in the same tube to increase the viral load.
Bronchoalveolar lavage	sterile container*	4 °C	≤48 hours: 4 °C >48 hours: -70 °C	There may be some dilution of pathogen, but still a worthwhile specimen
Tracheal aspirate, nasopharyngeal aspirate or nasal wash	sterile container*	4 °C	≤48 hours: 4 °C >48 hours: -70 °C	Not applicable
Sputum	sterile container	4 °C	≤48 hours: 4 °C >48 hours: -70 °C	Ensure the material is from the lower respiratory tract
Tissue from biopsy or autopsy including from lung	sterile container with saline	4 °C	≤24 hours: 4 °C >24 hours: -70 °C	Autopsy sample collection preferably to be avoided
Serum (2 samples - acute and convalescent)	Serum separator tubes (adults: collect 3-5 ml whole blood)	4 °C	≤5 days: 4 °C >5 days: -70 °C	Collect paired samples: • acute – first week of illness • convalescent - 2 to 3 weeks later

*For transport of samples for viral detection, use VTM (viral transport medium) containing antifungal and antibiotic supplements. Avoid repeated freezing and thawing of specimens.

Treatment:

- The only approved treatment as of today is **Social Distancing, quarantine and in affected cases symptomatic treatment only.**
- The following are few of the treatment regimens have been used so far but they are not validated by RCT's.
- Based on available data, the following drugs are in pipeline for COVID-19¹⁰ as of 21/03/20

Drugs	Types	Mechanisms of action	Past evidences
Chloroquine	4-aminoquinoline	Not clearly known, changes the pH of endosomes and believed to prevent viral entry, transport and post-entry events	Inhibits infection of cells by SARS-CoV-2 in vitro, approved for malaria treatment and prophylaxis
Hydroxychloroquine	4-aminoquinoline	Not clearly known, changes the pH of endosomes and believed to prevent viral entry, transport and post-entry events	Inhibits infection of cells by SARS-CoV-2 in vitro, approved for malaria prophylaxis and autoimmune disease (e.g. rheumatic diseases). Approved for treatment of T2DM in India
Remdesivir	Adenosine nucleotide analogues	Inhibits viral application	Effective against SARS and MERS
Ribavirin	Nucleoside analogue	Inhibits viral RNA synthesis and mRNA capping	No evidence in SARS (potential harm) and MERS
Ribavirin plus Interferon		Inhibits viral replication	Mixed result against MERS
Camostat Mesilate	Protease inhibitors	Blocks viral maturation and entry to cells	Effectively blocked SARS-CoV-2 in lung cells in vitro
Lopinavir/Ritonavir	Protease inhibitors	Blocks viral cellular entry	Effective against SARS-CoV-1 both in vitro and human studies, approved for HIV-1 treatment
Darunavir/Cobicistat	Protease inhibitors	Blocks viral cellular entry	Established anti-HIV medication. No activity against coronavirus-es or other respiratory viruses. No in vitro or clinical data

Research Society for the Study of Diabetes in India (RSSDI) Guidance for People with Diabetes on COVID - 19 for Healthcare Professionals



Drugs	Types	Mechanisms of action	Past evidences
Favipiravir	RNA polymerase inhibitors	Inhibits viral RNA-dependent polymerase	Broad-spectrum anti-viral-against influenza, arenavirus, bunyavirus and filovirus
Umifenovir	Fusion inhibitor	Inhibits fusion between viral and cellular membrane	Antiviral against other Corona viruses
Interferon-β1	Cytokines	Stimulate innate antiviral immunity	MERS-CoV appears to be more sensitive than SARS-CoV in vitro studies. Anti-MERS-CoV action noted in animal studies.
Interferon beta plus Lopinavir/Ritonavir		Interferon beta inhibits viral replication	Ongoing study for SARS-Cov-2 and MIRACLE trial for MERS
Aerosolized interferon α	Cytokines	Stimulate innate antiviral immunity	Case report suggested benefit in MERS
Oseltamivir	Neuraminidase inhibitor	Inhibits viral replication	No effect in SARS in vitro studies. No evidence in SARS and MERS
Baloxivir marboxil	Viral endonuclease inhibitor	Inhibits influenza virus multiplication	Approved for uncomplicated influenza only. Oral route.
Tocilizumab, Sarilumab, Eculizumab	Monoclonal antibody	IL-6 inhibitor, blocks cytokine storm.	No data on SARS or MERS. Tocilizumab reduced fever and oxygen requirement in COVID-19, approved for rheumatoid arthritis.
SARS-Cov-2 specific protease drug candidate	Protease inhibitors	Blocks viral infectivity	No data available
SARS-Cov-2 specific antibodies	Antibody	Binds to virus and block infection, binds to infected cells and change the immune system	Inhibits SARS-CoV-2 entry into cells in vitro

SARS- severe acute respiratory syndrome, MERS- Middle-East respiratory syndrome, HIV- Human Immunodeficiency syndrome, T2DM – type 2 diabetes, COVID-19- Corona virus disease 19.

As of 21/03/20, the following guidelines¹⁰ have been recommended by various centres and organisations

Study/Guidelines/Country	Dose (adults)
Expert consensus from Department of Science and Technology and Health Commission of Guangdong province, China ²¹	Chloroquine phosphate 500 mg BID for 10 days.
Central Clinical Task Force, Korea ²²	Moderate to severe COVID-19: Lopinavir 400mg/Ritonavir 100mg BID or Chloroquine 500mg orally per day or Hydroxychloroquine 400mg orally per day for 7-10 days.
Centre for Disease Control and Prevention, Atlanta, MICC Version 1 (March 12, 2020) ²³	URTI plus positive PCR: <ul style="list-style-type: none"> • Chloroquine phosphate 500 mg BID for 5 days. • Oseltamivir 150 mg BID for 5 days. COVID-19 Pneumonia: <ul style="list-style-type: none"> • Chloroquine phosphate 500 mg BID for 5 days plus Darunavir 800 mg/Cobicistat 150 mg OD for 2 weeks. • Atazanavir 400 mg OD for 2 weeks plus Oseltamivir 150 mg BID for 5 days.
The Dutch Center of Disease Control ²⁴	600 mg of Chloroquine base followed by 300 mg after 12 h on day 1, then 300 mg × 2/day per person on days 2-5.
Italian Society of Infectious and Tropical Diseases (Lombardy Section) ²⁵	Mild to moderate COVID-19: Lopinavir/ritonavir plus Chloroquine 500 mg × 2/day or Hydroxychloroquine 200 mg per day for 10 days. Severe or critical COVID-19: Remdesivir plus Chloroquine 500 mg × 2/day or Hydroxychloroquine 200 mg per day for 10-20 days.
Mount Sinai Health System, Canada ²⁶	Mild to moderate COVID-19: Hydroxychloroquine 400 mg BID x 2 doses then 12 hours later start 400 mg OD for 5-10 days.
Surviving Sepsis Campaign, The Society of Critical Care Medicine and the European Society of Intensive Care Medicine. ²⁷	Insufficient evidence to issue a recommendation on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19 at this point of time.
Clinical guidance for patients with suspected or confirmed COVID-19 in Belgium ²⁸	Mild/Moderate/Severe COVID-19: Hydroxychloroquine 400 mg at diagnosis, 400 mg 12 hour later, followed by 200 mg BID for 5 days,



	<p>Or,</p> <p>Chloroquine 600 mg at diagnosis and 300 mg 12 hour later followed by 300 mg BID for 5 days</p> <p>(Consider lopinavir 400 mg/ritonavir 100 mg BID for 14 days as a second choice only if HCQ and chloroquine is contraindicated, provided it can be administered within 10 days after onset of symptoms)</p> <p>Critical COVID-19: Remdesivir 200 mg loading dose i.v within 30 minutes followed by 100 mg OD for 2-10 days</p> <p>(Hydroxychloroquine is second option if Remdesivir is unavailable)</p>
Clinical guidance for patients with suspected or confirmed COVID-19 in Netherland ²⁸	<p>Mild/moderate/severe COVID-19: Chloroquine 600 mg on day 1, then 300 mg BID for 5 days (lopinavir/ritonavir as second option)</p> <p>Critical COVID-19: Remdesivir for 10 days plus chloroquine for 5 day</p>
Gautret et al, Marseille, France ¹⁹	Hydroxychloroquine 200 mg TID for 10 days.

OD- once daily, BID- twice daily, TID- thrice daily, URTI- upper respiratory tract infection, PCR- polymerase chain reaction, i.v - intravenous

Is there a role for Chemoprophylaxis? The following data is available

- As per the recommendation of ICMR as released on 23/03/20, the advisory provides placing the following high risk population under chemoprophylaxis with hydroxychloroquine

a) Asymptomatic Healthcare workers involved in the care of suspected or confirmed cases of COVID-19

b) Asymptomatic household contacts of laboratory confirmed cases



Other data available based on experimental and 2 human studies¹⁰

Timing of intervention	Proposed
Chemoprophylaxis	<ul style="list-style-type: none"> • No conclusive evidence so far; however, chloroquine or HCQ could be researched as a prophylactic agent in endemic areas. Recent guidelines from Indian Council of Medical Research recommend it as a prophylactic agent (see reference 42 for indication and dose). • Note: HCQ can be used as an adjunct to control glycemia in adult patients with type 2 diabetes (approved for treatment in India). However, role of such adjunctive treatment for testing its potential role as prophylaxis of COVID-19 in diabetes has not been researched but could be attempted (in view of above) considering a higher mortality in patients with diabetes, as compared to non-diabetic subjects with COVID-19.
Confirmed COVID-19	<p>A. Chloroquine phosphate: @\$</p> <ol style="list-style-type: none"> 1. COVID-19 URTI: 500mg BID for 5 days. 2. COVID-19 LRTI: 500mg BID for 10 days. <p>B. Hydroxychloroquine: @\$</p> <p>Loading dose: 400 mg BID day 1, then Maintenance dose: 200 mg BID for 5-10 days.</p> <p>C. Monitor and watch for side effects*</p>

@ watch for hypoglycemia in diabetes especially with concurrent use of lopinavir/ritonavir,

\$ should not be used concurrently with lopinavir/ritonavir and remdisivir due to increased QTc prolongation,

* complete blood count, renal, hepatic profile and ECG – watch for QTc prolongation, URTI- upper respiratory tract infection, LRTI- lower respiratory tract infection, HCQ- hydroxychloroquine, BID – twice daily

Administration of Lopinavir/ Ritonavir: **

Administration of Lopinavir/ Ritonavir to be considered in Laboratory confirmed cases of COVID – 19 when the following criteria are met:

• **Symptomatic patients with any of the following:**

- a) hypoxia,
 - b) hypotension,
 - c) new onset organ dysfunction (one or more)
- Increase in creatinine by 50% from baseline, GFR reduction by >25% from baseline or urine output of <0.5 ml/kg for 6 hrs
 - Diabetes Mellitus, Renal Failure, Chronic Lung disease
 - Immunocompromised persons
 - Dosage
 - Lopinavir/ Ritonavir (200 mg/ 50 mg) – 2 tablets twice daily
 - For patients unable to take medications by mouth: Lopinavir 400mg/ Ritonavir 100 mg – 5ml suspension twice daily
 - Duration: 14 days or for 7 days after becoming asymptomatic.

a) Advisory for Prophylaxis for SARS-CoV-2 infection

As per the recommendation of ICMR as released on 23/03/20, the advisory provides placing the following high risk population under chemoprophylaxis with hydroxychloroquine

- b) Asymptomatic Healthcare workers involved in the care of suspected or confirmed cases of COVID-19
- c) Asymptomatic household contacts of laboratory confirmed cases

** It should be noted however, that a recent RCT conducted with Lopinavir/Ritonavir failed to show any benefit in 199 case of COVID-19 and drug was stopped at day 13 due to adverse events.¹¹

NOTE: A large fast-tracked pragmatic open-label RCT (n=3200) is already underway named SOLIDARITY trial on behalf of WHO comparing standard of care head-on with 4 drug (HCQ vs. Remdesivir vs. Lopinavir/Ritonavir vs. Lopinavir/Ritonavir plus Interferon Beta) and is expected to report its result within a month. This trial expected to be a final nail in the coffin to show which drug is most effective against COVID-19.¹²

Drugs to be avoided in COVID-19:

- Ibuprofen
- Anti Hypertensives: Regarding ACE/ARB'S - most guidelines strongly encourage continuing them in all categories of patients



Status of Vaccination

- Coronavirus vaccine are in early trials. We have to wait for the results.

**“ Let’s keep our hopes alive and our attitude positive!
Remember, even the darkest clouds have a silver lining.”**

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This document has been prepared by experts from Research Society for Study of
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