

### FROM THE PEN OF THE PRESIDENT...

Dear All

It appears that we at a low peak of the SARS-COV-2 activity as of march end. But this is no cause for complacency as several medical organizations have warned of the possibility of CORONA peaks. Particularly in the aftermath of a vaccination program which has set in a sense of false security. However, it is still too early to say what the repercussions of Corona are and for how long we will remain under the yoke of COVID-19. Despite all these the New Year is coming and it is more than probable country will be in a merry making mood of having been released from the lockdowns and curfews. Because of this several medical organizations including SLMA, GMOA have forewarned the country of impending disaster if the basic public health measures are not adhered to.

We had a successful CPD activity at the Galle Face Hotel which was well attended. Several key topics were discussed at the ex-co meeting and an agenda for activities was set.

#### Dr. Ananda Perera

President IMPA

#### **EDITOR'S COLUMN**

I have received two articles related to Covid 19 pandemic. The editor will not publish the 2<sup>nd</sup> article as suggested before. This will be on Vaccines against covid 19. This will appear in the May Newsletter.



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#### The wider picture

The Corona viral infection (Coronavirus -2 (SARS-CoV-2) / COVID-19) which was said to have appeared in China Wuhan in 2019, causing severe acute respiratory syndrome has currently invaded the entire world with approximately 15 million cases and more than three million deaths.

The different variants of this virus seem to vary in severity. South Asia alone has reached a case rate of more than two million and more than 100,000 deaths due to COVID-19. This number keeps rising, overwhelming the health sectors in the region. The healthcare personnel frequently educate their patients about the proper wearing of masks, practicing social distancing and proper hand washing te chniques. The General Practitioners (GPs) and other primary care professionals have commenced the practice of telemedicine. At the same time, the health-seeking behaviour of the public seems to have reduced drastically, owing to the lockdowns, isolations and the fear of contracting this infection. A considerable number of people in the communities engage in selfmedication and using home remedies rather than going to the GP clinics.

All frontline healthcare workers, including social workers have a much higher risk of contracting COVID-19 due to repeated exposure and therefore arrangements have been made to get them vaccinated worldwide. In countries such as the United Kingdom, mental health support to all staff who are closely working with COVID-19 positive patients has been arranged.

#### The 'hospital at home' model

In this terrifying situation of the recent pandemic and the limitations of healthcare facilities, home-based services for the treatment of COVID-19 infection have come into light. These services may be best given by the healthcare personnel who are closest to the community and its people. A General Practitioner could manage the asymptomatic or patients with mild symptoms who are ideally below the age of 60 years, without co-morbidities, if given the responsibility, thus reducing the burden to the hospitals and hospital staff. This system of home-based COVID-19 care has already been implemented in the U.S.A, Italy and a number of other European countries. The use of tele-monitoring methods with real time audio-video messaging tools, digital blood pressure monitoring, digital thermometers, digital oxygen saturation devices which may be connected via Bluetooth devices / activity trackers (e.g., fit-bit) and other devices, could come in handy, when offering home-based or remote medical care for COVID-19 patients. Having a simple pulse oximeter in the household would be helpful to identify low oxygen levels in the blood for early action and management. Like in every case, the 'hospital at home' model too has its challenges including the need of personal protective equipment (PPE) and the need to dispose of these PPE with minimal risk of viral transmission.

The COVID positive patients in England and Scotland are being managed with the use of video consultations. In instances where the video consultations are inadequate and the physical examination is essential, home visits are done after triage. All precautions to prevent the spread of COVID-19 infection like wearing of PPE in advance to the visit, frequent and proper hand washing, physical distancing, and proper disposal of clinical waste are to be followed whenever home visits are done. The World Health Organization (WHO) stresses that the healthcare staff providing home care for suspected or confirmed COVID-19 patients must be trained sufficiently to minimize risk of infection, including the aspects of proper wearing, removal and disposal of PPE.

In the case of treating the COVID-19 suspected or confirmed patients in their homes, the chance of transmitting the virus to other family members at home, should be looked into.

According to the recommendations of the WHO, the decision whether to isolate the infected person and care to be given at home should depend on;

- 1. Clinical evaluation of the COVID-19 infected patient
  - a. Evaluation should be on, case by case basis. The clinical presentation, requirement for supportive care and other risk factors like age, Non-Communicable Diseases (NCDs), cancers, other immune compromising states, smoking, alcohol intake and obesity are to be evaluated thoroughly.
  - b. Patients who are asymptomatic, with mild symptoms (without pneumonia or hypoxia),

with moderate symptoms (adult or adolescents with clinical signs of pneumonia, symptoms like fever, cough, dyspnoea, SpO2 > 94% on air) with no risk factors and not requiring any emergency interventions and or hospitalization, could be isolated at home under close monitoring done by trained healthcare staff. This could be applied to both pregnant, postpartum mothers and children. It is important to ensure that both caregiver and the patient wear appropriate PPE.

- 2. Evaluation of the home setting and facilities available
  - a. Is the COVID-19 suspected / diagnosed patient living alone? If so, support and network?
  - b. Living conditions of the patient and the family? How feasible and practical to implement home care for this patient and the family?
  - c. Disabilities of the patient and the needs of the household members?
  - d. Knowledge and awareness of the patient and the family on COVID-19 infection its prevention, transmission, signs and symptoms?
  - e. Could the patient and the family be able to cope up with the situation?
  - f. The psychological impact of Person with COVID-19 and family members?
  - g. Financial constraints that the patient and the family may face?
  - h. Possibility of follow up and maintenance of care?
- 3. The ability to monitor the clinical evolution of the patient at home; monitoring, availability of facilities and line of communication should be established throughout the home care period.

#### Advice to be given to patient and the family:

- Limit the number of household members coming in contacting with the patient
- Minimize contact while using the washroom / toilets if only one is available
- Avoid sharing of personal items
- Adhere to strict hand hygiene
- Maintain distance and wear mask while coming in contact with the patient
- Make arrangements for proper waste disposal route

On the other hand, the GP or other relevant healthcare personnel should consider the following before handling COVID-19 suspected / diagnosed patients at home,

- Availability of adequate room
- Availability of natural air and light

The GP should lay out a proper treatment plan

which consists of symptomatic treatment, adequate nutritional management and hydration.

#### The General Practitioner and the community

The General Practitioner could also play the role in educating the community on how this infection could be spread, prevented and controlled. He should counsel the individuals in the community to cope up with the various problems that may arise due to the isolation, quarantine procedures and contracting of the disease itself. He must practice according to the health guidelines in diagnosing and notifying the COVID-19 infections in the patients who may present to the general practitioner for help. Moreover, the General Practitioner could continue to prevent and control the other non-communicable diseases that exist in the community such as cardiovascular diseases, diabetes melllitus, chronic lung diseases, chronic kidney diseases, without delay.

In Sri Lanka too, GPs and their staff should be in the priority list for vaccination against COVID-19. They could be liaised with the local Medical Officer of Health and relevant authorities under the Ministry of Health to handle and manage asymptomatic and mild COVID-19 patients at home. Thus, reduce the burden to the health sector in this time of need.

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#### MANAGEMENT OF COVID 19 INFECTION (ASYMPTOMATIC/MILD)

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#### Introduction

Covid 19 infection is caused by 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2). As of the day of writing, there have been over 169 million infections worldwide and over 3 million deaths(1). Up to April 2021, Sri Lanka had recorded 106,484 cases and only 667 deaths. Resurgence of Covid 19 infected cases from Mid-April, has become a national emergency, necessitating lockdown measures. This brief communication hopes to identify the clinical features of the present wave and offer management practices.

# Categories of patients seen by first contact doctors

Category 1 - First level Covid contacts who develop symptoms while they await PCR testing or have been tested and are awaiting the result. For some this has taken 10 days or more. During which time symptoms appear. Category 2 – Those who develop symptoms at home without PCR testing as they did not consult any medical officer or when they consulted, it was treated as a passing infection.

Category 3 – Stayed at home in spite of contact history and developed no symptoms but recovered on their own

#### Pathogenesis

Spike protein (S protein) of SARS-CoV2 virus is known to attach to angiotensin-converting enzyme-2 (ACE2) receptors, in the upper respiratory tract, in gaining entrance to the human body. The virus will gain access to alveolar tissues very quickly. If the virus spreads and the immunological inflammation is not arrested with early treatment, the body's immunological response will affect the lung, specifically air diffusion - oxygen and carbon dioxide diffusion via alveolar capillary membrane (ACM) (2).



Figure 1. Staging of COVID infection (Staging system was proposed by Siddiqi et al. Reproduced from https:// emcrit.org/pulmcrit/steroid-covid/(3)

#### **Clinical Progression**

- Gets worse after 4<sup>th</sup> day with early lung involvement
- Mild symptoms worsening on 8<sup>th</sup> day. Observation needed from 7<sup>th</sup> day.

Worsening symptoms

- Characteristic feeling of being unwell, "unfit to do usual work".
- Initial low-grade fever which spikes or afebrile initially and sudden onset fever
- Mild throat scratch/soreness
- Cough
- Difficulty in breathing You may be able to pick up early lung involvement with breathlessness on exertion (eg: one minute sit to stand test- few times as they can or stop if any discomfort) and with use of a pulse oximeter. (4)
- Sudden persistent headache
- Worsening diarrhea, severe loss of appetite

#### **Proposed management**

Prevention of thrombotic complications and supportive care

#### Non-pharmacological

- Steam inhalation (ensure safety), coriander water, warm fluids
- Avoidance of alcohol and smoking

#### Pharmacological

- 1. Promethazine H1 antagonist to prevent further lung damage by inhibiting viral replication at the lysosome level(5).
- 2. Vitamin C is a known antioxidant though conclusive evidence on its role in COVID-19 immunity response is lacking. Zinc sulphate 50 mg daily known antiviral action (6). However, many of the expert protocols for the treatment and prevention of covid-19 included vitamin D3, vitamin C 500mg and zinc. Vitamin D has an immunomodulatory effect (7). Loading dose is given to achieve adequate serum vitamin D3 levels within a short period of time. There is no consensus on the recommended dose and should be prescribed with caution due to possible vitamin D toxicity.
- 3. Inhaled budesonide 800 mcg twice daily Early administration improves recovery time and is an effective treatment when started early. (8) DPI was used in this RCT. In Sri Lanka only Budesonide MDIs are available.
- Dexamethasone (oral or intravenous(IV) resulted in lower mortality in those needing respiratory support(9). Methyl prednisolone (IV) – has been given on 4<sup>th</sup> day after symptoms. While viraemia increased, patients improved clinically because of immune inhibition action. This will prevent

thrombosis later. Better results rather than waiting until worsening hypoxia occurs. In hypoxic COVID-19 patients, methylprednisolone (IV) showed better clinical effect compared to dexamethasone(3) (9). Ministry of Health Sri Lanka recommends corticosteroids for patients with moderate to severe COVID in hospitalized patients.

5. Appropriate antibiotics as indicated for possible bacterial infection

#### Repurposed drugs under review

#### Aspirin

Low dose aspirin – 75 mg daily - Aspirin may be associated with decreased severity of COVID-19 and death by preventing platelet aggregation (6)

#### Hydroxychloroquine

Early therapy with hydroxychloroquine for high risk patients or patients with worsening symptoms - HCQ 400 mg twice daily loading dose on day 1, 200 mg twice daily for 7 days with Zinc has been recommended by Peter Macculough et al (6). HCQ blocks spike protein attachment to ACE2 receptor. HCQ also increases pH in lysosomes & reduce vital replication. HCQ blocks IL 6 which is a major mediator of cytokine storm (5) (6).

#### Ivermectin and combination therapy

Ivermectin has potential to reduce viral load. The high binding activity of ivermectin to the SARS-CoV-2 spike protein could limit binding to either the ACE-2 receptor or sialic acid receptors, respectively, either preventing cellular entry of the virus or preventing hemagglutination, a recently proposed pathologic mechanism in COVID-19 (5).

Early treatment with Ivermectin at onset of disease promoted faster viral clearance which may prevent significant immune system involvement and quicker recovery. Early intervention also reduced the viral load faster and this may hinder disease transmission in the general population (5).

Conclusions drawn from the British Ivermectin Recommendation Development meeting held in February 2021 were to use ivermectin for the prevention and treatment of covid-19 in order to reduce morbidity and mortality and to prevent covid-19 infection among those at higher risk (10).

Statistically significant reductions in mortality, clinical recovery time, and virus clearance were shown in the meta-analysis of 18 treatment RCTs and 3 prophylaxis RCTs of ivermectin in COVID-19 which included more than 2500 patients. The research panel found robust evidence for ivermectin's effects on mortality benefit and they recommended unconditional adoption for

use in the prophylaxis and treatment of COVID-19. (11). It was also noted multiple, large "natural experiments" occurred in regions that initiated "ivermectin distribution" campaigns followed by tight, reproducible, temporally associated decreases in case counts and case fatality rates compared with nearby regions without such campaigns (11). In another meta-analysis consisting of 21 RCTs involving 2741 participants, Bryant et al reports similar findings and suggests early treatment could reduce number of people progressing to severe disease. The apparent safety profile and cost effectiveness further supports the use in a pandemic (12).

Combination with ivermectin and doxycycline may inhibit viral entry and enhance viral load clearance in SARS-CoV-2 infection (13). Doxycycline is a known inhibitor of IL-6, TNF-alfa and MMP enzymes which play a pathological role in Covid-19(14). These mechanisms are independent of viral strains.

These findings propose using ivermectin as an add on therapy for treatment and prevention of COVID-19. Trials are ongoing on the treatment dose for treatment and prophylaxis and the use of combination therapy.

In another development the Ministry of health and family wwelfare, India revised its guidelines on home isolation of mild/asymptomatic COVID-19 cases on 28<sup>th</sup> April 2021 to include Ivermectin (200 mcg/kg once a day, to be taken empty stomach for 3 to 5 days) and budesonide inhalation (800 mcg twice daily for 5 to 7 days) for fever and/or cough persisting for more than 5 days.

#### Conclusion

Early treatment with Ivermectin with other combination medications for prevention of pulmonopathy and severe disease have been used. As first contact doctors in the community there is a responsibility of averting death, reduce hospital admissions and reduce need for ventilation and ICU care. It's time to read up and be up to date in scientific knowledge at a time science is politicized. Further randomized clinical trials are ongoing to establish conclusive evidence.

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