Review Article

Covid-19 and Surgery

ABM Moniruddin[1], Hossain Md Sabbir Raihan[2], Tanvirul Hasan[3], Salma Chowdhury[4], Baikaly Ferdous[5], M Rashed Khan[6], M Abdur Rouf[7].

Abstract

The severe acute respiratory syndrome (SARS) caused by the super-infectious, super-spreading, super-mutating novel coronavirus-2 (Covid-19) is responsible for the worldwide overwhelming panic and pandemic with a huge burden of suffering patients at a time. It has been causing alarming morbidity and unexpected mortality, shortening life span of many people that hadn't happened since the second world war. It was first identified in Wuhan, China in the last months of 2019. The clinical scenario presents in the form of asymptomatic, mild, moderate and severe illnesses. More than 80% patients are either asymptomatic who transmit it to others and have a mild influenza-like illness clinically not different from common cold. The moderate and severe cases commonly need supervised home or institutional treatment. Many of the latter need intensive therapy that includes non-invasive and invasive ventilation along with other measures and medications. The treatment is principally conservative, HDU- and ICU-dependent. Surgery has no role as its primary treatment. But protection of surgical team and non-infected patients remains as a challenge to surgeons and hospital authorities. Many of the mutant variants now show resistance to antibodies generated by spike protein based and m-RNA based vaccines. The threat of infection still persists making surgeons overwhelmingly concerned while performing emergency, elective and cancer surgeries. This article describes some guidelines to be followed by the operating surgeons, hospital and regional health authorities to minimize the risks of spreading the disease and to protect the surgical team and other non-infected people from being infected.

Key words: *: Cytokine storm, DIC, HRCT, Multiple Organ failure, SARS.*

Date of received: *27.05.2021*

Date of acceptance: *20.08.2021*

DOI: https://doi.org/10.3329/kyamcj.v12i3.56561

KYAMC Journal.2021;12(03): 172-181.

Introduction

A series of multiple severe acute atypical respiratory infections had been noted in the Wuhan city of Hubei province in China during the last quarter of 2019. The unique pathogen responsible for those atypical infections was soon identified as to be a new (novel) coronavirus belonging to the family Coronaviridae and was then incriminated as a cause of severe acute respiratory distress (SARS), to be named as the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2 virus) by the ICTV (International Committee on Taxonomy of Viruses) on the 11th February, 2020, as this virus is genetically related to the coronavirus responsible for the SARS pandemic outbreak that had spread during the 2002–2003 period.[1,2,3] After being declared as a public health emergency on the 30th January, 2020, Covid-19 was subsequently announced as a pandemic disease on the 11th March, 2020 by the WHO (World Health Organization). The SARS-CoV-2, which caused severe lethal pneumonia in China, has now tremendously super-spread throughout the world. It was supposed initially to rise slowly during the last months of 2019 in the Wuhan City, but soon it had started to rise steep geometrically and exponentially throughout the world attacking in multiple waves in many countries. This pandemic disease was postulated to have started via a zoonotic transmission from a seafood and wild animal flesh market in the Wuhan city of China.[4-6]

1. Professor & HOD, Department of Surgery, Khwaja Yunus Ali Medical College Hospital, Sirajgonj. Bangladesh.
2. Senior Registrar, Department of Surgery, Khwaja Yunus Ali Medical College Hospital, Sirajgonj, Bangladesh.
2. Medical Officer, Institute of Nuclear Medicine & Allied Sciences, Bangladesh Atomic Energy Commission, Dinajpur
4. Ex-Prof of Obs & Gynae, Dhaka Medical College, Dhaka.
5. Honorary Medical Officer, Shaheed M Monsur Ali Medical College, Sirajganj
6. Senior Registrar, Surgery, Khwaja Yunus Ali Medical College Hospital, Sirajgonj, Bangladesh.
7. Associate Professor, Department of Surgery, Khwaja Yunus Ali Medical College Hospital, Sirajgonj, Bangladesh.

Correspondence: ABM Moniruddin, Professor & HOD, Department of Surgery, Khwaja Yunus Ali Medical College Hospital, Sirajgonj, Bangladesh. Mobile: +8801795078217, E-mail: abmmu@yahoo.com

Thereafter, human-to-human transmission was identified to be responsible for the community and global transmission of the disease, being reported in approximately over 200 countries and territories in the world.[4,7] Bangladesh is also facing the toll of this highly super-infectious disease with community transmission at extremely high rates across the country. This newly identified coronavirus is still mutating and evolving, and has puzzled the scientists all over the world. Its dramatic upsurge has collapsed the health systems of the affected countries with tremendous morbidity, mortality and panic. The WHO considers the virus as unimaginable extremely infectious and urges all nations to take it with utmost priority. As on Sept 10, 2021, there were almost over 224 million cases worldwide, with over 4.62 million documented deaths.[6] The Covid-19 pandemic has substantial effects on working surgeons and patients who require surgical care. Providing care for patients with surgical diseases needs a unique and intimate relationship between the patients and the surgeons. The surgical workforce has faced distinct challenges compared with nonsurgical specialties during this Covid-19 pandemic.[7-9]

History of Coronaviruses

For the prehistoric period, using molecular clock analysis, the commonest ancestor of coronaviruses seems to have appeared 8,100 BC, and the predecessors of alpha-coronavirus, beta-coronavirus, gamma-coronavirus and delta-coronavirus had appeared approximately 2,400 BC, 3,300 BC, 2,800 BC & 3,000 BC respectively. Now the coronaviruses are actually a family of hundreds of viruses, most of them are infecting such animals as humans, many other mammals and animals like pigs, dogs, cats, bats, ferrets, hamsters, lions, tigers, pangolins, camels, raccoon dogs, rabbits, minks, tree shrews, many primates, domestic fowls, poultry birds, peafowls, guinea fowls, partridges, nongallinaceous birds, teals, greylag geese, mallard ducks, pigeons, turkeys and pheasants etc.[10-12] The scientists postulate that the bats and the birds are the ideal hosts for the genetic sources of coronaviruses (bats for the alpha- & the beta-coronaviruses and the birds for the gamma- and the delta-coronaviruses). Officially, following the discovery of microscopes and microbes, the first coronavirus was discovered in chickens in late 1929 and 1930s.[11,13] Then it followed few decades to detect human coronaviruses in 1960s. Four endemic coronaviruses [229E (an alpha-coronavirus), NL63 (an alpha-coronavirus), OC43 (a beta-coronavirus), HKU1 (a beta-coronavirus)) are well-known for their mild diseases (10 to 20% of all common colds) in a year. Any person is said to be infected by any one of these coronaviruses at least once in their lifetime.[14,15] But in this 21st century, three other coronaviruses namely SARS-CoV, MERS-CoV, SARS-CoV-2 were identified that are responsible for more serious fatal diseases. The well-known SARS-CoV, HCoV-NL63 (human coronavirus NL63) and HCoV-HKU1 were first described in 2003, 2004 and 2005 respectively.[16-18] The HCoV-HKU1 and the HCoV-NL63 are respiratory coronaviruses and are commonly found to cause upper and lower respiratory tract infections that have spread worldwide and that prefer the cold seasons. These characteristics simulate the symptoms described for the so-called 'old' viruses HCoV-229E and HCoV-OC43 the old ones being reported in mid-1960s. Coronavirus disease-2019, now abbreviated as COVID- 19 caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 virus) was named by the ICTV on the 11th February, 2020.[19,20] (Fig. 1).

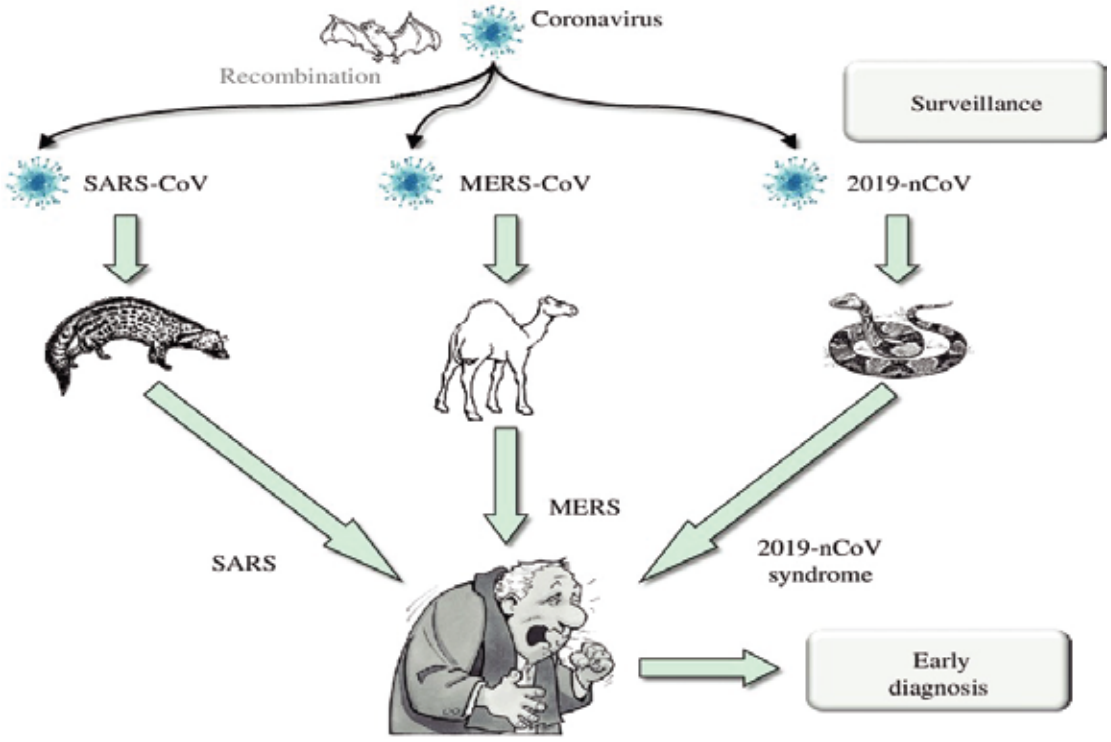


Fig. 1: Natural history of coronaviruses as a zoonotic disease infecting humans; (Courtesy: ResearchGate).

Aetiological agent

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had been an unknown beta-coronavirus until its discovery and identification in the Wuhan city of China in late December of 2019. Now it can be detected in the broncho-alveolar lavages, sputum, blood etc. from patients who presents with Covid-19 symptoms.[21,22] This viral spike proteins have special affinity to human ACE2 receptors that are believed to be an ancestral trait shared with bats' viruses and not one that had been acquired currently through recombination. Coronavirus are in the Realm- Riboviria, Kingdom Orhtornavirae, Phylum- Pisonviricetes/Incertae sedis, Order- Nidovirales, Suborder- Cornidovirineae, Family- Coronaviridae. Subfamilies and genera: Letovirinae- Alphaletovirus, Orthocoronavirinae- Alphacoronavirus, Betacoronavirus, Gammacoronavirus, Deltacoronavirus.[23,24] SARS-CoV-2 belongs to the Sarbecovirus subgenus of the Coronaviridae family of the Nidovirales order, and has been identified as the seventh coronavirus known to infect humans. The virus has been found to be similar to SARS-like coronaviruses from the bats, but it is distinct from SARS-CoV and MERS-CoV. The full genome has been determined and published in the GenBank.[25,26]

Structure of Coronaviruses

Coronaviruses are relatively large, grossly & roughly spheroidal particles with unique characteristic surface spiky projections. Their sizes are remarkably variable with average diameters being 80 to 120 nm (variably from 50 to 200 nm). The average total molecular mass is about 40,000 kiloDaltons. Each virus has a bilayer lipid envelope in which the membrane & spike proteins are anchored. This bilayered lipid envelope, the membrane proteins, and nucleocapsid protect the virus from circum-ambient adverse situations. The viral genome length is about 26 to 32 kilobases. The viral particles are typically endowed with large (about 20 nm) club shaped or petal shaped surface projections (called the peplomers or the spikes or the spike proteins). The viral particles under electron microscope are seen as spheroidal particles creating the image simulating and reminding the solar corona.[27-29] (Fig. 2).

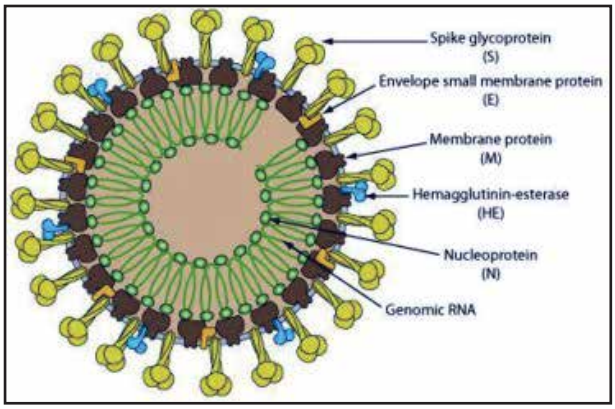


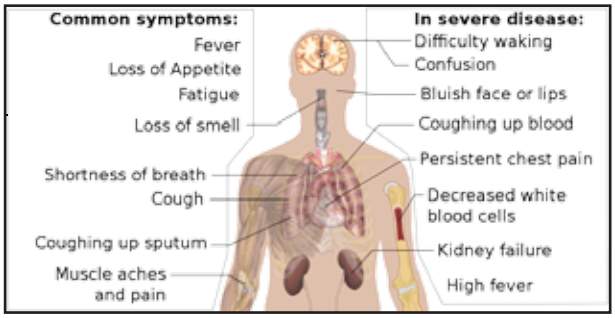
Fig. 2: Basic structure of a covod-19 virus; (Courtesy: ScienceDirect.com)

Peculiarities of COVID-19 virus

Since the time immemorial, no other virus was found so much super-mutating and super-spreading. Since the discovery of the parent Wuhan Covid-19 virus in December, 2019, several thousands of its variants have already been isolated by the scientists all over the world. Many of the new variants specially the lambda and mu ones are threatening the world by their ability to escape the classical natural anti-corona antibodies and the induced antibodies produced by mass vaccination (by vaccines of Oxford Astrageneca, Pfizer, Moderna, Jhonson & Jhonson, Russian Sputnik, Covaxin of Bharat Biotech, CanSino Biologics and Sinovac Biotech vaccines of China, the Queensland University vaccine of Australia, the, The ZyCov-D vaccine by Zydus Cadila of India etc.). The deadly waves have created dangerous panic across the globe and many more pandemic waves are supposed to knock us in the days to come. It has paralysed the world civilization including its trade, commerce, education, recreation, productivity and civilization. We don't know when these deadly waves of covid-19 will end. Scientists are not yet unanimous about its origin, modes of transmission, causes of its super-mutation and super-spreading nature, its variegated pathologies involving several organs and tissues in dying patients.[30,31]

Pathology

Coronaviruses are RNA viruses that are pathogenic to many mammals and many birds. They cause mild to lethal RTIs (Respiratory Tract Infections). In humans, they cause 15 to 20% of common colds, diarrhea, SARS, MERS & COVID-19.



In cattle and swines, they can cause diarrhea, while in mice they can cause hepatitis and encephalomyelitis. SARS-CoV-2 is considered a member of the beta-coronaviruses (β-CoVs) family, which also includes SARS-CoV and MERS-CoV. The CoV family members are composed of enveloped, positive-sense single-stranded RNA viruses.[32,33] They are spheroidal or spherical or oval in shape with large glycoprotein spikes on the surface displaying a crown-like shape on negative staining when seen or photographed by electron microscope. The CoV family is sub-divided into four subfamilies genotypically and serologically as follows: α-, β-, γ-, and δ-CoVs. Among them, α- and β-CoVs are pathogenic to humans. Generally, all human CoVs are stated to be of zoonotic origin, and the bats are the most likely natural hosts of CoVs. In addition, before infecting humans, they may need one or more intermediate animal hosts, that may civet cats and dromedary camels for SARS-CoV and MERS-CoV, respectively.

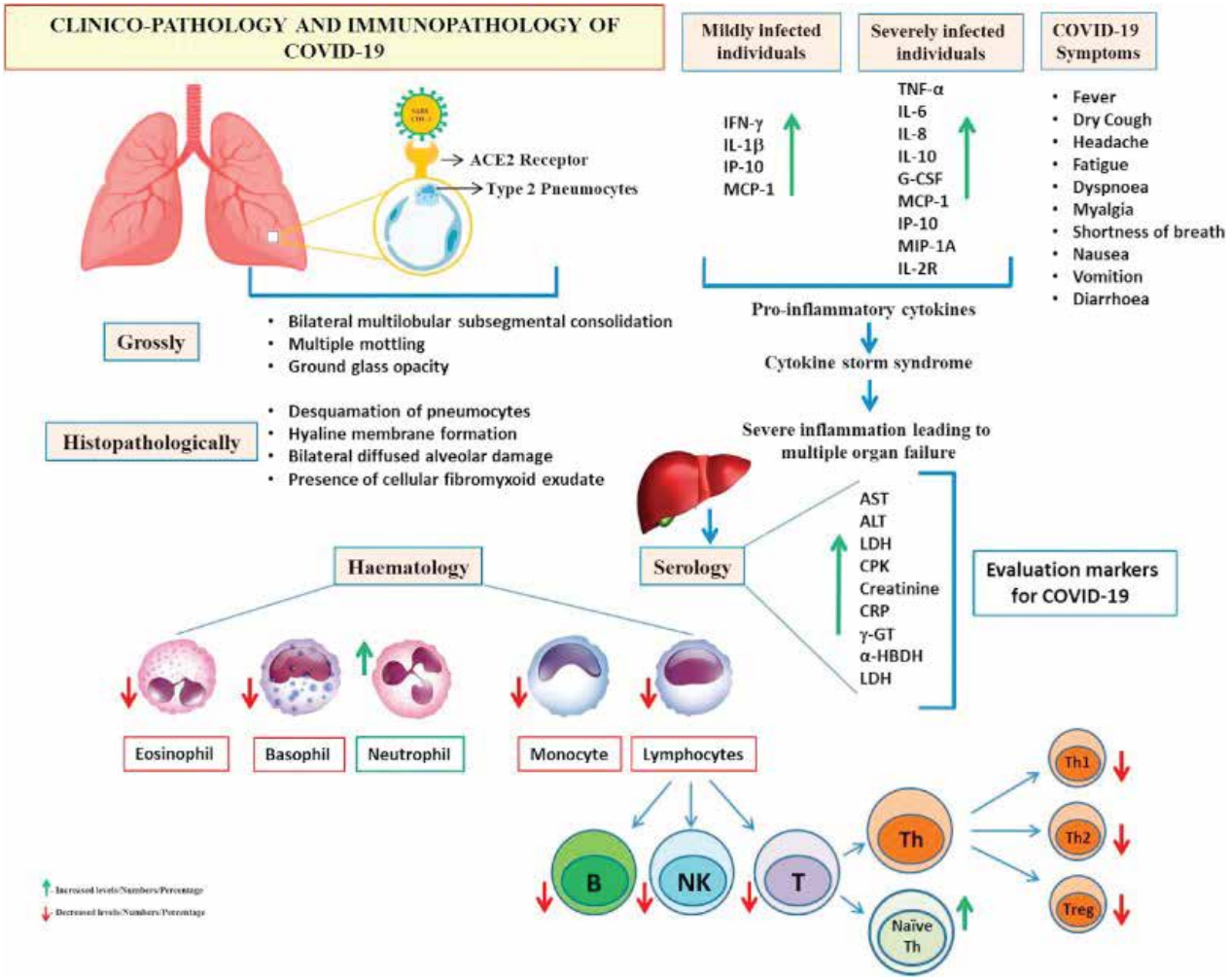


Fig.4: Clinico-Immuno-Pathology of Covid-19 virus, (Courtesy: ScienceDirect.com).

The discovery of pangolin's CoVs and their about 99% genetic similarity to SARS-CoV-2 indicate that pangolins may be a probable intermediate host for SARS-CoV-2. Currently, COVID-19 patients are the main sources of infection of this prevailing pandemic. Asymptomatic carriers have also been incriminated to disseminate the virus. Respiratory droplets from coughing, sneezing and close contact are considered as the principal transmission routes. The SARS-CoV-2 has also been isolated from blood, feces and urine.[30,33] Thence, aerosol or contact transmission as a result of contamination by blood, feces and urine of infected individuals are to be borne in mind. Since almost all people are commonly susceptible to SARS-CoV-2, Covid-19 has spread rapidly & exponentially across the globe. Smoking as it causes immunosuppression and respiratory illnesses is a high-risk factor for infection. Covid-19 patients principally presents with tiredness, pyrexia, dry cough. Few patients may have the symptoms of a running or stuffy nose, headache, muscle-ache, and diarrhea, dizziness, impaired consciousness, ataxia, epilepsy, hyposmia, hypogeusia, hypoxia, and neuralgia. More critically ill patients develop hypoxia and dyspnea, one week after the onset of symptoms. On rapid progression, ARDS (Acute Respiratory Distress Syndrome), septic shock, and metabolic acidosis will develop. Beyond the respiratory tract, SARS-CoV-2 can attack many other such tissues and organs as the spleen, the liver, the heart, the kidneys, the brain, the neurospheres, the brain organoids, the pluripotent stem cells–derived human neural progenitor cells. Cytokine storms and sepsis can cause hemolysis, DIC (Disseminated intravascular Coagulation) etc. and complications thereof.[10,22,33] (Figures 3 and 4).

Diagnosis Covid-19

Definite detection depends on detection of the specific Covid-19 virus from the of specimens collected from the suspected patients. Specimens include 1. Upper airway specimens like Oropharyngeal swabs, nasal swabs, nasopharyngeal secretions/swabs; 2. Lower airway specimens like sputum, bronchoalveolar lavage fluid, airway secretions etc. 3, Blood (rarely). Here sputum and other lower airway specimens have a high positive rate of nucleic acids and should be collected ideally preferentially. SARS-CoV-2 viruses preferentially grow and proliferate in type II alveolar cells (AT2) and peaks of viral shedding occur 3 to 5 days after the onset of symptomatic disease.[2,12,14]

Therefore, if the nucleic acid test may be negative at the beginning, samples should be continued to be collected and tested on subsequent several days/occasions. The viral nucleic acid is detected by the RT-PCR test. The RT-PCR test is the gold standard and absolute test for diagnosis of covid-19 infections. The sensitivity of viral nucleic acid detection/diagnosis depends upon following factors: 1. Specimen site, 2. Quality of the specimen, 3. The temperature of specimen storage, 4. Faulty collection techniques, 5. Faulty transport, 6. Non-contamination of the PCR machine, 7. Proper extraction of the viral nuclear material etc. Nasopharyngeal swab is most commonly used where false negative reports may be as high as 30 to 40%. No single test is confirmatory, as it may be false negative as well as false positive. Serological tests are cheap, can be performed more rapidly. But these are not cent percent confirmatory. These are: Rapid antigen & Rapid Antibody tests. These serological can detect covid-19 virus indirectly & non-specifically. Suspicious results need to be verified by RT-PCR test. Rapid antigen test is not specific as other non-covid-19 corona-viral antibody can give false positive result. Rapid Antibody tests need at least 7 to 10 days to detect Ig M antibody.[18-20]

For earliest indirect diagnosis in a symptomatic patient, a HRCT (High-Resolution CT) is highly preferable. The latter shows such classical findings as bilateral involvement in most patients, multiple areas of consolidation, ground-glass opacities (GGO), bilateral, subpleural, peripheral opacities, crazy paving opacities/appearances (GGOs and inter-/intra-lobular septal thickening), Bronchovascular thickenings in the lesion, traction bronchiectasis etc. Chest x-ray are not as sensitive as HRCT for early diagnosis as an indirect evidence. Chest x-ray may be valuable & suggestive if there is bilateral COVID-19 pneumonia, which is fairly common in worsening conditions.[21,22] USG of chest has definite specific sonographic findings in Covid-19 lung involvement, but it needs an experienced skilled operator who is accustomed with on Pulmonary Ultrasonography. All these techniques (HRCT, Chest x-ray and sonography) are nonspecific. Patchy ground-glass opacities (GGOs) may be caused by a variety diseases (like other viral and bacterial pneumonias). That is to say that the imaging gives only a bit of information which must be integrated & translated into clinical and epidemiological perspective.[22] Other supportive investigations include 1. CBC for evidences of lymphopenia (83%) or progressive lymphopenia, leukopenia (9–25%), leucocytosis (24–30%), thrombocytopenia. 2. Specific markers of sepsis like a). CRP (C-Reactive Protein), b). Procalcitonin, etc. Most patients with COVID-19 have a normal level of procalcitonin with significantly higher levels of C-reactive protein. A rapidly and significantly higher C-reactive protein levels indicate the likelihood of sepsis complicating bacterial superinfection. e). Blood culture to detect specific bacterial superinfection. 3. Miscellaneous tests like a) LFTs (Liver Function Tests), b). RFTs (Renal Function Tests), c). Arterial blood gas analysis. d) D-dimer (marker of DIC (Disseminated Intravascular coagulation) or intravascular thromboembolic disorders), e). Serum Ferritin (marker of increasing inflammation), f). S.LDH (marker of organ or tissue damage), g) S electrolytes etc.[18,19] Contemplating the co-incidental regional endemicity of other febrile diseases like malaria, dengue and tuberculosis, respective tests need to be be performed to exclude other diseases. It is to be remembered & highlighted that the combination of normal or low leucocyte count, remarkably elevated CRP level, and bilateral Pneumonia on Chest x-ray or Ground Glass Opacities (GGOs) on HRCT of chest is suggestive & diagnostic of COVID-19 during its pandemic, despite the negative RT-PCR report.[21,22]

Medical treatment

Treatment is mainly medical, that is symptomatic, supportive with or without administration of antiviral drugs, oxygen, steroids, monoclonal antibodies, and those of complications and co-morbidities. Surgery itself has no role to get cure of or prevent Covid-19. Asymptomatic patients actually need no medication other than the isolation protocols (either at home or at institution depending on regional and national strategies. Mildly symptomatic case may be treated in isolation in an isolated single room at home (where home isolation protocols are to be strictly followed). Symptomatic patients in risk group (like DM, HTN, IHD, Present or periodic or past Asthma/COPD (Chronic Obstructive Lung Diseases)/ Bronchiectasis/ Chronic bronchitis/ ILD (Interstitial Lung Diseases like Fibrosing Alveolitis) patients, Known CKD (Chronic Kidney Diseases), CLD (Chronic Liver Diseases), Known Malignancy, High risk pregnancy, Obesity (BMI>25) need admission to an isolation room in an isolation ward of a CDH (Corona Dedicated Hospital). Tab Paracetamol (500mg) as required if core temp is more than 101 degrees Fahrenheit. One may add anti-histamine like desloratadine if there is rhinorrhea, anti-tussive like dextromethorphan if there is dry cough, thromboprophylaxis for mild COVID-19 cases with risk factors by Enoxaparin 40 mg, SC, once daily and for obese patients 40 mg 12 hourly. Doses to be adjusted if Creatinine Clearance is less than 30ml/min or Unfractionated heparin 5000 unit S.C. per day is to be started with strict monitoring.

In Moderate cases as evidenced by Clinical or radiological pneumonia, the following treatment protocols are followed (in addition to the above mentioned isolation, antipyretic, antihistamine & thromboprophylaxis): 1. Antiviral drugs like Favipiravir may be used in non-hospitalized moderate cases at dosage of 800 mg 12 hourly on day 1 followed by 600 mg 12 hourly from day 2 to day 10; 2. Routine antibiotic use is not recommended in COVID-19 cases, however, antibiotics are used in a). older people and children less than 5 years of age, that ensures empirical treatment for probable bacterial pneumonia; simple antibiotics like amoxycillin and clavulanic acid are prescribed at discretion of treating consultants and if there is strong suspicion of bacterial super-infection as evidenced by high procalcitonin levels; 3. Oxygen through nasal canula maximum 5 L per min if required; 4. Proning- Prone position at least 4-6 hourly a day; 5. LMWH (Low Molecular Weight Heparin), i.e., Inj enoxaparin 1mg/kg SC 12 hourly, adjusting the doses if the Creatinine Clearance is less than 30ml/min, Or if LMWH can't be given or contraindicated, one is to use Inj UFH (Unfractionated heparin)as follows: 60 U per kg bolus followed by 12 units per kg per hour infusion; If there is ACS (Acute Coronary Syndrome), 80 U per Kg bolus plus 18 units per kg per hour infusion; if there is Venous Thrombo-Embolism (VTE) and if there is AF (Atrial Fibrillation), thromboprophylaxis should be given until symptom resolves or improves and followed by Oral tablet rivaroxaban 10 mg once daily for 1 month. For moderate to severe cases who need oxygen therapy and/or are hospitalization, antiviral drugs are given as follows: Inj Remdesivir 200 mg

IV infusion within 30 min to 2 hours on Day 1 followed by 100 mg infusion within 30 min to 2 hours from Day 2 to Day 10; Once Remdesivir is started, the other antiviral drugs like Favipiravir are to be stopped. Remdesivir is used at the discretion of treating consultants in the hospital and can be used in the treatment of all hospitalized adult and pediatric patients aging more than 12 years (having suspected or lab-confirmed COVID-19), irrespective of severity of the disease.[27]

If moderate cases on treatment show no improvement or show deterioration at 24 hours in hospital, then oral dexamethasone 6 mg per day in single or in two divided doses for 10 days or oral methylprednisolone 60-80 mg daily in a single dose or in two divided doses for 7 days after food with anti-ulcerant proton pump inhibitor and anti-helminthic coverages. Additional treatment for severe cases with respiratory symptoms that include ARDS (Adult Respiratory Distress Syndrome) includes Intravenous Tocilizumab (that blocks Interleukin 6) in adult dose schedules (18 years or more) 8 mg per kg (maximum 800 mg/dose) or in Pediatric dose schedules (less than 18 years): if body weight <30 kg to give 12 mg per kg; if body weight >30 kg to give 8 mg/kg (Maximum 800 mg per dose); Duration: 1 dose; Can be repeated after 12 hours if no clinical improvement for a maximum of 2 doses. Indications of Intravenous Tocilizumab: 1. COVID-19 positive and all of the following respiratory findings: a). Abnormal chest imaging consistent with COVID-19; b). Rapidly worsening gas exchange/respiratory status over 24 to 48 hours and requiring more than 6 L O2 per min or on mechanical ventilation; 2. Absence of systemic bacterial, fungal or parasitic co-infection; 3. High clinical suspicion for Cytokine Storm (cytokine release syndrome) and clinical deterioration of the patient. CPT (Convalescent Plasma therapy) is advocated provided the donor is healthy who recovered from COVID-19 and preferably after 28 days with neutralizing titre more than 1:160 and binding titre more than 1:1000; Criteria/indications for CPT: **1.** Age more than 18 years old, **2.** Positive SARS-CoV-2 and symptoms more than 8-10 days, **3**. IWC (Informed written consent) or SDM (Shared Decision Making), **4.** Severe or life-threatening disease as evidenced by at least one of the following: **a).** Increasing dyspnea, **b).** Respiratory rate more than 30 per min, **c).** SpO2 less than 88%, **d).** P/F ratio [the arterial pO2 ("P") from the ABG divided by the FIO2 ("F") less than 300, **e).** Lung infiltrate more than 50% within 24 to 48 hours, **f).** Septic shock, **g).** MOF (Multi organ failure).

Additional management of moderate case protocol (Excepting oral steroid) who needs injectable steroids include:
a). Inj Dexamethasone IV 6 mg daily for 10 days or Inj Methylprednisolone 250 mg IV daily for 5 days (switch over to IV from oral if already started), **b).** Maintain euvolaemia (avoiding fluid load), **c).** Early norepinephrine for hypotension, **d).** broad spectrum antibiotics IV at the discretion of treatin consultants plus If cytokine storm is considered as evidenced by HLH (Hemophagocytic lymphohistiocytosis) picture, one is to give then IV Tocilizumab with or without CPT (Convalescent Plasma therapy).[3,24,25,29,30,31,32]

STRATEGIES AT OUT-PATIENT DEPARTMENT (OPD)

To minimize transmission of infection, the most important strategy is to limit direct, close and intimate physical interaction among all people, including physicians, paramedics, attendants and patients. OPD (Out-Patient Department) activity should be rearranged successfully to curtail the risk of cross-infection, particularly of frail, elderly patients or those with co-morbidities who are at increased risks of serious adverse outcomes and complications with Covid-19 infections. Tele-communication and tele-consultation are effective strategies for maximizing the uses of resources and minimizing contacts. All patients including the new ones & the new referrals are to be triaged, with a view to consulting as many as possible through tele-consultations. "Forward triage" can be arranged, which, in essence, minimizes the patients through prior sorting before they reach the hospital. The objective of all such practice is to minimize admission for non-urgent & non-emergent cases during the pandemic period. Patients with suspicious cancers can be triaged straight to diagnostic tests, which can be pre-scheduled at a convenient appropriate time, based on the local facilities and amenities. Referrals requiring in-person examination are to be postponed. Patients are to be advised not to attend non-covid-19 OPD if they develop respiratory symptoms or fever, or if they are diagnosed with Covid-19 infection. Special fever clinics are to be set to separate these patients who attend hospitals. Surgical teams are to be trained to identify and respond to the possible Covid-19 infections during face-to-face consultation, tele-consultations and tele-communications.[7]

SURGICAL STRATEGIES AT ELECTIVE SURGERY

Reducing elective surgical activity, has three key benefits: a). It releases general ward and ICU beds that can be kept reserved for Covid-19 patients; b). It releases surgeons and theatre teams; c). It reduces the risk of cross-infection of elective patients and hospital visitors with Covid-19 by infected patients and staff, preventing subsequent spread of infection to the community at large. ''Stay-at-Home" as an early measure, most elective surgeries (non-essential) should be postponed. There are three types of elective surgeries. They are essential, semi-essential, and non-essential surgeries. Essential surgical services have been defined as those that cannot reasonably be delayed for more than eight weeks without causing significant harm to the patient or progression of the disease/disability. This judgment is difficult even in simple conditions. An example is chronic calculus cholecystitis. The patient may get acute attacks of cholecystitis, obstructive jaundice, cholangitis, or pancreatitis during the extended waiting period, which significantly increases morbidity, hospitalization rate and time, that complicates the decision to operate and subsequent postoperative outcome. All patients should be tested for COVID-19. If found positive, the surgery is to be postponed until after 1 month following achieving a negative report. The Covid-19 patient is to be discharged providing the home treatment plan with advice regarding the need for hospitalization if symptoms appear or worsen. If the report is found negative, the operating team can, proceed with the proposed treatment plan.[4]

AT CANCER SURGERY: Cancer treatment in the pandemic remains a challenge. Radiological and endoscopic investigations for patients triaged by telephone with prioritizing the high-risk symptoms that should continue for as long as possible. Significant problems are as follows: a). Delayed diagnosis and definitive treatment would worsen oncological outcomes; b). A cause of distress for patients and their families; c). High risk of COVID-19 complications because of suppressed immunity

(cancer related, treatment related); d). The duration of pandemic-related disruption is unpredictable. Some authorities recommend that, if possible, these patients should be offered such alternate therapy as neoadjuvant chemotherapy or radiotherapy. But, the multimodality treatment of cancer needs multiple visits, follow up visits, and hence enhanced exposure and increased chances of contacting the viral infection. As the patients may harbor asymptomatic infection, testing them at every visit will burden the already overwhelmed resources specially in resource-poor settings. It will cause intense mental agony to the already suffering patients. Virtual Tumour-Board should be arranged for SDM (Shared Decision Making). It should include all the stakeholders, such as the patient, family members of the patient, surgeon, medical oncologist, and radiation oncologist for the SDM. The final decision is be documented clearly in the case file. The main determinants of SDM for cancer treatment include: a). Patient factors (age, general fitness); b). Tumor-related factors (type, stage, grade, biology); c). The current status of Covid-19 pandemic at that region; d). Availability of resources; e). Availability of non-surgical treatment options. Surgery should be offered to most of those patients where non-surgical options are not available or delay in surgery will threaten the patient's life. Non-surgical treatment should be considered whenever needed in consultation with medical and radiation oncologists. Patients who present with onco-surgical emergencies should be operated upon with all precautions and recommendations laid for any surgical emergency. Tele-consultation should be used for those who have completed treatment or those who are disease-free.[3,4]

AT EMERGENCY SURGERY: Indications of emergency surgery remain the same during this Covid-19 pandemic as before. The only difference is achieving a balance between timely treatment and protection of HCWs (Health Care Workers) from this notorious virus. Surgeons across all specialties need to be prepared to encounter Covid-19 in all key areas. Patients already admitted to hospital for treatment of Covid-19 infection may develop additional health problems that may require surgical intervention where mortality and morbidity rates are high. Operative decision is dependent on a). Risk stratification; b). Multidisciplinary discussion with patient party, surgeon, critical care specialist, infectious disease specialist; c). Non-operative treatment options should be considered carefully, particularly if resources are limited and survival after major surgery is unlikely. Patients admitted with acute surgical pathologies, some of whom would require emergency surgery may have concurrent COVID-19 infection, when surgeons should be trained to recognize and respond to possible COVID-19 infection. After surgery, patients may develop respiratory symptoms or PUO (Pyrexia of Unknown Origin), indicating possible nosocomial COVID-19 infection, where surgical teams are to be trained to isolate patients with suspected infection early, and to ensure that individuals at risk of exposure are tested rapidly.[3,26]

AT MINIMALLY INVASIVE SURGERY (MIS): A perceived threat that the virus may be found in tissue and body fluids and concentrated virus-aerosol can occur due to pneumoperitoneum has suggested limiting use of MIS. Appropriate precautions are of utmost importance when laparoscopic techniques are used to reduce the duration of hospital stay and faster recovery.[1,3]

AT POSTOPERATIVE CARE: Surgeons are to be prepared to manage a range of complications in patients with Covid-19 infection. Patients who develop PUO or respiratory symptoms should be isolated, and chest HRCT performed or Covid-19 laboratory testing ordered. To prevent cross-infection, such patients are to be cared for by Covid-19-specific surgical team if possible, rather than teams who are also caring uninfected patients.[3,4,5]

AT DISCHARGE: When planning patients' discharge from the hospital, surgeons are to consider their psychosocial needs. If there is a possibility that patients are still infectious, they should be given clear advice on how to avoid transmitting COVID-19 to the family members and others.[4]

AT FOLLOW-UP: Follow-ups may be arranged through tele-consultation or audio/video calls to curtail unnecessary hospital attendance. These patients may need early re-intervention (with testing for Covid-19 and adequate protection for HCWs) in case of any post-operative surgical complication. Even patients who recover have a higher risk of future infection and a more complicated recovery pattern.[26] Additional recommendations for safe surgery: Training of all members of the operating team (i.e., surgeons, anesthetists, nurses, technicians, clinical attendants, cleaners, housekeeping staffs) regarding all possible measures to prevent the spread of Covid-19 to and from the operating and Postoperative rooms. The essential training includes: a). Training in proper way of Donning and Doffing; b). Appropriate ways of disposal of used items; c). Appropriate Sterilization of surgical equipment; d). Cleaning of theatre after every case.

ESSENTIAL PREOPERATIVE MEASURES include a). Triage, Teleconsultation, Forward Triage; b). Complete diagnostic tests and review through tele-consultation; c). COVID-19 testing; d). HRCT of chest, when needed.

PATIENT TRANSPORT system should be a). Through a pre-defined safe area; b). With proper communication beforehand; c). Through shortest possible route; c). Using dedicated elevators; d). With no or minimal holding time.

OPERATING ROOM is to be a). designated with Donning and Doffing areas; b). a dedicated Covid-19 operating room should be designated; c). with close entry and exit; d). with negative air pressure or with facilities of switching off 30 minutes before and restarting 30 minutes after sanitization at the end of surgery.

INTRA-OPERATIVE MEASURES include a). Preference for regional anesthesia to avoid aerosol generating general anesthesia for protection of HCWs; b). as to follow the guidelines laid down by the airway and anesthesia societies for intubation; c). an operation theatre adequately stocked with the equipment required for specific procedures; d). Safe equipment transfer through non-infected area on demand; e) facilities for Proper scrubbing, Donning, Doffing, proper fitting masks, eye protection; f). The surgeon should enter the Operating Room 15 minutes after intubation; g). Duration of the surgery should be kept to minimum, and lengthy and complex procedures should be avoided; h). Using the most surgeon-friendly procedures and

limiting the aerosol-producing gadgets such as electrocautery, laser, and ultrasonic scalpel; i). Ensuring minimal bleeding, spillage; j). Disposable items should be used as far as possible; k) After completion of the surgery, HCWs are to follow a well-planned exit sequence from the Operating Room. The surgical team should leave first, followed by the patient after extubation, then the anesthesia team, and, last of all, the cleaning and sterilization crew; k). Minimum gap of 1 hour should be there between two cases.

SPECIAL PRECAUTIONS IN LAPAROSCOPIC SURGERY include a). small port incisions to prevent gas leakage; b). low CO2 insufflation pressure; c). careful evacuation of smoke by using filtration systems; d). Proper desufflation can decrease the chances of infection transmission; e). Controlled smoke evacuation should be done by a designated team member, using the port's side-channel; f). If commercial smoke evacuation system is not available, a simple evacuation system using HME/HEPA filters can be made; g). When no smoke evacuation system is at hand, it is best not to opt for laparoscopy; h). use of drains should be kept minimal; i). Specimen removal, either hand-assisted or with a wound protection device, should be done only after desufflation; j)..Fascial closure is a must after desufflation.

POST-OPERATIVE MEASURES include a). Closely monitored and tested by RT-PCR in the event they developing symptoms. B). In highly suspicious case who are RT-PCR negative, HRCT chest should be done; c). Patients with COVID-19 should be kept in isolation; d). Using of 2 to 3 antiemetics to control nausea and vomiting more aggressively; e). Low flow supplemental oxygen should be provided through a nasal cannula, unless the patient requires oxygen supplementation through other devices (e.g., HFNC, Ventilator); f). Every effort is to adhered to enhanced recovery protocols should be made; g). Dedicated team should manage these patients to prevent exposure to Covid-19 negative patients.[1-5,26]

PITFALLS and LIMITATIONS in safe surgical care: Some barriers exist with tele-consultation. In times of need, many people want a physical interaction with the physician. Patients may be unaware that they have tele-consultation as an option and do not know how to get access to it. The interactive communication has some regulations as it involves providing sensitive information and also financial transactions. Quality of tele-consultations vary on the quality of facility, resources, and workforces available. Specific issue of privacy and data protection remains there too. Physical examination is not possible until the patient is admitted or physically appeared. The primary purpose of isolating Covid-19 positive patients is to curtail the risk of infection transmission to others. Accordingly, many hospitals have divided medical facilities into a dedicated Covid-19 and non-Covid-19 zones and a testing protocol for all admitted patients. However, two situations need special attention. These are a). The patient treated as non-Covid-19 may have an attendant who turns out to be Covid-19 positive. As the patient and attendant both remain in the non-Covid-19 zone, where HCWs are likely to be working without full PPE (Personal Protection Equipment). This attendant is potentially at risk of spreading the infection to other patients (in a large facility) and all HCWs; b). a non-Covid-19 patient who turns out to be positive during his/her hospital stay. Informed Written Consent (IWC) or SDM for surgery addresses to the risks and expected benefits, the likely outcome of the proposed operative procedure, and other alternative options. There is an increasing assertion among health care authorities that the risks of infection transmission & acquisition with Covid-19 should be a part of IWC or SDM for surgery. Long hours of surgery with wearing full PPE will lead to burnout and exhaustion of the surgical team. Patients with malignancies are already immunocompromised, which may increase the risk of Covid-19 infection. In addition, operated patients are under psychologic, physical and metabolic stresses and temporarily immunocompromised due to surgical intervention, which puts them at increased risk of acquiring SARS-CoV-2 infection. An ICU (Intensive Care Unit) bed may not be available in an already compromised hospital setting, which can compromise and jeopardize postoperative care following a lengthy or complicated surgery.

A retrospective study conducted by Wang et al. reported that 41.3% of their patients had the nosocomial transmission of Covid-19, out of which the many were HCWs. It calls for attention to undertake regular staff rotation, testing, and designating Covid-19 and non-Covid-19 areas in a hospital, which are necessary measures to limit unwanted spread. Doubling or cross-covering of duty rotations anticipating staff absence due to sickness or quarantine, reducing doctor-to-patient ratios in some parts of the hospital, and strengthening surgical teams by recruiting retired surgeons, clinical academics, or final-year medical students are some of the possible approaches to meet and solve the anticipated crisis. There has been a trend from an operative to delayed-operative management of surgical conditions such as intestinal perforation, intestinal obstruction, or intra-abdominal inflammation. However, it is still a question of whether to wait and watch management in acute surgical conditions should increase and be the norm. Approximately 330 million operations are done worldwide annually, with an average of about six million procedures per week internationally. The cancellation of elective operations creates a massive pile-up of patients. There are no robust data available to calculate the number of operations postponed and how this backlog will be dealt with after the pandemic. We have to take care that our workforce does not get exhausted once the elective surgeries start in the later pandemic stages. Data on the effects of surgical cancellation on psycho-social and physical health of the patients are lacking, but surely it will damage their health and wellbeing. The Covid-19 pandemic has also created challenges in the education of the future surgical workforce. Most medical students were removed from clinical care rotations. With the shutdown of nonurgent, nonemergency surgery, surgical trainees were no longer gaining experience in the operating room and clinic. The implications for these are far-reaching. More residents may graduate who are not fully prepared to enter independent practice. Regarding the medical students, their exposure to surgery is now limited. Fewer medical students may choose careers in surgery due to limited exposure. The pandemic has also has affected research and career development. All researches, including clinical trials, has slowed or stopped. The ultimate effect of this shutdown is there on new scientific discovery and innovation.[5,26]

Prognosis

Operating surgeons are to know that Covid-19 patients with absolute lymphopenia at the beginning of the disease generally have a poor prognosis. Severely ill patients have a progressively decreased number of peripheral lymphocytes. A ratio of Neutrophil to lymphocyte more than 3.5 is a very poor sign. D-dimer and Ferritin levels are significantly elevated in severe cases, which are highly potential risk factors for poor prognosis. Aged patients who have co-morbidities like hypertension, diabetes mellitus, cancer, ischemic heart disease, cerebro-vascular disease, high LDH (lactate dehydrogenase level), any overt or subclinical organ failure, D-dimer more than 1 μg/mL are more likely to show deterioration and development of serious illness with a worse prognosis. In addition, male sex, incidental serious illness, respiratory expectoration, myalgia, and hypoalbuminemia are independent risk factors that can exacerbate the clinical course and outcome of Covid-19 patients. Moreover, seriously ill men with a myocardial injury, hyperglycemia, and high-dose steroid use have a higher risk of death.[2,24]

The Covid-19 pandemic is currently a global health emergency. Interpersonal transmission has enormously and rapidly multiplied the spread of this disease, making it even the most difficult to prevent and contain its spread. A Covid-19 patient may be completely asymptomatic with a positive test result, or may present with a mild common cold-like illness or may present with severe symptoms requiring admission to a hospital. There is currently no specific effective gold standard antibody test available for rapid diagnosis, but High Resolution CT (HRCT) scans of the chest have been proved to be quite the most sensitive.[21,22]

In the absence of an ideal effective polyvalent vaccine covering all of its mutant pathogenic variants, its treatment is principally supportive with oxygen administration, antiviral drugs, steroids and antibiotics. Complicated and resistant cases, in addition to standard treatment regimen may necessitate immunomodulatory medication and PET (Plasma Exchange Therapy) using convalescent plasma from recently recovered patients with no other transmissible diseases. The profound effect of this pandemic super-infectious and super-mutating disease has left Health Care Workers (HCWs) and the healthcare industries across the world in a critical condition. The management models are not adequate in all dire situations and proper dynamic trainings are pre-requisites to work in critical situations, while continuous protection of HCWs by themselves is equally important. Many of the current protocols and therapeutic guidelines are based mostly on experience, observation and opinion. Specific guidelines need to be updated frequently to incorporate the emerging needs as the duration of pandemic is progressing. Non-infected communities that have no experience of facing this Covid-19 pandemic, planning should be built to lesson them urgently. All these challenges and changes are expected to build a "new normal world" as early as possible.[23,33]

Main messages

1. The Covid-19 pandemic is currently super-spreading with super-mutating by Covid-19 virus throughout the world, resulting in unexpected morbidity and mortality and creating a huge panic.
2. To date, there is still a high need of an effective gold standard, rapid and sensitive specific serologic test for Covid-19.
3. Several effective treatment regimens are now available, including antiviral medication, immunomodulating drugs, potent steroids with minimal side-effects and PET (Plasma Exchange Therapy by convalescent plasma).
4. The search for a potent polyvalent vaccine should be started by health research institutes all over the globe.

Acknowledgement

We are very much grateful and thankful to Prof Md. Zulfikar Ali for his continuous and active inspiration in preparing and publishing this time-demanding highly important burning issue "Covid-19 and Surgery".

References

1. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: a review article. 20 April 2020]. Clin Immunol2020; 215:108427.
2. Cascella M, Rajnik M, Cuomo A, et al. Features, evaluation and treatment coronavirus (COVID-19). Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing, 2020 Jan. (Last Updated 18 May 2020).
3. Joint Statement by American College of Surgeons, American Society of Anesthesiologists, Association of peri-Operative Registered Nurses, American Hospital Association.: Roadmap for Maintaining Essential Surgery during COVID-19 Pandemic. Available at: https://www.facs.org/-covid-19/clinical-guidance/roadmap-maintain-essential-surgery. Updated August 10, 2020.
4. Prachand VN, Milner R, Angelos P, et al. Medically Necessary, Time-Sensitive Procedures: Scoring System to Ethically and Efficiently Manage Resource Scarcity and Provider Risk During the COVID-19 Pandemic. J Am Coll Surg. 2020; 231(2):281-288.
5. Wall Street Journal. Available at https://www.wsj.com/podcasts/the-journal/dr-anthony-fauci-on-how-life-returns-to-normal /. April 16, 2020.
6. Global Corona Situation. The daily "The Prothom Alo". 2021, September 11. Available at https://www.prothom-alo.com
7. American College of Surgeons. COVID-19: Guidance for Triage of Non-Emergent Surgical Procedures. Accessed April 17, 2020. Available at https://www.facs.org/-COVID-19/clinical-guidance/triage. March 17, 2020.
8. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: a review article. Clin Immunol. 2020; 215:108427.

9. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020; 382:1199–1207.

10. He Y, Wang J, Li F, et al. Main clinical features of COVID-19 and potential prognostic and therapeutic value of the microbiota in SARS-CoV-2 Infections. Front Microbiol 2020 ;11:1302.

11. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B beta coronaviruses. Nat Microbiol 2020; 5:562–569.

12. Ou X, Liu Y, Lei X, et al. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nat Commun2020; 11:1620.

13. Yang N, Shen HM. Targeting the endocytic pathway and autophagy process as a novel therapeutic strategy in COVID-19. Int J Biol Sci 2020; 16:1724–1731.

14. Wan Y, Shang J, Graham R, et al. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. J Virol2020; doi: 10.1128/JVI.00127-20.

15. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020; 8:420–422 .

16. Chan J, Yuan S, Ko kK, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020; 395:514–523.

17. Huang C, Wang Y, LiX, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497–506.

18. Goyal P, ChoiJJ, PinheiroLC,et al.Clinical characteristics of COVID-19 in New York city. N Engl J Med 2020; 382:2372–2374.

19. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382: 1708–1720.

20. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. JAMA 2020; 323:1488–1494.

21. Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology 2020.

22. Huang P, Liu T, Huang L, et al. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology 2020.

23. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect 2020; 9:386–389.

24. Kollias A, Kyriakoulis KG, Dimakakos E, et al. Thromboembolic risk and anticoagulant therapy in COVID-19 patients: emerging evidence and call for action. Br J Haematol 2020; 189:846–847.

25. Kowalewski M, Fina D, SłomkaA, et al. COVID-19 and ECMO: the interplay between coagulation and inflammation: a narrative review. Crit Care 2020; 24:205.

26. Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of COVID-19 - preliminary report [published online ahead of print, 2020 May 22]. N Engl J Med 2020; NEJMoa2007764.

27. Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 days in patients with severe COVID-19. N Engl J Med 2020. Doi: 10.1056/NEJMoa2015301.

28. Yao TT, Qian JD, Zhu WY, et al. A systematic review of lopinavir therapy for SARS coronavirus and MERS coronavirus-a possible reference for coronavirus disease-19 treatment option. J Med Virol 2020; 92:556–563.

29. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe COVID-19. N Engl J Med 2020;382: 1787–1799.

30. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395:507–513.

31. Buonaguro FM, Puzanov I, Ascierto PA. Anti-IL6R role in treatment of COVID-19-related ARDS. J Transl Med 2020; 18:16.

32. ZhuFC, Li YH, Guan XH, et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. Lancet 2020;395: 1845–1854.

33. Zhou P, Yang XL, Wang XG, et al.A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020; 579:270–273.