63

<u>Review Article</u>

COVID Management and Prophylaxis among Rural, Hilly and Tribal Population of India

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The Covid-19 pandemic has been around us for more than a year now, with millions of confirmed cases and related deaths around the World.

Recently, during second wave in India we observed a large number of infected cases with high mortality and scarcity of health infrastructure and manpower. The worst hit states were Rajasthan, Maharashtra, Uttar Pradesh, Karnataka, Andhra Pradesh and Kerala.

The uncertainty and hopelessness of the disease is more exaggerated in remote rural, hilly and tribal areas of our country because of scarcity and inefficiency of health care facilities.

A streamlined treatment and prophylaxis protocol is the need of the hour. Uttar Pradesh was the first State in India that issued a Government order for Ivermectin prophylaxis to household contacts, health care workers and to treat mild to moderate cases of Covid-19 with combination of Ivermectin and Doxycycline.

This author was one of the external experts who was behind the formulation of this Government order. He further observed the miraculous effect of combination of ivermectin and doxycycline which became the backbone of the treatment protocol designed by him for the people living in remote areas of the country. Author's concept is just the simplified version, mainly based on Indian Council for Medical Research (ICMR) protocol and the Government order issued by Uttar Pradesh which is more applicable and feasible and accessible in such resource poor localities of our country.

Author's strategy for such areas is simply based on COVID symptoms and pulse oximetry measurement to diagnose, categorise and treat the mild and moderate cases of COVID. This innovative strategy can be very helpful for rapid and prompt treatment of Covid-19 in remote areas considering the scarcity of COVID testing, health infrastructure and difficult connectivity and transport facilities in these areas.

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Key words : Covid Treatment, Rural, Hilly, Tribal, Remote Areas.

The coronavirus disease 2019 (Covid-19) is a global pandemic that was first detected in China in December, 2019.¹The pandemic affected around 200 countries² with number of cases reported globally now exceeding 180 million till now³. The virus is rapidly changing and new variants being discovered. The second wave of this deadly disease emerged with new mutant variant with higher virulence and higher mortality⁴. Newer strains are not only more transmissible but also affect the younger population. Presentation with unusual symptoms, higher rate of infections among younger people and anexponential rise in daily cases leading to delayed RTPCR test reports, have been seen in the second wave of COVID.

India was among the badly hit countries by the second wave, with more than 3 crore confirmed cases and around 4 lakh total deaths.⁵ The two main

Editor's Comment :

Health Infrastructure, healthcare facilities, and healthcare workers are very poorly available in rural, hilly, tribal remote areas of India hence presumptive covid diagnosis based on symptoms only and monitoring of Oxygen saturation by Pulse Oximeter is a key diagnostic approach in these remote areas, Covid 19 treatment strategy based primarily on ICMR Protocol and Ivermectin-Doxycycline regimen can be the best strategy for Covid-19 treatment in the remote areas.

challenges faced by India in fighting the pandemic are the population size and poor healthcare infrastructure.

Furthermore, there is vast diversity in the availability of healthcare facilities between rural and urban India. There are approximately 7 lakhs villages across India and around 70% of Indian population lives in rural areas with scheduled tribes contributing to 11.3% of the total population of rural areas and 2.8% of urban areas.⁶ There is only a single health care centre at every 40 kms and that too mostly with no oxygen beds and with untrained staff and doctors. There is scarcity of

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qualified medical professionals in this region with a shortfall of 11.6% of medical officers at the primary health care level and 81.2% of medical specialists at community health centres as reported in 2016.⁷ The doctor-patient ratio of 1:1445 is way less than the ratio suggested by the World Health Organisation (WHO) in this regard (1:1000)⁸. Furthermore, this ratio is even lesser in villages and tribal areas. Transportation facilities are poor, making access to medical facilities even more difficult. Providing health care to people in rural areas is thus the biggest task faced by the country which worsens with pandemics such as Covid-19. The relocation of the urban crowd to small towns and villages post-lockdown led to a surge in rate of COVID infection in rural India.

Challenges for Covid Management in Rural, Hilly and Tribal areas :

It has been reported in May 2021 that rural districts accounted for almost 50 percent of all new cases in the country and therefore to win the battle against COVID adequate management strategies should be adopted for both prevention and treatment of the disease.

Challenges faced in COVID management of these patients were,

Scarcity of health care facilities

 Scarcity of healthcare workers including doctors, nurses, paramedical staff (ANM, ASHA worker etc)

- Lack of ambulance services
- Lack of transport and connectivity

• Lack of standards of home isolation, small houses and no attached bathroom facility

- Non availability of medicines
- Lack of COVID health awareness

• Improper information and management system by untrained nonqualified fellows (quacks)

• If a fellow residing in these areas complains of symptoms consistent with Covid-19 infection where diagnostic tests like Rapid Antigen Test and RT PCR are not easily accessible, samples are sent to closest town and the reports are always delayed by 4-5 days.

These problems are a hurdle in providing optimum health care facilities to the residents of these areas. Though Government is trying to make test accessible to all, practical scenarios indicate that there is a long way to go.

To overcome this, the author has

come up with a pulse oximeter-based treatment strategy to initiate the basic treatment of Covid-19. Before going into to the details of the treatment there are few points regarding the appropriate diagnosis of Covid-19 infection that should be kept in mind. Those patients who have signs, symptoms and /or radiological findings suggestive of COVID with negative RTPCR report are assumed as presumptive COVID.

Author has modified this definition for early detection and prompt management of COVID.

Protocol for pre-sumptive COVID (without waiting for test reports) (Fig 1):

The author recommends early treatment with a combination of Ivermectin and Doxycycline along with symptomatic and supportive therapy in patients with mild disease who have oxygen saturation above 94 % and early institution of a short course of steroid in patients who have oxygen saturation between 90-94%.

These patients actually belong to the MODERATE category of COVID infection who are recommended hospitalization according to ICMR protocol (Fig 2) and any delay in instituting treatment in these patients can lead to increase in severity of the disease from MODERATE to SEVERE category which leads to a higher mortality in these patients. This strategy highlights the use of Ivermectin as a frontline drug in the treatment of Covid-19 infection.

Role of Ivermectin in COVID Prophylaxis and Moderate Infection :

There have been more than 100 trials Worldwide for the use of Ivermectin in the treatment of COVID infection. Ivermectin not only has role in treatment but is also useful as a preventive therapy.





An observational study, conducted in a tertiary hospital in Dhaka that enrolled 118 health care workers showed that Ivermectin has a role in Covid-19 prevention as well. Another study done at AIIMS, Bhubaneswar also reemphasized that Ivermectin prophylaxis reduces the risk of contracting COVID infection.

The author was a part of a group of experts,all having enormous clinical experience who gathered and explored the role of Ivermectin, an old molecule in Covid-19 management. After critical panel discussion, they all came to an inference that Ivermectin can be a prospective molecule for prophylaxis and treatment of people infected with Coronavirus because of its Anti-viral activity and good safety profile and tolerability.

Following this White paper on lvermectin as a potential therapy for Covid-19 came in July 2020 which later also became a part of global literature on coronavirus diseases available on the official World Health Organization webpage.

Later, Government order for prophylaxis of healthcare workers and household contacts along with the order for treatment with Ivermectin and

doxycycline was released on 6/8/2020 by the UP Government. Ivermectin in combination with doxycycline has shown to have a synergistic effect in inhibition of spike protein of ACE 2 receptors and therefore the combination used in this protocol is a good choice in prevention and management of COVID infection.

Treatment Strategy based on Symptoms and Oxygen Saturation for Rural, Hilly and Tribal Areas :

A simplified protocol has been suggested here, for patients to whom RTPCR/RAPID ANTIGEN TESTING is not readily available (Fig 3). This simplified protocol can be beneficial for the doctors working at CHCs/ PHs for early detection, better management and monitoring of such patients.

• If the oxygen saturation (SpO2) is>94 %: The patient should be isolated and given ivermectin and doxycycline. Symptomatic and supportive treatment should also be provided.^{9,10}



Fig 2 — ICMR/AIIMS COVID 19 Treatment Protocol



Fig 3 — Treatment Algorithm Based On Clinical Experience

• If the SpO2 is between 94 to 90 %: The patient should be placed inprone position and asteroid can be added to the above treatment regimen after consulting the physician.

• If the SpO2 is <90%: The patient needs oxygen support/ hospitalization

For patients living invillages where COVID testing as well as other diagnostic modalities are readily available, the initial management can still be based on SpO2 level of the patient (Fig 4). Following stepwise treatment protocol has been suggested:

If the patient is Covid positive or has presumptive Covid (Symptoms/ Chest X-Ray/HRCT Thorax Suggestive of Covid but Covid Test Negative) and the SpO2 is:

Above 94%

- Isolation
- Ivermectin(12 mg)- two hours after dinner for 5 days

• Doxycycline (100 mg) twice daily after meals for 5 days

• Paracetamol (500 MG), when body temperature is >99°F

Between 94 to 90%

Isolation prone position

 Ivermectin (12 mg) - two hours after dinner daily for 5 days

Doxycycline (100 mg) twice after meals for 5 days

• Prednisolone (20mg) one daily after breakfast for 5 days

• Paracetamol (500 mg), when body temperature is >99°F.

The patient should be carefully monitored and hospitalization will be required if SpO2 falls below 90% or patient develops unconscious-ness, bluish discoloration of lips, tongue, nails, breathlessness or the body temperature does not fall below 104°F.

Currently Available Medications for Treatment of Covid-19:

With no effective antiviral drugs in sight, the repurposing of many currently available drugs has been considered the mainstay of treatment.

Ivermectin was formerly approved as an antiparasitic agent but it has been shown to also exhibit antiviral



NOTE 1 -RED FLAG SIGNS - If SpO2 is < 90% or patient has unconsciousness and bluish discoloration of lips tongue, nails breathlessness and temperature does not fall below 104 THESE FEATURES ARE INDICATION OF HOSPITALIZATION

NOTE 2 -Doses of IVERMECTIN

 Adults with weight
 < 60 kg</td>
 12 mg

 Adults with weight between 60 – 80 kg
 18 mg

 Adults with weight more than 80 kg
 24 mg

 Children between 6 – 12 years of age
 6 mg

 Children between 2 –6years of age
 3 mg

Fig 4 — Treatment Strategy Suggested By Dr . Surya Kant (Based Mainly On ICMR Protocol) For Covid 19 Patients in Rural Population Where Covid Testing is Unavailable

activity against a wide range of viruses. Ivermectin is an excellent composition that has the potential to treat various classes of diseases because it has antimicrobial, anticancer and antiviral properties. Therefore, Ivermectin is investigated and studied to be used in the treatment and prophylaxis of Covid-19 as well because of its multidimensional mechanism of action including inhibition of viral replication, blockade of the entry of the virus into the host cell, action as an ionophore molecule, and prevention of microvascular thrombosis.¹¹

Uttar Pradesh was the first State in India to use Ivermectin. Government order of UP Government for the use of Ivermectin in treatment and prevention of Covid-19 was released on 6/08/2020 and since then it has been adopted in treatment and prevention of the disease in various States of India — West Bengal, Maharashtra, Karnataka, Kerala, Assam and Goa. Goa Government recommended a new Covid-19 treatment protocol which endorses prescription of five tablets of the Ivermectin to all residents >18 years of age in order to prevent the steep and sometimes fatal viral fever, which accompanies a Covid-19 infection.

The recommended dose of Ivermectin in adults with

body weight <60 kg is 12 mg/day, weight between 60 to >80 kg is 18 mg/day and for those with weight >80 Kg, it is 24 mg/day. Children in between 6 to 12 years of age can be 6 mg/day.

Doxycycline : Doxycycline is a broadspectrum antibiotic class which is used in treatment of various bacterial infections like community acquired pneumonia, acne, chlamydia infections, Lyme disease, cholera, typhus and syphilis. It has an established safety profile with a potential efficacy against viral pathogens leading to dengue fever and chikungunya therefore, it may regulate pathways important in initial infection, replication, and systemic response to SARS-CoV-2. Ivermectin-Doxycycline vs Hydroxychloroquine-Azithromycin in mild to moderate cases [Bangladesh Study] showed that Ivermectin – Doxycycline to have a faster rate of recovery.¹²

Steroids: Covid-19 is a multisystem inflammatory disease and not just a disease confined to the lungs. Covid-19 triggers an hyperinflammatory response in the form of cytokine storm which is often lethal and is the main reason for increasing mortality in these patients. These deleterious effects can be prevented or mitigated by Anti-inflammatory effects of corticosteroids. The Randomised Evaluation of Covid-19 Therapy (RECOVERY) trial in patients admitted to hospitals with Covid-19, that the mortality from Covid-19 was lower among patients who received Dexamethasone than among those who were given the standard of care¹³.

Isolation in Rural Setup for COVID Patients :

It is important to isolate the patient to reduce the risk of infection spread. If dedicated COVID Care Centres are available in rural areas, the patient should be kept there under the observation. If not, following method of home isolation should be followed:

• People having only one room should use that room as isolation room and rest of the members should sleep outside in the portico area outside the house.

• The patient using the common washroom should sanitize it with commercially available sanitizer (if available) or 1% Hypochlorite solution (if available) or simply soap water can be sprayed for sanitization.

• Other family members should use bathroom after 3hours as virus remains in air for 3 hours. This will reduce the chance of other members getting infected.

• All members of the house including the patient, should use mask at the time of using washroom and should sanitize before and after using washroom.

For the monitoring of patients, we can use the services of ASHA workers. ASHA workers should be

sensitized about the symptoms and basic management of the COVID disease when it is in mild form and to identify the Red Flag Signs (Box). They should visit the patient twice in a day and monitor their oxygen saturation level and inform the doctors at nearby CHCs/PHCs. They should also take with them glucometer and monitor random blood glucose levels of diabetic patients. ASHA workers should also inform about any Red Flag Signs to doctors immediately, thus speeding up the transfer of such patients to hospital facility.

RED FLAGSIGNS

- 1. PERSISTENT FEVER
- 2. BREATHLESSNESS
- 3. DECREASING OXYGEN SATURATION
- 4. INCREASED BREATHLESSNESS
- 5. UNCONSIOUSNESS
- 6. BLUISH DISCOULOURATION OF LIPS, TONGUE OR NAILS

Role of ASHA workers :

Since community participation is an irreplaceable strategy for strengthening of health system in a densely populated country like India, a new cadre of community health volunteers [Accredited Social Health Activists (ASHA)] was created across all villages in India with a goal of increasing community engagement with the health system. ASHA worker is primarily a woman resident of the village preferably in the age group of 25 to 45 years and her services are of prime importance for managing the diseased and suspected cases of COVID. In order to properly avail their services ASHA workers should be sensitized about the symptoms and basic management of the COVID disease specially when it is in its mild form so that the disease can be nipped in the bud (Fig 5). She should be fully aware of her responsibilities which are as follows -

• ASHA worker is responsible to take pulse oximeter and glucometer door to door with her to screen for suspected COVID patients.

 Send a photograph of patient's oxygen saturation and random blood sugar to the doctors available at the PHC/CHC so that they can advise appropriate treatment and take an informed call for starting steroids in a patient.

• She should provide a detailed information about the Red Flag Signs of COVID infection.

• She should provide her contact number to the family and tell them to report if they notice any red flag signs in their family members.



Fig 5 — Role of ASHA Workers in Management of COVID patients (Endnotes)

• If Red Flag Signs are noted in any member of the village she should immediately inform the doctors at the PHC/CHC.

• She is responsible for the arrangement of safe transport of the sick patient to the nearest PHC/CHC.

• If none of the Red Flag Signs are noted in a COVID patient then he should either be isolated at isolation centres established in the village or be in home isolation.

• ASHA workers also have the responsibility to inform the Gram Pradhan of the respective village about the number and health status of COVID patients in his village so that accordingly he can help to arrange for any emergency services such as ambulance for the patients.

PROTOCOL FOR COVID-19 PROPHYLAXIS IN VIEW OF UPCOMING THIRD WAVE

In a densely populated country such as India, with a population of around 1,39 billion people, just treatment doesn't suffice. Prophylaxis is needed to arrest the spread of COVID cases.

Ivermectin is not only a potent antiviral agent but also an effective drug for prophylaxis of Covid-19 infection. It possesses potent antiviral properties and also helps in eliminating parasitic diseases — by mass administration that too with negligible side effects and cost.

A systematic review and meta-analysis of 24 RCTs (n = 3328) showed that ivermectin treatment reduces inflammatory markers, achieves viral clearance more quickly and improves survival compared with standard of care. This was especially so in mild/moderate patients, with stronger viral clearance at higher doses and longer durations of treatment. There was a 70%

improvement in survival in the subgroup of mild/ moderate participants¹⁴.

Another meta-analysis based on 18 randomized controlled treatment trials of ivermectin in Covid-19 has found large, statistically significant reductions in mortality, time to clinical recovery, and time to viral clearance¹⁵.

Efficacy of ivermectin in Covid-19 is supported by evidence from clinical trials in animal models and humans. It has been seen that Ivermectin prevents transmission and development of Covid-19 disease in those exposed to infected patients. It hastens recovery and prevents deterioration in patients with mild to moderate diseasetreated early after symptoms. Ivermectin leads to temporally associated reductionsin case fatality rates in regions after ivermectindistribution campaigns¹⁵.

Uttar Pradesh was the first state that released a Government order, with the author as one of the experts involved in formulation, for Ivermectin prophylaxis in household contacts and health care workers way back in August 2020, followed by Karnataka, Kerala, Rajasthan and West Bengal.

Vaccination along with mass prophylaxis with ivermectinare the only means of safe guarding the population from the tide of the upcoming waves of COVID.

Strategy for mass prophylaxis to general population (based on extrapolation from a study done in Bangladesh for weekly prophylaxis with Ivermectin)

Dose of Ivermectin recommended for mass prophylaxis by the author is as follows

- 2-6 years of age: Ivermectin 3 mg once weekly
- 6-12 years of age: lvermectin 6 mg once weekly
- More than 12 years of age: lvermectin 12 mg once weekly

DISCUSSION

The medical practitioners in rural areas are the first contact person where patients present with symptoms suggestive of Covid-19 infection. However, the knowledge about the disease is rapidly changing and with growing number of cases, the healthcare providers in these areas are not often adequately trained and equipped to deal with these infections¹⁶. Thus, there is a need of handy guideline that would aid the diagnosis and management of Covid-19 infection at the level of first contact of the patients in rural India.

In this simplified treatment protocol that has been proposed, SpO2 measurements using pulse oximeter,

which is readily available and does not require specialized training, is the only requirement. Before the confirmatory diagnosis is made using the Rapid Antigen Test or a RT-PCR, treatment can be initiated using this protocol that includes Ivermectin.While repurposed antimicrobials such as, hydroxychloroquine, lopinavir/ritonavir, remdesivir and interferon-beta have shown no significant survival benefit, ivermectin has shown benefits in mild/moderate disease and subsequent survival¹⁴. Use of this protocol before getting a confirmatory result would prevent aggravation of the disease for the lack of proper management and also help decreasing the healthcare cost to certain degree.

Involvement of the local Non-governmental Organizations like ASHA workers is also vital to boost up the human resource dearth that the country is facing. Educating people to recognize the symptoms and seek support and treatment whenever necessary is equally important. It should be noted that rural India often lives in houses that does not have more than 1 room, the washroom used is also common. In such situation, isolation and social distancing are distant reality. Measures to overcome these issues should also be brainstormed; opening more isolation centres for the infected may help to deal with this issue.

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