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Why Not Lose Faith in Science in the Fight Against Coronavirus

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ABSTRACT

Background: One of the most vulnerable group to cope with the consequences of COVID-19 pandemic are women, particularly pregnant ones. **Objective:** The aim of this article was to make review of the scientific literature to show clearly that pandemic is not so dangerous neither for mother nor her unborn and newborn children. **Results and Discussion:** It should be stated that most of the scientific papers on COVID-19 are currently being conducted in a way that would probably be completely unacceptable to serious science in any other circumstances. Taking into account everything we have learned about the SARS-CoV-2 virus so far it comes as a surprise that there has not been a more intense scientific debate on whether the blind lockdown model, implemented by most national governments, was truly an appropriate response to the challenges posed by the pandemic. **Conclusion:** Deep analysis what science in perinatal medicine did assess and what it recommended to perinatal world it may be followed by principles that the research of the members of the Academy will not be the first to be published, but we certainly aim that the scientific evidence published by Academy is fast, reliable and implementable.

Keywords: Corona pandemic, scientific approach, Internation Academy of Perinatal Medicine, global issue of pandemics.

1. BACKGROUND

Significant scientific and technical progress has been made in the second half of the XX century. We will just mention a few of the breakthrough events that took place in the 1960s and 1970s, usually with very positive results and considerable social impact: the first Intensive Care Units were introduced, patients began to be regularly treated with dialysis, which for the first time was performed in their own homes; kidney transplants were made and more knowledge acquired about the immunological mechanisms of rejection; brain death was diagnosed; a great deal of progress was made in molecular biology; in psychopharmacology, in hormone treatments aimed at regulating human procreation and in pre-natal diagnosis (1).

These biomdical advances in new technologies caused such bewilderment not to say fear that doctors and biologists understandably became interested in clarifying concepts such as what is good, who has the authority to decide what is good and what is not good, and on what this authority is based. They also began searching for ethical decision-making criteria which could be broadly applicable. Where are we now living with corona? COVID-19 has already changed the world in the magnitude never seen before. The invisible devil has already affected the life of virtually every single human being on the planet. These issues are reviewed in recently published paper on Pandemic corona virus issue – how do we respond? (2-8).

2. HOW STRONG COVID-19 IS DANGEROUS?

These real numbers of COVID-19 infections are much higher due to the lack of testing capacity and underreporting. COVID-19 is, although dangerous, very fair one choosing not only poor, homeless, old people with chronical diseases, but also Prime Ministers, Crown Princes, celebrities and wealthy people. In an elegant recent editorial Cadmus (9) sent a message.

The unanticipated consequences of COVID-19 are impacting every sector, field of activity and level of global society today. They are raising unemployment and inequality, compelling adoption of unconventional economic policies, polarizing societies, activating political extremism, aggravating competitive nationalism,

contesting the veracity of scientific knowledge, undermining international cooperation and the functioning of the multilateral system.

At a more fundamental level, the Pandemic has exposed a plethora of hidden threats to human wellbeing which challenge prevailing notions of security, laid bare the inadequacy of partial theories and siloed disciplines, revealed the limitations of narrowly framed sectoral policies and strategies implemented by specialized agencies, and highlighted fundamental questions regarding the complex, interconnected nature of the social reality on which our understanding of the world and ourselves is based.

A new approach to security is urgently needed which relates and synthesizes the multiple dimensions of human life to present a comprehensive, integrated concept of human security. The Sustainable Development Goals identify all the major components but deal with them separately as independent dimensions. Human Security places people at the center and views all these elements as inseparable and interdependent dimensions of an indivisible social whole.

The pandemic thus reiterates the need for fundamental changes in theory, intellectual disciplines, educational curricula and content, the structure and coordination within and between different departments and levels of government, policy-making institutions, programs for implementation and measures for assessment.

At the international level it has profound implications for our conception of multilateralism and the type, structure and relationship between the complex array of international institutions established to foster peace and human security for 'we the people'. At a still deeper level it points to the need for a fundamental shift from analytic thinking about specialized, compartmentalized subjects to comprehensive perspectives that include all parts of global society and also perceive the deeper forces and process of social evolution by which the various fields, sectors, levels, ideas, values and aspirations are related and integrated with one another as dimensions of a single transdisciplinary knowledge of the whole.

COVID-19 is a call for new ways of thinking, knowing, educating, decision-making and practical execution of measures to promote human security of all for the common good. Humanity is called on today to change many things, but most of all our understanding of the world we live in, our place in it, and our relationship to it and to one another (9).

One of the most vulnerable group to cope with the consequences of COVID-19 pandemic are women, particularly pregnant ones. The data about outcome of pregnancies with COVID-19 infection are scarce and the results of the current studies are inconsistent and are obtained mostly from mid- or low-income countries with different health care systems, non-equal access to pregnancy care low-income and pregnancy surveillance.

The knowledge gained from previous human coronavirus outbreaks, namely the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Ebola Virus Disease (EVD), suggests that pregnant women and their fetuses may be particularly susceptible to poor outcomes.

The prevalence of the COVID-19 infection during pregnancy in the epidemic areas is largely unknown. So far, eighteen articles reporting data from only 108 pregnancies between December 8, 2019 and April 1, 2020 have been summarized in the recent systematic review.

There was one neonatal death and six admissions to the intensive care unit. Although it seems that severe pregnancy and neonatal complications during COVID-19 pandemic are due to the premature birth and cesarean delivery complications (as the predominant delivery mode), there are also case-reports on maternal deaths.

While most of the reported cases focused specifically on the maternal outcomes and possible vertical transmission, less attention has been payed on fetus as a patient in such pregnancies. It should be stated that most of the scientific research on COVID-19 (also during pregnancy) is currently being conducted in a way that would probably be completely unacceptable to serious science in any other circumstances.

The research has been published fast-tracked and possibly without proper peer-review process, using small and often insufficiently representative samples, numerous imperfections in the research design are being overlooked as well as many other details which are usually taken into account. All of these factors resulted in a flood of superficial research, all in a desire to get answers as fast as possible. Unfortunately, rush and wrong answers can cause greated damage than an accurate but slow one.

It is realistic to expect a whole series of daily reports on various „scientific research results" which will in a week or two turn out to be wrong or unfounded. The number of domestic violence cases reported to a police station in Jingzhou, a city in Hubei Province, tripled in February 2020, compared to the same period the previous year. Security, health, and money worries create tensions and strains.

More than half of the world's population was under lockdown conditions by early April. Violence against women remains a major global public health and women's health threat during emergencies. One of the solutions may be the extended use of mobile devices and tablets that has revolutionized healthcare for some of the hardest to reach communities across Asia, Africa and the Middle East.

3. CROSS-SECTIONAL STUDIES ABOUT COVID-19 IN THE SCIENTIFIC LITERATURE

The second author, Olus Api, did review of literature which is included in this paper, and made the next description.

Vertical transmission is defined as the transmission of the infectious pathogen from the mother to the fetus during the antepartum and intrapartum periods, or to the neonate during the postpartum period via the placenta in utero, body fluid contact during childbirth, or through direct contact owing to breastfeeding after birth. Although multiple infectious vectors have been shown to be capable of vertical transmission, the possibility of vertical transmission of SARS-CoV-2 from the infected mother to the fetus or neonate has been a point of a recent debate with previous systematic reviews, albeit with a limited number of studies, concluding that there is no evidence of vertical transmission. No known cases of vertical transmission have been noted with similar coronaviruses such as SARS

and MERS, although the number of cases has been limited. COVID-19 shares 50% and 79% sequence homology with SARS and MERS, respectively; despite this homology, a similar lack of vertical transmission cannot be assumed. A concern over vertical transmission in the case of COVID-19 exists for several reasons.

First is the known tissue tropism of COVID-19. The main receptor that COVID-19 binds to enter a cell is the angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is expressed in the placenta and is found in the syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle from both primary and secondary villi. A recent systematic review also found evidence that ACE2 is expressed in gynecologic organs such as the ovary, uterus, and vagina. Overall, ACE2 expression is seen in numerous tissues that are in direct communication with a developing pregnancy. These data were further bolstered by a recent single-cell RNA sequencing analysis that found ACE2 expression in stromal, perivascular, placental, and decidual cells at the maternal-fetal interface. However, a single-cell RNA sequencing analysis looking at the coexpression of ACE2 and the transmembrane serine protein for virus spike (S) protein priming, transmembrane serine protease 2 (TMPRSS2), showed that only a minimal number of placental cells express both proteins in any trimester.

Furthermore, this group showed that chorioamniotic membranes from the third trimester exhibit minimal coexpression of both proteins. Nonetheless, the authors suggested that viral entry into placenta cells may still occur using a combination of ACE2 and a noncanonical cell-entry mediator. In addition, animal data indicated that oronasal inoculation of pregnant mice withmouse hepatitis virus (MHV), which is part of the Coronaviridae family, led to the dissemination of the virus to the fetus in each trimester. However, the dissemination was dependent on the strain of MHV and the strain of mice, with BALB/cByJ mice being the most susceptible. In addition to this biological plausibility, there are several lines of clinical evidence concerning vertical transmission. Initial reports from China have documented immunoglobulin M (IgM) antibodies in neonates born to mothers who had positive results for COVID-19 raising concerns for in utero transmission because IgM cannot cross the placenta.

Moreover, several recent case reports provided evidence that COVID-19 can infect the placenta as confirmed by the presence of SARS-CoV-2 viral RNA and protein in the placenta and evidence of virions found within the syncytiotrophoblast.

Answering the question of vertical transmission is crucial for guiding patient counseling regarding COVID-19 related risks before and during pregnancy and obstetrical care for women infected with COVID-19.

The most recent meta-analysis published in the latest issue of AJOG is able to answer this difficult question. The authors of this meta-anaysis conducted a systematic search of the literature from Cochrane Library, DisasterLit, Ovid, Embase, Ovid Medline, Google Scholar, LitCovid, MedRxiv, Pubmed, Scopus, and Web of Science Core Collection databases to find relevant articles published from inception of the database to May 28, 2020, to identify cohort studies, case series, and case reports of pregnant women with COVID-19 that include information regarding fetal or neonatal COVID-19 testing.

This systematic review included 30 eligible case reports describing a total of 44 SARS-CoV-2 positive pregnant women with outcomes available for 43 neonates and 39 cohort or case series studies describing a total of 936 tested neonates born to SARS-CoV-2 positive pregnant women. Data in this review were limited to pregnant women who had laboratory-confirmed SARS-CoV-2 infection diagnosed by RT-PCR in an NP swab specimen, which is considered the gold standard for the diagnosis of COVID-19. Because of the recent onset of the pandemic, the vast majority of data came from pregnant women in their third trimester, whereas the greatest paucity of reports involved patients in the earlier stages of pregnancy.

Of the 30 case re- ports, 29 reports described neonatal outcomes of women in their third trimester, whereas only 2 case reports described outcomes of women in their second trimester. To date, no reports are available describing the assessment for the presence of SARS-CoV-2 in products of conception of a first-trimester pregnancy. The details of this syudy is as follows:

936 neonates from mothers with COVID-19, 27 neonates had a positive result for severe acute respiratory syndrome coronavirus 2 viral RNA test using nasopharyngeal swab, indicating a pooled proportion of 3.2% (95% confidence interval, 2.2e4.3) for vertical transmission. Of note, the pooled proportion of severe acute respiratory syndrome coronavirus 2 positivity in neonates by nasopharyngeal swab in studies from China was 2.0% (8/397), which was similar to the pooled proportion of 2.7% (14/517) in studies from outside of China. Severe acute respiratory syndrome coronavirus 2 viral RNA testing in neonatal cord blood was positive in 2.9% of samples (1/34), 7.7% of placenta samples (2/26), 0% of amniotic fluid (0/51), 0% of urine samples (0/17), and 9.7% of fecal or rectal swabs (3/31). Neonatal serology was positive in 3 of 82 samples (3.7%) (based on the presence of immunoglobulin M).

4. KEY FINDINGS OF THIS STUDY

The vertical transmission of COVID-19 in the third trimester is approximately 3.2% (22/936) by infant nasopharyngeal swab testing, with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA positivity in other test sites ranging from 0% (0/51) in amniotic fluid and urine (0/17), 3.6% (1/28) in the cord blood, 7.7% (2/26) by placental sample analysis, 9.7% (3/31) by rectal or anal swab, and 3.7% (3/81) by serology.

5. WHAT DOES THIS ADD TO WHAT IS KNOWN?

There is evidence of SARS-CoV-2 vertical transmission when the infection occurs in the third trimester of pregnancy. To conclude, vertical transmission of severe acute respiratory syndrome coronavirus 2 is possible and seems to occur in a minority of cases of maternal coronavirus disease 2019 infection in the third trimester. The rates of infection are similar to those of other pathogens that cause congenital infections. However, given the paucity of early

trimester data, no assessment can yet be made regarding the rates of vertical transmission in early pregnancy and potential risk for consequent fetal morbidity and mortality.

The activities of the International Academy of Perinatal Medicine had the remarkable impact of perinatal care worldwide. Naturally, the future depends on role of its members because no academy can be appreciated by itself but by the reputation of each and all its members. Indeed, science is true global activity because its very nature is global.

Most of us welcomed positive globalization process but with the recent pandemic of corona disease we are introducing negative part of globalization with many unpredictable developments. In science we do not have good and bad work. By following our principal duties we justifiably expect that creative and visionary members of the Academy show again its intellectual power in order to solve this global pandemic.

Taking into account everything we have learned about the SARS-CoV-2 virus so far it comes as a surprise that there hasn't been a more intense scientific debate on whether the blind lockdown model, implemented by most national governments, was truly an appropriate response to the challenges posed by the pandemic.

Today, when we know more about the transmission modes of SARS-CoV-2 (primary mode is by respiratory droplets) as well as how dangerous it truly is (much less than previously thought), it is time to reassess the first radical epidemiological reactions. This needs to be done not to accuse someone of mistakes, but in order to plan future action.

It is clear that in the beginning numerous countries opted for radical epidemiological measures because we didn't have enough information about the COVID-19 pandemic but now the time has come to ask the questions about the weirdly mingled responsibility of politicians and epidemiologists who persist in scaring the populace with threats of the virus without considering the general consequences.

Individuals who bravely provoke the world scientific community by insisting on a discussion based on data and not assumptions are actually very rare.

One of the most famous 'provocateurs' is Michael Levitt, the Nobel prize winning biophysicist and structural biology professor who's made a name for himself by developing multiscale models for complex chemicals. Since the COVID-19 pandemic started, he has been spending 18 hours a day analyzing all available data, drawing conclusions, making prognoses and publicly debating his findings.

Levitt's biggest sin was that he warned, early in the pandemic, that the spread of the virus will not be as rapid or dangerous as it seemed by initial findings from Wuhan. That was brave.

A Jew born in South Africa with an unquestionable scientific reputation who bravely and precisely diagnosed the development of the pandemic. His tweets were sensational and far removed from the political-scientific mainstream

Back in March, he calculated that the growth of the death toll in China will slow down. He also announced the reduction of the infection rate and explained why, dealing with the SARS-CoV-2 virus, we can't speak of exponential growth even though that word became a buzzword in media and scientific reports.

He warned the scientific doomsayers that they're highly exaggerating the expected death rates, and his greatest 'sin' was pioneering the attitude that blind lockdown will not save lives but that it will cause dramatic economic consequences and indirectly cause more deaths than COVID-19.

Until recently, statements like this seemed wildly extravagant. It didn't help that Levitt was backing everything with mathematical analysis of exact data.

Today Levitt is a resentful scientist calling out the entire epidemiological profession; he is warning that epidemiologists are guided by the idea that it is better to implement radical epidemiological measures and prevent the pandemic from escalating, but that they're irresponsibly disregarding the damages caused precisely by those radical epidemiological measures. The biggest problem of the COVID-19 pandemic is that it caused economic damage of epic proportions. Levitt is the first one in the scientific community who is demanding not just that we discuss the data but that we assign responsibility for the wrong assessments.

Anyway, it needs reminding that the huge scope of damage caused by the COVID-19 pandemic is actually impossible to asses: between GDP losses, the rise of debt, social problems and death toll caused by other acute and chronic diseases... We should instead take account of how much has COVID-19 changed our future.

Those who have the nerves and knowledge to read studies with complex mathematical models should read „Scarring Body and Mind: The Long-Term Belief-Scarring Effects of Covid-19". The analysis was published by three scientists employed by American institutions with the best access to statistical data in the world – the Federal Reserve system and the National Bureau of Economic Research

The authors of "Scarring Body and Mind" reason that the greatest economic consequences will be due to changes in behavior after the current health crisis is resolved.

They stipulate that expecting new shocks will become a permanent issue and that living in fear will cause greater damage to the long-term growth than this short-term reduction in output. Which was in itself a frightening experience.

6. LONG-TERM CONSEQUENCES

Long-term consequences projections in several scenarios of the authors are, at the very least, twice as bad – precisely because they're long-term: the fear and uncertainty rob us of perspective, rob us of a future, rob us of the growth which the future generations should inherit.

The coordination of scientific resources on a global scale was completely nonexistent, while at the same time two thirds of scientists are boasting of being globalists. The world today would probably be much less different from the pre-pandemic time if the global coordination of science didn't fail so miserably.

He believed that his measures would keep the number of infected below 20 thousand. So, he not only overestimated the danger of the virus, but also the efficiency of his measures in protecting against a virus which turned out to be much less dangerous than he announced.

Although Ferguson was called out by other virologists for strained assessments on which he based his models (e.g. that 50 percent of households will not observe quarantine),

Ferguson didn't resign his position in the Scientific Advisory Group for Emergencies for making wrong projections.

He only resigned after it was discovered that he was meeting with a married woman, undermining the governments social distancing message. "I acted in the belief that I was immune, having tested positive for coronavirus and completely isolated myself for almost two weeks after developing symptoms."

Ferguson didn't do anything illegal because he didn't leave his house. He was only visited by a certain woman. Twice. That doesn't seem like too much. Twice is still twice, and he had enough free time to respond to the emails of the anxious Levitt. But, he did not. Both authors are members of IAPM which is performing large research on corona in pregnancy. Interested reader will find more details in the quoted list of references (11-25).

International Academy of Perinatal Medicine and, also, other Academies in this field, including Academy of Medical Sciences of Bosnia and Herzegovina (which organized in November 2020 in Sarajevo Special Topic Conference about COVID-19 pandemic, regarding Bosnian and Herzegovinian experiences) have both - the RESPONSIBILITY and PRIVILEGE to conduct scienfitic research on COVID-19 pandemic impact on maternal, fetal and neonatal health (26-32).

Without any doubt, this will open up again new visionary solutions and one of them will be deep analysis what science in perinatal medicine did assess and what it recommended to perinatal world. The principle of the Academy should not be: „any information is better than none".

7. CONCLUSION

We repeat again that the information should be feasible, usable and implementable and proven according to the best scientific principles.

It may be that the research of the members of the Academy will not be the first to be published, but we certainly aim that the scientific evidence published by Academy is fast, reliable and implementable.

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