Develop – DeVos Cardiovascular Research Program's Emergency Letter on the Pandemic

Scientific Stream Update on the COVID-19 Pandemic – 4.16.20, 1400

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Not All Recovered Patients Have High Titers of Neutralizing Ab Against SARS-CoV-2

Article Title: *Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications*

https://www.medrxiv.org/content/10.1101/2020.03.30.20047365v1

Source: *MEDRXIV*

Clinical Field: *Infectious Disease*

Article Type: *Clinical Report*

Study Type: *Non-Randomized Controlled Trial*

Patient Group: *COVID-19 pats with mild disease*

Intervention: *Observational*

Reviewer	*Disha Geriani*
Study Design	*Minor concerns*
Study Design Concerns	*Patients with severe disease and those critically ill were excluded. Unable to understand the natural progression of the disease.*
Main Results	*-Most COVID-19 patients developed SARS-CoV-2-specific neutralizing antibodies (NAbs) around the convalescent phase of infection (titers reaching peak around 10-15 days)* *-Convalescent plasma from COVID-19 patients specifically inhibited SARS-CoV-2, but not SARS-CoV infection.* *-About 30% of recovered patients generated very low titers of SARS-CoV-2 specific NAbs The levels of NAbs did not coorelate with the duration of disease as these patients had similar times to recovery as compared to those that generated higher titers.* *-There were ten recovered patients with antibody titers with undetectable antibody titers, indicating that other immune responses such as T-cell mediated and cytokine-mediated immunity may have played a role towards their recovery. Although it is unclear whether these patients were at higher risk for reinfection or rebound.* *-NAbs titers were related to the age. Elderly and middle-aged patients had significantly higher titers of NAbs than younger patients. Of note,*

	elderly patients also had higher CRP levels and lower lymphocyte count, indicating a stronger immune response in these patients. *-COVID-19 recovered patients age and SARS-CoV-2-specific NAbs titers negatively correlated with lymphocyte count and positively correlated with CRP levels on admission.*
Comments	*-The highly variable levels of NAbs in the patients of COVID-19 indicates that convalescent plasma and serum from recovered donors should be titrated before use in passive antibody therapy, an easy task that can be performed using the PsV neutralization assay.* *-Further studies are needed to assess whether the high level of NAbs protect the patients from progression into severe and critical conditions.* *-Further studies of the immunological characteristics of COVID-19 patients may reveal key determinants in the generation of NAbs and effective cell-mediated immune responses, which is important for the development of an effective vaccine against SARS-CoV-2 virus.*

Case Fatality Rate 7.2% in Italy May Be Due to Under-Reporting of Cases But Also Higher Degree of Elderly

Article Title: *Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy*

https://jamanetwork.com/journals/jama/fullarticle/2763667

Source: *JAMA*

Clinical Field: *Infectious Disease*

Article Type: *Clinical Report*

Study Type: *Retrospective Study*

Patient Group: *Epidemiologic study of mortality in COVID-19*

Intervention: *N/A*

Reviewer	*Vinu Perinjelil*
Study Design	*Minor concerns*
Study Design Concerns	*1) Case fatality rate (CFR=deaths/overall cases) can be skewed in Italy as sufficient testing at beginning of pandemic not widely available therefore more critical cases resulting in death are reported while overall cases are under-reported (smaller denominator). An over-estimation of CF rate can also occur due to defining death in any COVID-19 positive patient independent from a pre-existing condition that could have been responsible for death in that patient* *2) This study does not take into account patient specific co-morbidities or immune status, thus Italy's rate in contrast to China does not give a perspective on patients with pre-existing conditions whose COVID positive status did not determine outcome.* *3) Data on cases in those aged over 90 in China were not reported, which would be a group highest at risk.* *4) Data from China until Feb 11, 2020 was compared with data from Italy until March 17,2020. Incomplete population pool from China.* *5) Testing policies are not uniform across countries and continues to vary as time passes, therefore transparent reporting of cases and accurate reporting of patient characteristics does not currently exist to make a more valid comparison of rates* *6) February 25th more stringent testing criteria implemented in Italy, so milder cases excluded and more severe cases represented. This could also mean worse cases are no longer counted in the numerator as they die before getting tested with hospitals getting overwhelmed* *7) ICU admission restrictions in the elderly (>70) in Italy could also be considered as impacting fatality rate, as a way to lower the ICU death rate/manage resources therefore elder patients die outside of hospital/ICU*

Main Results	*After China, Italy has the 2nd largest number of COVID-19 cases yet a higher reported case fatality rate. The Italian NIH collected information regarding the overall fatality rate of persons with confirmed COVID-19 in Italy based on data up to March 17, 2020 and their overall CF rate of 7.2% is substantially higher than China (2.3%).* *This could partly be explained by the demographics of the Italian population with 23% of the population comprised of individuals over 65 years of age. Individuals aged 70 years or older comprise 37.6% of cases in Italy while only 11.9% in China. A second possible explanation could be attributed to definitions of COVID-19 deaths, as any death in a COVID-19 positive patient is considered a COVID-19 fatality since there is no consensus on what constitutes a COVID-19 related death. This variation could be a reason why the CF rate is high and warrants a detailed chart review of deaths in these patients. Thirdly, since testing for asymptomatic patients in Italy was increasingly limited starting February 25th as a strategy to prioritize resources, this resulted in a higher proportion of positive results (only patients with more severe disease tested). Patients with less severe disease were no longer represented which could be the reason for increased CF rate (3.1% in February 24th to 7.2% in March 17th). The elimination of these milder cases in Italy is evident when compared to Korea (CF=1%) where their strategy of widespread testing has identified a large number of mild cases.*
Comments	*The idea of comparing fatality rates is critical however challenging as pandemic is unfolding and countries vary in testing and treatment strategies. This study reviews what is currently available regarding the Italian experience and more details regarding admission and testing criteria would be valuable as a basis for comparison. Future research focused on demographics based on more explicit chart review or treatment strategies would help understand the variety in CF rates across countries and demographics*

Summary of Advices for Intensive Care Patients With COVID-19

Article Title: *Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations*

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30161-2/fulltext

Source: *Lancet*

Clinical Field: *Critical Care*

Article Type: *Other*

Study Type: *Other*

Patient Group: *COVID-19 Patients requiring ICU*

Intervention: *n/a*

Reviewer	*Kathrine A Kelly-Schuette*
Study Design	*N/A*
Study Design Concerns	*Review from Asian Critical Care Clinical Trials Group* *Nice summary of clinical considerations and current literature on COVID19*
Main Results	*Clinical Features:* *most common are fever, cough, dyspnea, fatigue.* *Onset of symptoms to pneumonia is 5 days, and ICU admission 7-12 days. CT demonstrates ground glass opacities* *Mortality is associated with older age, DM, HTN, CAD, chronic lung disease, and cancer, higher d-dimer and CRP.* *Median time to recovery is 6-8 weeks.* *Diagnosis: RT PCR assay (sensitivity still unknown), sampling from lower respiratory tract is recommended by the WHO, via sputum or endotracheal aspirates. Avoid bronchoscopy to minimize exposure. Repeated sampling may be necessary if clinical features.* *Management of Acute Respiratory Failure: Minimal data to support or refute the safety of NIV or HFNC. Delay in intubation may increase mortality.* *Lung protective ventilation, prone positioning early (outcome data is pending)* *ECMO may improve survival (MERS data), but is very resource dependent.*

	Other considerations: Re-assessment of fluid status is essential due to cardiac dysfunction. *ICU infrastructure: if airborne isolation room is unavailable, patients should be in single room with doors closed. Shared rooms with dedicated staff is another option. A substantial increase in ICU capacity includes beds, medications and staffing.*
Comments	*Take home points: clinical features of COVID-19 are non-specific, and clinicians should have a high index of suspicion* *Surge prep should focus on increasing ICU beds, infrastructure, supply, and staff protection and mental health* *Be aware of associated myocardial dysfunction, co-infection with influenza or bacterial pneumonia.* *Benefits of steroids are unclear* *Minimize patient transfers out of the ICU* *Viral Shedding continues beyond 10 days after symptom onset in severe COVID 19* *Intubation drills for staff are crucial.* *Very nice summary table of experimental therapies. The use of new therapies must be balanced with ethical and scientific safeguards.* *Research during COVID 19 should focus on high quality trials, sharing data, collaboration, and maintaining ethical integrity.*

Transmission Dynamics of COVID-19 In China

Article Title: *Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study*

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30230-9/fulltext

Source: *Lancet*

Clinical Field: *Other*

Article Type: *Other*

Study Type: *Other*

Patient Group: *COVID-19*

Intervention: *N/A*

Reviewer	*Stefan Jovinge*
Study Design	*Minor Concerns*
Study Design Concerns	*n=8579 . Unclear of how the cases were selected; consecutive cases or any other mechanism.*
Main Results	*1. As disease progressed the major increase was seen in the older (>64) and the younger groups.* *2. Incubation time in the first half decreased from 4.4 to 2.6 days. Over the whole observation period it was estimated to be 5.2 days.* *3. Rt was initially estimated 1.71 at highest. It fell below 1.0 (the epidemiological threshold) within three weeks (after travel restrictions were imposed).*
Comments	*The Rt estimates (2.35) are far below all other estimates made (between 3-4) that the epidemic was controlled within three weeks (rt <1) doesn't match what was seen from an outside perspective.* *Major disease peek run for about four weeks.*