ACTA SCIENTIFIC PAEDIATRICS (ISSN: 2581-883X)

Volume 3 Issue 8 August 2020

Short Communication

SARS-CoV-2 (COVID-19), What We Do Not Know So Far?

Amar Al Shibli and Ghassan Ghatasheh*

Department of Pediatrics, Tawam Hospital, United Arab Emirates

***Corresponding Author:** Ghassan Ghatasheh, Department of Pediatrics, Tawam Hospital, United Arab Emirates.

Received: June 23, 2020

Published: July 30, 2020

Introduction

Coronavirus is a single stranded RNA virus that belongs to a family of viruses called *Coronoviridae*, which can cause disease in both human and animals. Human coronaviruses tend to cause mild upper respiratory tract infections; on the other hand; SARS coronaviruses are sub-classes of Corona virus that cause severe respiratory infection such as SARS-CoV and Middle East Respiratory Virus Syndrome virus (MERS-CoV).

A new strain of coronavirus has emerged since December 2019 in Wuhan city in China, which was categorized by the WHO as a SARS-CoV-2 and announced as a global pandemic in March 2020. The current clinical evidence indicates that the incubation period for SARS-CoV-2 is ranging from few days up to 2 weeks. In adult patients; the clinical features can range from asymptomatic to symptomatic in about 80% of patients while 10% might require hospitalization and 5% might develop severe symptoms requiring critical care. In pediatrics the disease is usually mild and most of the affected patients will recover completely; However, Pediatric death due to SARS-CoV-2 was reported in few patients.

Several countries across the globe and continents got the infection, different strategies were applied by different countries. We start to know more about the virus.

What we don't know about COVID-19 so far

Why the disease severity varies between different countries

It was evident through monitoring the pandemic that some countries were having aggressive disease with very high mortality rates while other countries got a mild disease and it was contained early. Several factors play a role including population density, household transmission, and/or race and ethnicity. Genetic predisposition is one of the most important factors. Was there a mutation in the virus that contribute to the difference in the pathogenesis and virulence? Human immune response is a known contributing factors for several clinic features and has a role in the cytokine storm with its sequels.

Certain geographical areas has lower incidence of infection and less severe manifestations. Most of those areas are tropical zone and areas that had previous epidemics with SARS and MERS. Does that means that there is immunity for COVID-19 if the patient had a previous infection with the same virus? Does that mean that there is possibility of have cross immunity with other infections in tropical countries? Or this is related to the genetic predisposition only?

Is this a natural virus that was mutated or it is a manufactured virus

There are different theories, one theory, the virus is a naturally occurring strain among bats and not a bioweapon, but it was being studied in Wuhan laboratory. On the other hand, there are raising concerns from several countries that "patient zero" worked at Wuhan National Biosafety Laboratory and the Wuhan. The lab employee was accidentally infected before spreading the disease among the common people outside the lab in Wuhan city. There are many reports that support any of the theories and this question will be repeatedly raised for scientific and political reasons.

Was the response from different the health organization appropriate

As the virus is novel there were different approaches that was accommodated by different health institutions/organizations throughout the globe. Some adopted identification and segregation of patients. Others adopted the herd immunity strategy. The strategy depends on people developing immunity from contracting the virus, which is believed to prevent reinfection. Hospitals across the word find themselves suddenly need to deal with excess load on

hospitals. There was shortage in equipments and personal protective equipments. The choice between the two strategies related to multiple factors related to the level of community education, economy and other factors. Which of the 2 strategies was better? How the health care organization will be ready and have a contingency plan for such thing in the future?

Did we contain the spread the pandemic as it should be

The virus was first reported on December 2019, there are reports that it was there even prior to this time. It was started in Wuhan and spread throughout China, different countries. The disease was epidemic in Wuhan city in China, interestingly enough is that, the disease has a very limited spread to the remaining of areas in China; However there was spread to different counties till the disease was declared a pandemic.

Are we going to have a vaccine?

Vaccine makers are racing to develop COVID-19 vaccines and have advanced ten candidates into clinical trials.

Vaccine development is typically a long game. On average, it takes 10 years to develop a vaccine. With the COVID-19 crisis looming, everyone is hoping that this time will be different. It might be. Already, ten vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) are in clinical trials. Although many infectious disease experts argue that even 18 months for a first vaccine is an incredibly aggressive schedule, a few optimists believe that hundreds of millions of doses of vaccine might be ready for roll-out by the end of 2020.

Are we going to have treatment?

Since the beginning of the disease many medications and treatment protocols were tried. So far there are no drugs or other therapeutics presently approved by the U.S. Food and Drug Administration (FDA) to prevent or treat COVID-19. Current clinical management includes infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated.

For example, the recommendations for using Remdesivir, chloroquine, and Hydroxychloroquine to treat COVID-19 have been revised based on data from recently published clinical trials and observational cohort studies. Several antivirals and other medications were tried. Several protocols were adopted. Some medications were initially advised and then proven to be useless or even showed significant side effects. Are we going to have a specific treatment for COVID-19 or not? This is crucial question which will help to get rid of the virus?

Ae we going to have a second wave of the disease

The new virus is rapidly spreading in humans and cases of severe acute respiratory syndromes are being reported worldwide. Health authority advisors and governments from small towns to large countries need to quickly manage and deal with growing epidemiological data on a daily basis. In this work, current available data from reported cases and deaths over time were analysed and treated. Lethality has been calculated by finding linearization of death cases against reported ones, using a time-delayed data transposition. A two-wave statistical model, 2WM, based on the superposition of normal distributions was used to fit current data and to estimate the evolution of infections and deaths, using Microsoft Excel®. The model showed good agreement even for apparent single wave behaviour in some countries and can easily be extended to any number of waves. A gamma distribution was used as a risk function to estimate death probability from patient admission to reported death. Evolution of fatality cases over time can then be estimated from the model with reasonable accuracy. Data from South Korea, China, Australia, Germany, Italy and Spain were used to validate the model. Data from The United States, United Kingdom and Brazil were used to study the epidemiology as the pandemic progresses. Additionally, the 2WM was applied to world data and to the Brazilian state of Santa Catarina. The model was implemented in MS-Excel, a popular and easy to use analytical tool. A template spreadsheet is provided as supplementary material. Constant lethality can be determined from the initial stage of the pandemic wave. Values ranged from 1.7% to 15.3%, depending on the degree of possible sub notification cases. Even for places with low testing, a linear relationship can be found. The two-wave model can be fine-tuned to properly adjust the data. The second wave pattern was estimated according to the first wave parameter. The accuracy for estimating COVID-19 evolution was compared to the classic SIR model with good agreement. According to the model, based on current trends, health protocols and policies, approximately 10,000,000 cases and 860,000 deaths will be recorded worldwide. Approximately 99% of that number would be reached by the end of July 2020 given constant conditions.

What is the link between the inflammatory syndrome and COVID

It has become increasingly clear that children are less frequently affected by severe COVID-19 than adults. However, a new 'hyper in-

flammatory syndrome' in children associated with SARS-CoV-2 has recently been widely reported in the media with notable clusters of cases in New York City and London. This hyper inflammatory syndrome has similarities to Kawasaki disease, Toxic Shock Syndrome, and hyper inflammatory syndromes such as Haemophagocytic Lymphocytic Histiocytosis (HLH) and SLE.

There are many similarities between the clinical presentation of PIM-TS and Kawasaki Disease, in particular, the unrelenting fever, rash, conjunctivitis and peripheral oedema. Vascular involvement has also been demonstrated with echo-bright coronary arteries in all children, and a giant coronary artery aneurysm in one child.

There are some particularly notable features of PIMS-TS including abdominal pain and gastrointestinal symptoms that are predominantly early symptoms. They are less commonly seen in Kawasaki Disease.

Then the Centre for Disease Control (CDC) in America came up with another name for the same syndrome, MIS-C, which stands for Multisystem Inflammatory Syndrome in Children. An individual aged < 21 years presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (> 2) organ or neurological) AND involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic No alternative plausible diagnoses And Positive for current or recent SARS-CoV-2 infection by RT-PCR serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptom

What evidence do we have currently?

The first case series to describe this cluster of children was published on May 7, 2020 in Lancet by Riphagen., *et al*. Subsequently, an observational cohort study of children in the Bergamo province, Italy, was published on May 13, 2020 showing a 30-fold increased incidence of KD during the SARS-CoV-2 pandemic. Interestingly, they highlighted a higher rate of cardiac involvement and features of inflammation ('macrophage activation syndrome'). A preprint from France has described a cluster of 17 cases within 2 weeks presenting in a similar manner. Clusters of children with similar presentations have been reported by news outlets in the United States and Spain. Abdominal pain, vomiting and diarrhoea have been the predominant early features so far in all cohorts.

Of note, there are yet to be similar reports from the Asian epicentres that were first affected by the virus.

Does infection gives immunity? How long it will last?

Existing limited data on antibody responses to SARS-CoV-2 and related coronaviruses, as well as one small animal model study, suggest that recovery from COVID-19 might confer immunity against reinfection, at least temporarily. However, the immune response to COVID-19 is not yet fully understood and definitive data on postinfection immunity are lacking. Amidst the uncertainty of this public health crisis, thoughtful and rigorous science will be essential to inform public health policy, planning, and practice.

The durability of neutralizing antibodies (NAbs, primarily IgG) against SARS-CoV-2 has yet to be defined; persistence up to 40 days from symptom onset has been described. Duration of antibody responses against other human coronaviruses may be relevant in this context. For example, following infection with SARS-CoV-1 (the virus that caused SARS), concentrations of IgG remained high for approximately 4 to 5 months before subsequently declining slowly during the next 2 to 3 years.4 Similarly, NAbs following infection with MERS-CoV (the virus that caused Middle East respiratory syndrome) have persisted up to 34 months in recovered patients.

Is the world after COVID-19 will be the same as the world before it?

It is really hard to answer that question, but what we are sure that even if this is the case then it will need time.

We are hoping that the world will be ready for such pandemics in the future and that the countries will invest more in health care systems. With time we will have more and more answers for this.