

SPECIAL ARTICLE

(Our) World with COVID-19

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ABSTRACT

The pandemic COVID-19 certainly has terrible impact to the world. Not only on health issue, but other aspects which are unavoidably involved are environment, economics, politics, social and the new way of living. This new normal way of life certainly influences medical practice. The physicians of every expertise should acquire additional knowledge and be competent in taking care of an individual, patients, and even themselves to stay safe from the deadly virus. Some health technologies have been rapidly emerging to serve the needs of the world. A distinct example is COVID-19 vaccine invention, manufacturing, and distribution. The deoxyribonucleic acid (DNA) or new technology of Messenger ribonucleic acid (mRNA) vaccines against the COVID-19 had extremely expedited production process and Food and Drug Administration (FDA) approval like it has never been before. Another example is a digital health which has been introduced for quite a while. A steep and expanding growth of various digital health technologies and artificial intelligence is more widely accepted and practiced e.g. telemedicine, health data sharing, medical applications, and etc. These digital health technologies are also incorporated with many business start-ups to serve necessities to live in a new way of life. The effects of COVID-19 to obstetrics and gynecology practices are also evidenced in both tangible and intangible aspects: safety issues related to the infection (medical care providers/ hospital management vs women/patients/ her family members), health outcomes (reproduction, perinatal, cancer), selective type of service (elective vs urgent vs emergent), education and training (face-to-face vs online), a balance of specialties needed now and in the upcoming future (reproductive endocrinologist, obstetricians, gynecologic oncologists), and etc. All of us, as a physician or as an individual, should stay safe, have knowledge and strength to sail safely through the virus-inducing storm.

Keywords: COVID-19, corona virus, vaccine production, digital health, Obstetrics and Gynecology.

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Introduction

The global panic over the new strain of a deadly virus, named by the World Health Organization as 'COVID-19', has been occurring for more than 1 year. After the beginning episode in China in December 2019, the infection has become a life-threatening pandemic all over the world. This viral catastrophic event of the century has similar feature with the rampant Spanish Flu in 1918. Both are a deathblow which killed or have killed millions of people. Until April 2021, the world is still struggling to control the rises of infection rate, severe illness, and death.

Impact of the pandemic COVID-19 is not only on health of an individual but also on people's livelihoods in all aspects. Major negative influences are on many systems, for examples, social, economics, environment, politics, etc. Everyone must inevitably live in a new way of life or the 'new normal'.

This article is gathering information from available evidence to draw a picture how the world of healthcare must be changed during and probably after the pandemic COVID-19. Aside from the effect on Obstetrics and Gynecology practice, an overview of other relevant situations is also covered.

Health Leading Policy

It is probably one of the first few revolutions in the world that 'health policy' is the arrowhead of the policy in all nations rather than politics, military, or economics. The goal of infection control had been challenged by some national leaders who concerned more on the economics. This irrational judgment has led more deaths among their people and unfathomable damage to their countries before a turn to public health directions. Many other countries also imply diplomacy led by health as never have been before. For examples, a vaccine diplomacy which was initiated by China by giving away the COVID-19 vaccines to her allied countries. This led other countries to express their positive act by providing medical support and supplies to their alliances as well. A collaboration of vaccine diplomats under an informal strategic dialogue between the United States, Japan, Australia and India, so called

'Quadrilateral Security Dialogue; QSD or Quad) has also been executed.

COVID-19 control is a major challenge to a national public health system. Thailand, one of the top 5 countries which have been recognized for the pandemic control achievement⁽¹⁾, uses health policy to lead the national direction. Our achievement is based mainly on the policy---'health of Thai people' should take preponderance over economics. We have implied many regulations and measures, a 'lock down' regulation to prevent or minimize a spread of the infection. Expert opinions and advice of physicians (especially infectious or viral disease doctors) are followed. The success of COVID-19 control in Thailand and other countries leads other countries to re-assess and to adapt their national health policies⁽²⁾.

The new normal practices are actively proceeding in different levels. The microscopic level of practice makes an emphasis on personal hygiene, social distancing, wearing mask, and frequent handwashing. The macroscopic social practice generally has the same principle; for examples, each hospital or health unit limits number of medical users/ patients to those with urgent or emergent conditions, effective screening and preventive measures of medical personnel; in-house of public services including restaurants and bars are withheld; home delivery services have become more common, and etc.

These new normal lives are expected to continue for uncertain duration. It must be carried on, at least, until an improvement of pandemic control when a herd immunity is developed (by nature or by adequate vaccination coverage) or a discovery of an effective treatment. Some educational institutions have attempted to develop a predictive model of COVID-19 spread and existence. However, they can foresee only a short-term of only 2-3 weeks pattern. Until then, a 'New Normal' way of life must be carried on to the "Next Normal", and probably eras after that.

Health Technology Leap

In a current era of advanced of information and technology (IT) especially in industrial development,

COVID-19 has provoked a leapfrogging advance in medical IT as has never been before. This was clearly demonstrated by biotechnology in vaccine development and digital health which included telehealth or telemedicine.

Biotechnology

A renowned example of the biotechnology is a development of an mRNA vaccine to fight against COVID-19. This mRNA vaccine (one of the nucleic-based vaccine) is based on a novel technology in designing an mRNA. The mRNA, which after injected into the body, will trigger cells to produce the virus-resembling protein. This protein will, in turn, trigger human immune system to function against the virus. The new technique of mRNA vaccine production has several advantages. It has higher safety than the DNA vaccine because the production does not involve genuine virus or viral particle. This vaccine material is not incorporated into the genome (non-integral platform) which can cause insertional mutagenesis^(3,4). Furthermore, higher immunity level was found due to varieties and large amount of designed protein antigens. This, in turn, leads to lower chance of vaccine resistance.

Not only an evolution of mRNA vaccine, the accelerated process of development must also be remarked. The vaccine development teams of 2 pharmaceutical companies, Moderna® (derived from 'modified' and 'RNA') and BioNTech (derived from 'Biopharmaceutical New Technologies') in collaboration with Pfizer⁽⁵⁾, could achieve the vaccine template within a week after having the genetic code of COVID-19⁽⁶⁾.

Development of COVID-19 vaccines in Thailand

A development of vaccine technologies also takes place in Thailand. There are many organizations which have missions in research, development, and manufacturing of COVID-19 vaccine. Examples are Chula Vaccine Research Center (Chula VRC), Mahidol University, Baiya PhytoPharm (a start-up project of two instructors from Faculty of Pharmaceutical Sciences, Chulalongkorn University), Bionet Asia, and the

Government Pharmaceutical Organization (GPO) of Thailand⁽⁷⁻¹⁰⁾.

One private segment which actively executed many activities to fight against COVID pandemic is the Siam Bioscience group, which all stockholders are Thai. This group is the only corporation in Thailand and Southeast Asia, which can use high technology to perform the whole process of biomedicine production: initiation, development, in-house preparation of raw materials and medicinal production, packaging, and delivery⁽¹¹⁾. During the COVID-19 pandemic, the Siam Bioscience group has collaborated with the Thai Department of Medical Science to develop and to produce the COVID-19 RT-PCR test kit. The test, which has high quality of WHO standard, has been manufactured in a rapid manner. Now, the test kits are patronizing delivered to all laboratories in Thailand⁽¹¹⁾.

The Siam Bioscience group also collaborates with AstraZeneca pharmaceutical company and Oxford University in a production of COVID-19 vaccine as many as 26 million doses for Thai people. With an additional 35 million doses purchased by the government, a total of 61 million doses will be available. A maximal capacity of vaccine production by the company may reach 180-200 million doses annually or an average of 15 million doses monthly. The Department of Disease Control under the Ministry of Public Health is planning to distribute the vaccines to target population in Thailand. The extra-doses as well as technology in vaccine production will be bestowed to neighboring countries in ASEAN⁽¹²⁾.

Chula Vaccine Research Center (Chula VRC), which was founded in 2017 under a supervision of Professor Kiat Ruxrungham, is another active organization which has conducted a research to develop COVID-19 vaccine. The objective of Chula VRC is to produce an effective, safe, and low-cost vaccine, in order to be widely accessible all over Thailand and other low-resources countries. The Chula VRC vaccine (ChulaCov19) uses similar platform mRNA as that of Moderna and Pfizer-BioNTech. The mRNA will be coated with lipid nanoparticle from Canada. The study was conducted as an animal testing (mice and monkeys)

in March 2021. A high immunity response was elicited among the COVID-19 affected animals (intranasal inoculation of virus) who had received 2 shots of ChulaCov19 (3-week apart). The nasal and pulmonary viral load were reduced by 10,000,000 folds, with a prevention of viremia and clinical symptoms compared to the unvaccinated animals who had high viral load with clinical symptoms in 3-5 days after inoculation. As of now, the 3-month clinical outcomes are in close follow-up. With the promising results, the clinical study in human will be launched in May 2021. Another benefit of ChulaCov19 is a simple storage process that it can be kept for at least 1 month in a regular freezer (at a temperature of 2-8°C). Hence, the vaccine can be conveniently distributed nationwide. With a benefit of mRNA vaccine which can be designed to fight with a resistant-strain of COVID-19, Chula VRC is in preparatory phase to develop ChulaCov19-2 for a resistant-strain virus to the current vaccines^(13,14).

Not only an innovation of vaccine for a current viral pandemic, another goal of Chula VRC is to develop a high and international standard vaccine to prepare for a fight with any global threats from other outbreak of infection in the future⁽¹³⁾.

The Government Pharmaceutical Organization (GPO) under Ministry of Public Health, Faculty of Tropical Medicine of Mahidol University, and Program for Appropriate Technology in Health (PATH) which is a non-profit organization (located at Seattle, USA) are collaborating to develop inactivated COVID-19 vaccine. The GPO had acquired this technology from Flu vaccine development. The initial Newcastle virus (known to infect only chicken but not human) was genetically modified (at Icahn School of Medicine at Mount Sinai in New York City and University of Texas) to possess spike protein as of COVID-19 virus. The simulated virus, which cannot infect cells, are cultivated and explicitly grown in chicken egg. This GPO COVID-19 vaccine, so called 'NDV-HXP-S' was approved by the Thai FDA to proceed with a clinical study after animals testing (toxicity testing in rat in India and efficacy in immunity production in hamster in the US). The clinical study was initiated in March 2021 and, if successful, is

expected to have a license for commercial production in 2022. The NDV-HXP-S is estimated to be less than 5 USD, and an annual production of 25-30 million doses are expected⁽¹⁰⁾.

A development of several other COVID-19 vaccines are in progress by few other sectors e.g., protein subunit (plant-based) vaccine by Baiya Phytopharm Co., Ltd. in collaboration with Faculty of Pharmaceutical Sciences, Chulalongkorn University⁽⁸⁾, DNA vaccine of Bionet Asia pharmaceutical company⁽⁹⁾, and etc.

The development and manufacturing of various platforms of COVID-19 vaccine in Thailand should be a pride of all Thai people. This important step in health care productivity will lead Thailand to a new arena of technology progression and being ready to fight against any other new pandemics in the future⁽⁹⁾.

Digital health

Everyone realizes that a 'distancing' has become a new normal way of life. It involves many activities of daily living, business, education, and medicine. In medicine, 'digital health' is a clear example of a means to keep distancing.

Digital health has a broad definition. Generally, it refers to a use of digital technology for health care. This includes not only electronic health record which has been used for over decades, but also other ITs which are coming about, such as, telehealth, telemedicine, remote patient monitoring, various wearables, artificial intelligence, health applications, and etc. Although these digital health technologies have been developed for quite a while, their usages are super-accelerated in the COVID era to minimize viral spread due to face-to-face communication. Data have shown a remarkable expansion of telemedicine or telehealth during the COVID-19 pandemic⁽¹⁵⁾. The applications of telemedicine are being used widely in many aspects. Many advantages are recognized e.g., minimization of the contagious rates of infection, provision of service to many consumers and in a timely manner, being practical even in areas with limited medical resources.

Another great area of improvement in digital health is a method of 'data sharing'. Traditionally in the past, the 2 major medias of medical data sharing are via peer-review journals and internet system. A paradigm shift of data sharing towards digital platform is intended to offer medical care in a timely manner. A concept of data sharing probably based on a lesson-learn from the management of Ebola outbreak in Africa during 2013-2016. In order to have an effective medical care, the World Health Organization (WHO) set up a meeting with other organizations, representatives from several countries, and authorities from medical journals in September 2015. The agreement from the meeting is to share important health data during public health emergency regardless of the publication proceeding thereafter⁽¹⁶⁾. By all means, rapid and news of the situation can be update in real time in the data sharing⁽¹⁷⁾. A great example of data sharing during the COVID-19 era is a disclose of full viral genome sequence. This consequently led to a rapid vaccine development and a timely diagnosis resulting in an appropriate management.

Digital health has been readily introduced in medicine prior to the COVID-19 pandemic. It can help or facilitate in both diagnosis and treatment. Examples of diagnostic aids are the Artificial Intelligence (AI) used in screening and diagnosis of diabetic retinopathy^(18,19), digital camera to transmit pulmonary images instead of film digitizer to diagnose pneumonitis⁽²⁰⁾, teleconsultation of a non-displaced or minimally displaced fracture film from digital camera via mail⁽²¹⁾ or images of brain lesions (acute ischemic stroke, intracerebral hemorrhage, or metastasis) via smart phone⁽²²⁾. The digital health is later expanded in therapeutic setting e.g., an endoscopist performing surgery (tele-NOTES) in Thailand on soft cadaver with an overseas remote control from Japan⁽²³⁾, or teleconsultation via line system between Chulalongkorn Stroke team and physicians from Mittaphab Hospital, Laos for a thrombolytic agent in a patient with acute ischemic stroke with a good result⁽²⁴⁾. With a new normal way of life from COVID-19, it is certain that the digital health will become more rapidly developed and widely used during the pandemic and

most likely they will persist and progress thereafter.

Despite clear advantages of digital medicine, some disadvantages are also encountered e.g., non-acceptance or unfamiliarity from providers and/or consumers, unsettled standard reimbursement system in telemedicine service, lack of an organization to run an effective management, etc. An urge to develop a good system to handle with upcoming problems and challenges is needed⁽²⁵⁾. There are some administrative managements which have been designed and incorporated with digital health. This led to a business initiation or so called 'startup-business'.

In 2017, a "Startup Thailand 2017" meeting was held among companies of health services or health products leading to a Health Startup Network (HSN). These entrepreneurs have brought technology and innovation to create products, technical and soft services e.g. telemedicine, health promotion service, search engine and appointment arranging with a physician, home care delivery service, health data analysis, block chain technology, hospital/ clinic/ drug store management, etc. Many supporting government sectors are available, such as, Thai Health Promotion Foundation, National Innovation Agency (NIA), Chaophraya Abhaibhubejhr Hospital, Thai Medical Council, etc⁽²⁶⁾.

As of November 2020, 56 entrepreneurs⁽²⁶⁾ had joined in the Thailand Health Tech Startup project. Few examples are as followed.

1) Chiiwii Live App⁽²⁷⁾

This application is a medical online-consulting program. The application will serve as an intermediary platform to fill or decrease a gap between a patient and his physician. The main objective is to provide a primary consultation or a follow-up process. A good sample is when an individual has a health problem outside the country and want to have an urgent consultation with a Thai physician for basic medical care.

2) QueQ App^(28, 29)

As a name implies, this app is to manage a queuing system. A customer can reserve the service by executing a transaction ahead of time, within a

2-kilometer distance. Other information can be obtained from the transaction i.e., waiting list, waiting time, reminder to customer's smart phone when a queue is approaching. This application has been used originally in business and is subsequently used in the hospital queuing management. Rayong Hospital is the first hospital using this application. Many other hospitals including Rajavithi Hospital which is usually crowded with a larger number of patients due to being a referral center of the Ministry of Public Health. One great advantage of the QueQ App is that the customers/patients can optimally manage their time and activities. For example, they may go to the cinema or shopping or back to work while waiting to see a doctor. In non-smart phone users, Rajavithi Hospital also set a self-check KIOSK for scanning (with or without a support from hospital personnel). With a clinical proven benefit that this QueQ App can decrease congestion of customers/patients, the app is moving towards a market share in other countries e.g., Singapore, Malaysia, Japan, Taiwan, and etc.

3) SenzE version 4 (MediTech Solution cpd., Bangkok, Thailand)⁽³⁰⁾

The SenzE system is designed to assist a physical disabled patient from any illnesses, such as, stroke, myasthenia gravis or other muscular disorders, postoperative immobilization, critically ill, bedridden or on respirator, old age or impaired verbal communication individuals, and etc. The SenzE uses software of the Eye Controlled System to function instead of verbal or body language communication. The high-definition camera (HD camera) and infrared sensor will monitor the patient's eye movement. A 2-second-stilled gaze at the menu will serve as a selection of 'enter' or 'print' function, hence the patient can communicate or even type a message in a computer using his eye. A dual 'touch screen' function is also available. This app allows a direct communication between a disabled patient and physicians effectively in a timely manner.

SenzE is first designed in Thai language and currently serves in 14 other languages (e.g. English, Chinese, Japanese, Arabic, Russian, German, and etc.). It is also equipped with interpreting and translating

system in every selected menu as well as voicing audio function.

This system has received many awards e.g., Startup Thailand 2016 Pitch Challenge, IP Champion 2015 (patent category), National Innovation 2014 (second runner up), IBM ASEAN Smart Camp 2014 (champion; at Singapore), Senate Thailand Center of Excellence Science 2013.

4) BLOCK M.D.⁽³¹⁾

The founder of this system learned from his own difficult experience about a drawback of referring system of his elderly relatives who required many expert opinions or second opinion from different hospitals. He found that this problem is due to an independent data holding of each hospital. Unless a great improvement of each hospital resulting in a genuine perfect hospital can be achieved, an alternative and reliable system which can function as a bridge to access data from different sites will be useful.

The system uses blockchain technology to assist a rapid, reliable, and safe health data sharing. BLOCK MD serves as a base to connect all health systems. It can be for the patient's own access, fax claim billing process, data sharing between hospitals, or even tracking. This allows each referring or referral hospital to access patients' data to expedite and increase a quality medical management. This system was selected as the finalist in the Thailand Startup Smart Camp 2016.

The question without an answer is how long this telemedicine or tele-practice is needed. There is a projection that the tele-practices will be continuing from now on, even after a pandemic control. Bill Gates, who frequently and accurately foresees the future, is one among the first panels who had predicted a hard-to-handle pandemic event since 2015. He made statement from his interview that telemedicine will be one among the digitalization trends which remains after the COVID-19⁽³²⁾.

Impact of COVID-19 to OB-GYN practices

The detrimental medical effects of COVID-19 to pregnancy have already been described elsewhere in many reports⁽³³⁻³⁵⁾. This impact is important with a global

trend of decreased birth rate in the current era⁽³⁶⁾. This must be emphasized especially in the countries which have low birth rates including Thailand which has the second lowest rate in ASEAN⁽³⁷⁾. Studies have shown that a pandemic (for example, 1918 Spanish flu) or natural disaster led to declined birth rates⁽³⁸⁻⁴²⁾. The effect was not evident abruptly but rather slowly in months^(38,41,42). Two different hypotheses were proposed. First is a biological effect i.e., infection may effect pregnancy by reduced conceptions, increasing miscarriage rate, or late fetal loss^(38,41,42). Second is a socio-economic effect i.e., poverty leading to undesired fertility, voluntary postponement of childbearing due to fear of infection^(36,41). Others also reported a trend of deferral the first birth, resulting in advanced age at conception and impaired fertility function⁽⁴³⁾. Although there is no direct effect of COVID-19 on abortion, it could possibly cause negative effect upon birth rates⁽³⁶⁾. This phenomenon will certainly result in higher proportion of aging population as have readily been a situation in many countries.

Other relevant effects of COVID-19 are a difficult access to health service of the patients and ineffective medical education. The 2 problems are inter-related. A lower number of patients especially for a long period of time should have negative influence on education especially training of post-graduated residents or fellows who need broad and deep knowledge, and skills. Changing in healthcare services due to COVID-19 pandemic has raised many questions regarding public health. For example; in oncology fields, many questions have been asked, such as, "Will there be an explosion of late-stage cancers after the pandemic?", "Will telemedicine and technological innovations revolutionize cancer care?", "Will virtual conferences continue after the pandemic?", "How do we prepare for the next pandemic or international emergency?"

Many questions regarding numbers and knowledge of Ob-Gyn specialists may arise from these impacts. How many obstetricians are required with a decreased pregnancy rate or birth rate? With an advanced age of married couples (women), more reproductive medicine specialists may be needed for specialized assisted reproductive techniques such as

eggs or ovarian tissue preservation for later use. With an association of cancer and advanced age, an aging society may need more gynecologic oncologists.

During preparing this article, the third wave of COVID-19 outbreak has occurred. Post pandemic world seems to be a far-away vision. We hope that our people will, once again, go through this hard time together with full courage and wisdom. Until then, we would be rising again with grace!

Potential conflicts of interest

The authors declare no conflict of interest.

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