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Letter to Editor

Covid-19: are we treating the wrong disease, the wrong way with the wrong attitude?

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Covid-19 is now a 6.0 months old disease. After its first identification and early encounter, many speculations about its natural course and various pathogenesis mechanisms have been made. From ACE-II Rs mediated viral attachment to pneumocyte damage, and diffuse endotheliitis, still a lot is left to answer on pathogenesis, immunity and other important aspects of this disease [1,2,3]. What we have now is some studies, observational lab and clinical data only that keeps us guessing what is going on with this novel disease.

But in an unusual response to a syndrome, various societies and governing authorities around the world got busy with their routine of prescribing treatment guidance. A thorough perusal of these documents let us conclude that the general theme is to provide what best can be done in such desperate scenarios. This data and guidance is largely based on the evidence which are hardly of a quality to believe religiously, mostly observations and extrapolations of data from previous viral illnesses [4,5].

In a hurry of prescribing treatment guidance, we might have done more harm than good. Especially in a developing world, where many times these guidelines are taken as a tool to avert treatment modalities and even deny new research on therapies. Let's focus on two major concerns of critical care physicians globally (sepsis and ARDS) and the research and guidance presently available on these topics. It may not be hard to spot various strategies that were recommended earlier and now almost banned from practice. Also it's not very difficult to spot 180 degree turns on some other non recommended strategies.

Simultaneously it's important to emphasize here that it took us 14 yrs to realize that low tidal volume ventilation protects lungs, and proning actually helps in moderate to severe ARDS mortality with adequate acceptable evidence. But now we don't have that much time to react.

Covid-19 is a new disease about which we know very little. How it originated, mechanisms by which it can spread, pathogenesis, how it interacts with the human body, reasons for different varieties of phenotypes, and lastly therapies which actually can help. But unanimously everyone would agree that it has pandemic concerns and is proving to be very lethal in the present day. Covid-19 also has a capacity to overwhelm any of the finest health care systems in world, and citing these reasons it is rather too early for us to provide guidance or produce a position statement which is based on old observations or mere little data of itself, rather societies should have taken the task of pushing for more and more research and allowing clinician on the front to take their own decisions for treatment part with rapid update of available data. All are already aware of what a best practice means for ICU general care, what fluid is safe in most of the scenarios, what vasopressor to choose if the need may arise, at what point an oxygen therapy is needed and so on. These are the well proven and well ingrained facts in practice.

What was actually needed, was a guidance about the experimental treatment strategies and how and when to use them in a given patient in desperate situations, which was not based on data (as obviously evidence and data is scarce for covid-19 and continuously evolving) but on physiological expectations from the known clinical course of the disease. We must not restrict them by providing statements of "use in a research setting" as not everyone is doing research and many are just struck with pandemic and epidemic as well.

Even in this desperate situation every data point and outcome (positive or negative) is a research setting, even if someone has an absolutely negative response with some experimental strategy that is also a valuable input of harm from such strategy.

For simple example, in a hurry, we have mistaken on covid-19 by labeling it as pneumonia and simply viral ARDS. At least present observations of front line doctors indicate so. Several terminologies for the disease in observational data have been coined, among them "HAPPY HYPOXIC" seems a very close and most frequent observation of severe covid-19 requiring hospitalization and even ICU care. It is truly a novel finding, as any of the ARDS and sepsis never had a hypoxic and un-distressed patient. Prominent authors even came forward with a similar view of having 2 different phenotypes of ARDS found in severe covid-19 [6, 7]. and among them typical ARDS (low compliance lungs) is seen late in the course of illness. It was clear that rather a diffuse alveolar damage (DAD), it may be a Diffuse pulmonary capillary damage (DPCD) and diffuse systemic capillary damage (DSCD) that is leading to typical covid-19 findings and it is our injudicious interventions (high PEEP, ARDS ventilation strategy etc) that is leading to typical ARDS phenotype later in the disease. Similarly some autopsy findings suggest diffuse endotheliitis and venous and arterial thrombosis [3,8]. Observational lab data (Rising D-dimer, CRP, Coagulopathy, cardiac stress, and elevated cTroponin) in the sickest of the covid-19 patient goes just in the line of these findings [9,10,11] For these patients "high peep strategy" for ventilation is largely proving to be detrimental and many of such cases

become non responsive to any therapy and their fate is sealed. Early prophylactic anticoagulation and even early aggressive therapeutic anticoagulation are the debated therapies for such subtype [12,13,14].

Similarly epidemiology and observational data suggest that the natural course of this disease can be categorized in 3 phases [15] First early infection phase is first 5-7 days, where antiviral drugs could have worked well. Second pulmonary phase when hypoxia starts developing after 5-7 days and diffuse sepsis like cytokine response starts building up. This is probably the best time to start immune modulatory (including steroid HCQs) therapies. And lastly, the hyper inflammatory phase, when most of the therapies would have failed, is the time for rescue and costly therapies (like convalescent serum therapy, extracorporeal cytokine filtration, anti cytokine therapies).

An approach like this could have been suggested and then treating physicians can come to a final decision considering many social, resource, economic and other factors. If by any of such strategies we could have avoided even ICU admissions, in present scenarios that would have been of great help.

These are desperate times, and desperate times have a quality. They make revolutionary changes in styles and patterns we do work. We were already transitioning from absolute evidence based care to a more individualized care (especially when a question is in a grey zone), and possible that Covid-19 have completed that transition too fast to be acceptable. If we don't move in the appropriate direction and keep on riding against the tide, we may lose many lives before we come to concrete evidence based conclusions.

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