



Update: 16 & 17 June, 2020

**UPDATE ON GLOBAL, REGIONAL AND NATIONAL
DEVELOPMENTS ON COVID-19**

THE KNOWLEDGE SYNTHESIS TEAM
CDT-AFRICA, ADDIS ABABA UNIVERSITY
www.cdt-africa.org

Summary

- Worldwide, as of June 17, 12:00 GMT, the novel coronavirus has caused 8,288,189 infections, 446,682 deaths and 4,342,553 recoveries.
- A total of 259,036 cases, 6,999 deaths and 118,472 recoveries were reported in Africa as of June 17th, 3:00 PM EAT.
- Two studies published in the lancet concerning asymptomatic and pre symptomatic cases of COVID-19 on the Diamond Princess cruise ship, indicated the presence of comorbidities did not appear to increase susceptibility to symptomatic infection or even disease outcome. Instead, older age was the only demographic factor that differentiated symptomatic from asymptomatic cases.
- The CXRs obtained from confirmed and symptomatic COVID-19 patients presenting to the emergency care were normal in 58.3% of cases, and normal or only mildly abnormal in 89% of patients.
- The emergency use authorization (EUA) of chloroquine phosphate and hydroxychloroquine sulfate for COVID-19 was revoked by the US FDA.
- Dexamethasone has been identified as the first drug to improve survival rates in ventilated and oxygen receiving COVID-19 patients in the RECOVERY trial.
- mandating face mask use in public had a greater impact in decreasing daily COVID-19 growth rates

Recommendations

- Dexamethasone could be a beneficial drug for patients requiring ventilation or oxygen supplement and should be considered in the care of such patients.
- Guideline on use of chloroquine (and hydroxychloroquine) in routine care needs to be revised
- Need to explore appropriate mechanisms of enforcing face coverings.
- Protection of healthcare professionals and monitoring for stigma and discrimination is necessary.

Update on pathogenesis

Disease Transmission

- Two cohort studies are recently published in the Lancet Infectious Diseases concerning asymptomatic and pre symptomatic cases of COVID-19 on the Diamond Princess cruise ship.

first study was done on 104 individuals who tested positive in Tokyo, Japan. These cases were immediately hospitalized, and their clinical characteristics were retrospectively reviewed until they were discharged from the hospital. The second study was conducted among 265 individuals who were on board and tested negative when the ship was docked in Japan. Hence, these individuals were returned back to China and quarantined in a public estate in Hong Kong. Therefore, participants were prospectively followed and both PCR & antibody tests were done at baseline, 4, 8, and 12 days of quarantine. The major findings from these two studies are;

- Among 104 cases on admission, 43 (41%) participants were classified as asymptomatic, 41 (39%) as having mild COVID-10, and 20 (19%) as having severe COVID-19.
- Of the 43 individuals positive for SARS-CoV-2 on RT-PCR who were asymptomatic at admission to a hospital in Tokyo, Japan, ten developed COVID-19, including severe pulmonary disease.
- Serum lactate hydrogenase concentrations were significantly higher in these ten participants compared with the 33 participants who remained asymptomatic throughout the observation period [Tabata, S., et al, 2020].
- Out of the 215 asymptomatic individuals who returned to Hong Kong for further quarantine, nine became RT-PCR positive and three of them eventually developed symptoms [Hung, I., et al, 2020].
- The presence of comorbidities did not appear to increase susceptibility to symptomatic infection or even disease outcome in these studies. Instead, older age was the only demographic factor that differentiated symptomatic from asymptomatic.
- About 50% of asymptomatic individuals showed radiographic abnormalities, including ground glass opacities on chest CT scans.
- Patients with CT scan abnormalities had higher concentrations of SARS-CoV-2 spike protein and nucleoprotein antibodies than those with normal CT scans, regardless of whether they were symptomatic or asymptomatic [Eng Eong Ooi 2020].

Update on Epidemiology (Incidence, mortality, recovery & epidemiologic parameters)

Global

- Novel coronavirus affected 213 countries and territories around the world causing cases 8,288,189 cases, 446,682 deaths and 4,342,553 recoveries as of June 17, 12:00 GMT.
- Comparing the last two days' report, the number of new cases is vastly increased from 124,600 on June 15th to 142, 557 on June 16th. Similarly, the number of new deaths is significantly increased between these two days (from 3,415 to 6,592).

- Consistently, United States of America (USA) is the leading country with both high number of cases and deaths in the world. As of June 17th, 12:00 GMT, more than 2.2 million (2,208,748) people were infected with the virus and 119,137 deaths were reported in the country contributing for more than one fourth (26.7%) of total cases and deaths in the world.
- Both the number of new cases and new deaths in USA is substantially increased in the last two days; (from 20,722 new cases & 425 new deaths on June 15th to 25,450 new cases & 849 new deaths on June 16th).
- Next to USA, Brazil (928,834 cases), Russia (553,301 cases), India (355,060 cases) and United Kingdom (298,136 cases) are other most affected countries with COVID-19.
- These countries also reported high number of deaths each accounting for large proportion of total deaths in the world; Brazil 45,456 (10.2%), United Kingdom 41,969 (9.4 %), Italy 34,405 (7.7%), France 29,547 (6.6%) and Spain 27,136 (6.1%). However, total number of deaths in India (11,922 deaths) and Russia (7,478) is very low compared to high number of cases reported in both countries.

Africa

- According to Africa CDC, a total of 259,036 cases, 6,999 deaths and 118,472 recoveries were reported as of June 17th, 3:00 PM EAT.
- South Africa remained the first country with a total of 76,334 cases and 1,625 deaths followed by Egypt (47,856 cases), Nigeria (17,148 cases), Ghana (12,193 cases), Algeria (11,147 cases) and Cameroon (9,864 cases).
- As compared to previous day's report, the number of new cases within the last 24 hours is decreased in majority of these countries; South Africa (3,495 to 2,801), Egypt (1,691 to 1,567), Nigeria (573 to 490) and Ghana (846 to 229), while it's significantly increased in Cameroon; from 369 on June 10th to 1,183 on June 15th.
- The highest number of deaths is reported from Egypt (1,766 deaths) which accounted for almost one fourth 25.2% of total deaths in the continent.
- Other African countries with high number of COVID-19 deaths include; Algeria 788 (11.3%), Sudan 477 (6.8%), Nigeria 455 (6.5%) and Cameroon 276 (3.9%).

Ethiopia

- According to the Ministry of Health report, a total of 10,376 laboratory tests were carried out within 48 hours and 238 additional COVID-19 cases were identified in the country.
- All of the additional cases are Ethiopians, their age ranges from 1 to 78 years and more than half 139 (58.4%) of them are males.

- More than two third 166 (69.8%) of these cases were reported from Addis Ababa, 14 from Somali, 14 from Oromia, 14 from Tigray, 11 from SNNPR, 9 from Amhara, 4 from Afar, 4 from Dire Dawa and 2 from Hareri region.
- The ministry also reported that additional 229 people (224 from Addis Ababa, 3 from Tigray and 2 from Dire Dawa) are fully recovered from the disease raising the total number of recoveries to 849.
- In addition, three people (2 males and 1 females) have passed away in the last two days raising the total number of deaths in the country to 63.
- Therefore, a total of 197,361 laboratory tests were conducted and 3,759 confirmed cases, 63 deaths and 849 recoveries were reported as of June 17th, 4:00 PM EAT.
- Out of the total 2,845 active cases, 30 of them are in critical condition and receiving treatment in the intensive care unit, while the others are having mild form of the disease

Update on Diagnosis

- One article reported the occurrence of contaminations in commercial primers/probe sets with the SARS-CoV-2 target sequence of the RT-qPCR as an example for pitfalls during PCR diagnostics affecting diagnostic specificity. It was stated that in several purchased in-house primers/probe sets, low quantification cycle values were measured for negative control samples. Based on the results, it was indicated that it is important to pre-test each batch of reagents using more than 50 negative samples before use in routine diagnosis to ensure high level of diagnostic accuracy (Wernike et al., 2020).
- One study analysed the performance of an antigen test called COVID-19 Ag Respi-Strip, an immunochromatographic assay for the rapid detection of SARS-CoV-2 antigen on nasopharyngeal specimen. Four hundred observations were recorded for the analytical performance study and thirty tests were analyzed for the cross-reactivity study. The clinical performance study was performed in a retrospective multicentric evaluation on aliquots of 328 nasopharyngeal samples. COVID-19 Ag Respi-Strip results were compared with qRT-PCR as golden standard for COVID-19 diagnostics. In the study, the reproducibility showed a between-observer disagreement of 1.7%, a robustness of 98%, an overall satisfying user friendliness and no cross-reactivity with other virus-infected nasopharyngeal samples. In the clinical performance study performed in three different clinical laboratories during the ascendant phase of the epidemiological curve, an overall sensitivity and specificity of 57.6 and

99.5%, respectively with an accuracy of 82.6% was found. It was demonstrated that COVID-19 Ag Respi-Strip may be implemented in clinical laboratories according to biosafety recommendations. The authors concluded the COVID-19 Ag Respi-Strip represents a promising rapid SARS-CoV-2 antigen assay for the first-line diagnosis of COVID-19 in 15min at the peak of the pandemic (Mertens et al., 2020).

- In another study, a database of a large emergency care company in the greater New York City area was reviewed for patients with positive SARS-CoV-2 PCR tests who also underwent chest x-ray (CXR). Out of 636 CXRs reviewed, there were 371 CXRs re-read as normal (58.3%). Of the 265 abnormal cases 41.7% (n=195) demonstrated mild disease, 65 demonstrated moderate disease, and five demonstrated severe disease. The vast majority of patients (566/636) had either normal or only mildly abnormal CXRs (89%), despite being symptomatic enough to warrant imaging as determined by the treating care provider. The CXRs obtained from confirmed and symptomatic COVID-19 patients presenting to emergency care were normal in 58.3% of cases, and normal or only mildly abnormal in 89% of patients. It was indicated the most common findings when abnormal were present in the lower lobes and the pattern was interstitial and/or multifocal. Pleural effusions and lymphadenopathy were uncommon (Weinstock et al., 2020)

Update on treatment

Hydroxychloroquine and chloroquine

- On June 15, 2020, the U.S. Food and Drug Administration (FDA) revoked the emergency use authorization (EUA) that allowed for chloroquine phosphate and hydroxychloroquine sulfate donated to the Strategic National Stockpile to be used to treat certain hospitalized patients with COVID-19 when a clinical trial was unavailable, or participation in a clinical trial was not feasible. The agency determined that the legal criteria for issuing an EUA are no longer met. Based on its ongoing analysis of the EUA and emerging scientific data, the FDA determined that chloroquine and hydroxychloroquine are unlikely to be effective in treating COVID-19 for the authorized uses in the EUA. Additionally, in light of ongoing serious cardiac adverse events and other potential serious side effects, the known and potential benefits of chloroquine and hydroxychloroquine no longer outweigh the known and potential risks for the authorized use. This is the statutory standard for issuance of an EUA(US FDA 2020).

Dexamethasone--Recovery trial

- The NIHR-funded and supported study RECOVERY (Randomised Evaluation of COVid-19 thERapY) has announced that the steroid dexamethasone has been identified as the first drug to improve survival rates in certain coronavirus patients. A total of 2104 patients were randomised to take 6mg dexamethasone once per day(orally or by injection) for ten days and were compared with 4321 patients randomised to usual care alone. Among the usual care control group, 28-day mortality was highest in those on ventilators (41%), intermediate in those on oxygen only (25%), and lowest among those who were not receiving any respiratory intervention (13%).The study, found that dexamethasone reduced the risk of dying by one-third in ventilated patients and by one fifth in other patients receiving oxygen only. There was no benefit among those who did not need respiratory intervention. Overall, dexamethasone reduced the risk of 28-day mortality by 17% with a highly significant trend showing greatest benefit among those on ventilators. No evidence of benefit was found for patients who did not receive oxygen and the study did not include patients outside the hospital setting. Follow-up is complete for over 90% of participants (University of Oxford 2020).
- The RECOVERY Trial is a large, randomised controlled trial of possible treatments for patients admitted to over 175 NHS hospitals in the UK with COVID-19. Over 11,500 patients have been randomised to the following treatment arms, or no additional treatment: Lopinavir-Ritonavir (commonly used to treat HIV), Low-dose Dexamethasone (a type of steroid, which typically used to reduce inflammation), Hydroxychloroquine (which has now been stopped due to lack of efficacy), Azithromycin (a commonly used antibiotic), Tocilizumab (an anti-inflammatory treatment given by injection) and Convalescent plasma (collected from donors who have recovered from COVID-19 and contains antibodies against the SARS-CoV-2 virus)(University of Oxford 2020).

Baricitinib

- Eli Lilly and Company announced today that the first patient has been enrolled in a Phase 3 randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of baricitinib, an oral JAK1/JAK2 inhibitor is approved in several countries as a treatment for adults with moderately to severely active rheumatoid arthritis (RA).Lilly expects to enroll 400 patients in the trial, with data expected in the next few months. The study will be conducted in the U.S., Europe and Latin America and includes patients hospitalized with SARS-CoV-2

infection who have at least one elevated marker of inflammation but do not require invasive mechanical ventilation at study entry(Lily 2020).

- The rationale for use in regards to COVID-19 infection is, increased disease severity can be associated with a hyperinflammatory state. It is hypothesized that through JAK1 and JAK2 inhibition, baricitinib may reduce the cytokine storm associated with the complications of this infection. In addition, baricitinib may have a role in inhibiting the host cell proteins that assist in viral reproduction, reducing the ability of infected cells to make more virus(Lily 2020).
- The primary endpoint for Lilly's study is the proportion of patients who die or require non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation by Day 28 in patients treated with 4 mg of baricitinib daily (with background therapy) compared to placebo (with background therapy). Patients will receive baricitinib or placebo for up to 14 days or until discharge from the hospital. Key secondary outcomes of this study include the proportion of patients with clinical improvement at different time points, time to recovery, duration of hospitalization, number of ventilator-free days and mortality over a 28-day period(Lily 2020).

Update on personal protective equipment

Face mask use

- One article provided evidence from a natural experiment on effects of state government mandates in the US for face mask use in public issued by 15 states plus DC between April 8 and May 15. The study examined the changes in the daily county-level COVID-19 growth rates between March 31, 2020 and May 22, 2020. The results showed mandating face mask use in public had a greater decline in daily COVID-19 growth rates after issuing these mandates compared to states that did not issue mandates. Estimates suggested as many as 230,000–450,000 COVID-19 cases possibly prevented by May 22, 2020 by these mandates indicating that requiring face mask use in public might help in mitigating COVID-19 spread (Lyu and Wehby, 2020).

Psychosocial wellbeing updates

- A commentary from Mexico indicated that health workers have started experiencing stigma and discrimination by the community. Even though this has resulted from fear of acquiring the disease from them, they highlighted that in some incidents this has reached the level of ostracism. Knowing their importance to the health system and contribution to save lives, the authors recommended that immediate actions need to take place and there should be “zero tolerance” to violence against health workers(Rodríguez-Bolaños et al., 2020).

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