

Review Article

COVID Management Strategy for Third Wave / Omicron Variant in India

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COVID-19, the worst Pandemic of this decade caused significant morbidity and mortality in the past 3 years and still continue to hit the human kind with its evil skills. After the first and second COVID-19 wave the third wave has emerged with new variants and with high transmission rate and reduced efficiency of treatments and vaccines. The main treatment strategy remain same as symptomatic and supportive treatments. Oxygen therapy, Steroid, Antivirals and some repurposed drugs like Ivermectin and newer drugs including monoclonal antibodies are used in this fight against COVID-19. Ivermectin is being the game changer in many states of India, they kept this medicine in their new treatment protocol also. Vaccination including additional Booster/Precautionary Dose along with the COVID appropriate behaviours, if we are able to maintain Physical distance, Wear mask properly, Wash our hands and Prevent crowd from gathering then we will not allow the virus to spread and prevent the emergence of another wave.

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Key words : COVID-19, Omicron, Ivermectin, Booster dose.

COVID-19 is one of the worst viral pandemic in the last 100 years. The origin of the virus in Wuhan city of China in early December 2019 is a mystery and most likely the emergence was from a bat lineage via an unidentified intermediate host with more frequent human contact, in which the progenitor virus might have been circulating undetected for decades. The origin and spread of the disease created a havoc and feeling of unrest in India as well, affecting a population of more than 3.5 crore in India and more than 25 crore people globally. During this pandemic India lost more than 2000 doctors of modern system of medicine, they sacrificed their life for the fight against COVID-19^{1,2}. We salute their sacrifice and pay tribute to their selfless services. Even though the spread of the disease in the country was very unfortunate the silver lining behind its spread was the COVID appropriate behaviour that the disease taught^{3,4}. Awareness was created across the country over a very large scale like never before about the proper use of masks, cough etiquettes, physical distancing hand washing and sanitization. But never the late while we were almost recovering from the 2nd wave of covid, a new variant named OMICRON was detected in South Africa which became the major cause of 3rd wave in India.

Current COVID-19 Epidemiology (Table 1) :

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Editor's Comment :

- Third COVID-19 Wave with new variant including Omicron variant emerged as a threat for the society. However, India has contained this threat effectively because of its largest and fastest COVID-19 vaccination program including additional booster doses and COVID appropriate behavior.

COVID-19 Variants and Emergence of Omicron :

Viruses like SARS-CoV-2 (COVID-19) continuously evolving and Genetic Mutations occur during replication of the Genome. A variant is a Viral Genome (Genetic Code) that contain one or more mutations. To assist with public discussion WHO proposed the name of this variants consisting of a Greek alphabet like Alpha, Beta, Gama etc. They are also classified them as Variant of Interest (VOI) and Variant of Concern (VOC) etc. VOI are the variant with Specific Genetic Markers associated with changes to receptor binding, reduced neutralizing antibodies by the Vaccine and reduced efficiency of treatments. VOC are those variant with high transmissibility, potential for severe disease, reduced effectiveness of treatments or Vaccines or diagnostic detection failure.

Some of the variants and the place of earliest documentation are given below :

Alpha (B.1.1.7)	– United Kingdom
Beta (B.1.351)	– South Africa
Gamma (P.1)	– Brazil
Delta (B.1.617.2)	– India
And finally Omicron (B.1.1.529) – South Africa	

The Omicron variant is a variant of SARS-CoV-2, the virus that causes COVID-19. It was first found in

COVID -19 Cases	Global	India	Uttar Pradesh
Total no of cases /Cases per million population	32.9 crores (329,009,077)/42,209	3.73 crores /26,683 (only 11.34% of total global morbidity)	18.3lakhs (only 4.9% of total national morbidity)
Mortality Total/per Million population	55.5 lakhs /713	4.86 lakhs/347 (only 8.75% of total global mortality)	22,963 (only 4.72% of total national mortality)/102
Case Fatality ratio	2.3	1.3	1.1

South Africa on 9th November, which was then reported to WHO on 24th November, 2021. On 26th November, 2021, the WHO designated it as a **variant of concern** and named it "Omicron", the fifteenth letter in the Greek alphabet^{5,6}. The variant has total of 60 mutations compared to the actual variant, significant number of mutations are affecting the spike protein, targeted by most COVID-19 vaccines at present. This level of variation has led to concerns regarding its transmissibility, Immune System Evasion and Vaccine Resistance. Omicron is believed to be far more contagious (spreading much more quickly), to multiply around 70 times faster than the Delta variant^{7,8}. But to be less able to penetrate deep Lung Tissue. However, the extremely high rate of spread, combined with its ability to evade both double vaccination and the body's Immune System, means the total number of patients requiring hospital care at any given time is still of great concern.

On 2nd January, 2022 Israel confirmed its first case of an individual infected with both the seasonal flu and COVID-19 at the same time named **FLURONA**, the two infections were found in an unvaccinated pregnant woman who had mild symptoms. Another strain of covid-19 that combines delta and omicron was found in cyprus "**DELTACRON**". WHO however has not given any official confirmation about the two strains and their nomenclature^{9,10}.

Owing to the rapid spread of the disease due to its high infectivity Indian Council of Medical Research (ICMR) gave a guideline for COVID testing, to contain the spread of the disease in the Country.

ICMR New Advisory for COVID Testing (10 th January) :

Current COVID 19 testing strategy is for early detection of symptomatic cases for quick isolation and care and, early detection of infection in elderly >60 years and individuals with co-morbidities (Diabetes, Hypertension, Chronic Lung or Kidney Disease, Malignancy, Obesity etc for quick care. Test may be a point of care test like home or self test / Rapid Antigen test or Molecular Tests like RT-PCR, TrueNat, Cartridge Based Nucleic Acid Amplification Test

(CBNAAT), newer SARS-CoV-2 Omicron or Variant detection RT-PCR assays. According to the ICMR protocol, in community setting the following persons may get tested ; (1) symptomatic patients (Cough, Sore throat, Fever, Loss of taste/smell, Breathlessness and / or other respiratory symptoms), (2) at risk contacts of confirmed cases (Elderly >60 years and individuals with co-morbidities (Diabetes, Hypertension, Chronic Lung or Kidney disease, Malignancy, Obesity), (3) Individual undertaking International travel, (4) International travellers arriving at Indian Airport or Seaports. In hospital settings the testing may be undertaken as per the decision of the treating doctor. However patient care should not be compromised due to COVID testing so they included the following considerations like; emergency procedures, should not be delayed, should not be referred to other facilities for lack of a testing facility, asymptomatic patients undergoing surgical / nonsurgical invasive procedures including pregnant woman should not be tested unless symptoms develop¹¹ (Fig 1).

TREATMENT

Similar to 1st and 2nd wave strategy, the main treatment of the disease is symptomatic and supportive treatment . The mass casualties of COVID cases in previous waves were treated by Oxygen Therapy,

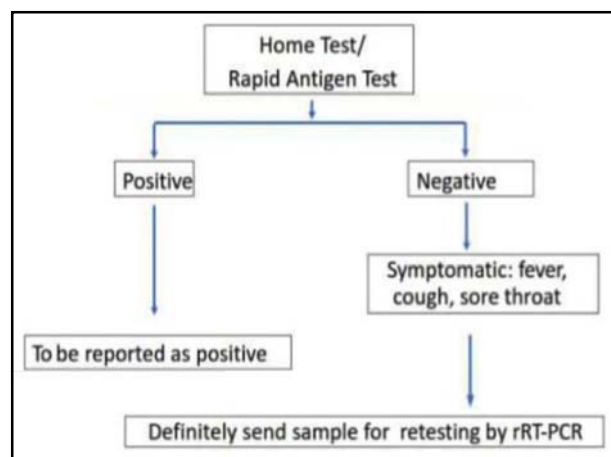


Fig 1 — Algorithm for COVID-19 Test Interpretation Using Home Test / Rapid Antigen Point of Care Test (Icmr, 10th Jan 2022)

Steroids and inhaled Budesonide and antivirals like, Remdesivir, Favipiravir. All of the drugs which are tried in the treatment of COVID-19 were repurposed drugs. The alternative treatment of COVID-19 consists of Ivermectin, Baricitinib (JAK inhibitor), Monoclonal Antibodies-Cocktail Therapy, Tocilizumab, Plasma therapy. The therapies recommended by AYUSH like Kadha, Steam, Yoga, Pranayama, Warm water etc were also widely accepted¹²⁻¹⁹.

Latest treatment protocol for the management of third wave of COVID-19 given below :

AIIMS / ICMR COVID-19 Treatment Protocol (14/1/2022) :

AIIMS/ICMR revised the COVID-19 treatment protocol on 14th January, 2022 . They approved the off label use of Remdesivir and Tocilizumab in specific circumstances (Fig 2).

Ivermectin is a FDA-approved broad spectrum Anti-parasitic agent, Commercialized since 1981 but no resistance is detected till date. High efficiency and safety profile along with low cost of this medicine made this a preferred medication for common people. Ivermectin is considered as a wonder drug because of its different mechanisms of action. MOA which make this effective against COVID-19 are, inhibition of viral replication, Blockade of the entry of the virus into the

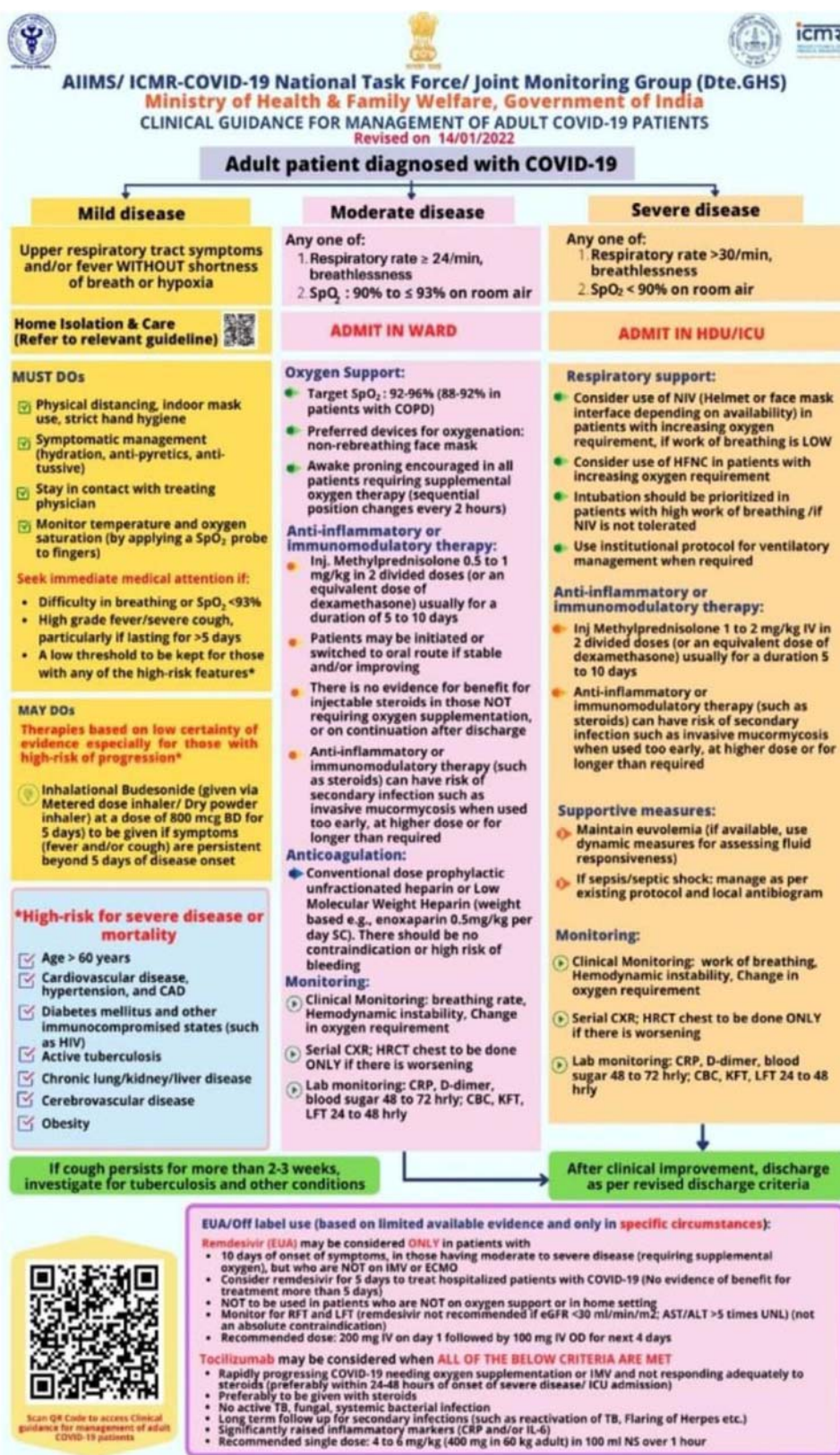


Fig 2 — Latest MOHFW/ICMR/AIIMS Guideline for Management of COVID-19 (Dated 14/1/2022)

Ivermectin for COVID-19: real-time meta analysis of 75 studies

Covid Analysis, Jan 16, 2022, Version 172 — added Abbas [BBC, GMK response]

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- Statistically significant improvements are seen for mortality, ventilation, ICU admission, hospitalization, recovery, cases, and viral clearance. All remain significant after exclusions. 49 studies from 45 independent teams in 21 different countries show statistically significant improvements in isolation (37 primary outcome, 34 most serious outcome).
- Meta analysis using the most serious outcome shows 66% [53-75%] and 83% [74-89%] improvement for early treatment and prophylaxis, with similar results after exclusion based sensitivity analysis (excluding all GMK/BBC team studies), for primary outcomes, for peer-reviewed studies, and for RCTs.
- Results are very robust — in worst case exclusion sensitivity analysis 60 of 75 studies must be excluded to avoid finding statistically significant efficacy.
- While many treatments have some level of efficacy, they do not replace vaccines and other measures to avoid infection. Only 25% of ivermectin studies show zero events in the treatment arm.
- Multiple treatments are typically used in combination, which may be significantly more effective.
- Elimination of COVID-19 is a race against viral evolution. No treatment, vaccine, or intervention is 100% available and effective for all variants. All practical, effective, and safe means should be used, including treatments, as supported by Pfizer [Pfizer, TrialSiteNews]. Denying the efficacy of treatments increases mortality, morbidity, collateral damage, and endemic risk.

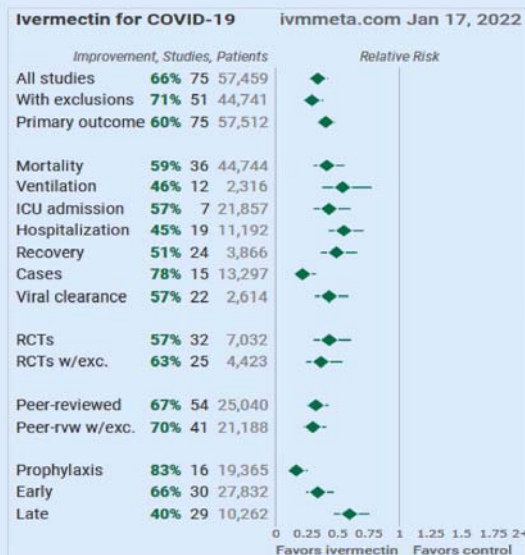


Fig 3 — Studies on the Effect of Ivermectin on COVID-19

Host Cell, Action as an Ionophore Molecule, Prevention of Microvascular Thrombosis and Sequestration in the pulmonary tissue. Currently there are 75 studies from 691 scientists in 24 Countries on the effect of Ivermectin for COVID-19 showed that there statistically significant improvement for viral clearance, hospitalization, mortality and recovery. They showed 59% lower mortality in 34 studies!²⁰⁻²⁵ (Fig 3).

Earlier the Indian states Uttar Pradesh, Uttarakhand, Goa, Delhi, Kerala etc were officially approved the use of Ivermectin in COVID-19 treatment protocol. Uttar Pradesh was the first state which has officially approved the use of Ivermectin for COVID treatment.

Uttar Pradesh, one of the biggest and populated state of India but during COVID-19 pandemic this state showed excellent disease containment and effective management. It had only 4.7% of the total National COVID-19 mortality and case fatality ratio is also less than National ratio. Apart from the political and administrative commitment, intensive use of Health Experts in COVID-19 mangement and sensitization, and policies like Triple “T” policy (Tracing, Testing and Treatment) and Containment policy; health experts

says that the use of Ivermectin in the treatment of COVID-19 was also a reason for this excellent results. Till date very few states have published their treatment protocol for third wave of COVID-19 pandemic, Uttar Pradesh government have kept ivermectin in their treatment protocol due to the excellent results of this drug (Fig 4).

Revised Covid Protocol of UP (JAN 2022)

- Treatment of Mild Covid

ISOLATION.

IVERMECTIN 200 mcg/ Kg Body weight per day for 5 days.

Doxycycline 100 mg twice daily / Azithromycin 500 mg daily for 5 days .

PARACETAMOL SOS.

Vitamin B ,C,D .

- Prophylaxis of family Contacts of COVID-19 patient

Two Doses of 12 mg of IVERMECTIN , 1st Day and 7th Day.

- Prophylaxis of Healthcare Workers

IVERMECTIN 12 mg once a Week

Fig 4 — Revised COVID Protocol of UP (Jan, 2022)

There are various studies are conducting for some new drugs for COVID-19, and some of the accepted amongst them in this third wave of COVID-19 pandemic are given below (Advised by The COVID-19 Treatment Guidelines Panel²⁶).

Pre exposure prophylaxis :

- Evusheld - Tixagevimab plus Cligavimab

Therapies for mild to moderate High risk non hospitalized patients

- Paxlovid Nirmatrelvir 300mg + Ritonavir 100mg BD for 5 days
- Sotrovimab 500 mg IV infusion
- Molnupiravir 800mg BD 5 days

Postexposure prophylaxis for people:

- Bamlanivimab and Eltesevimab 700mg + 1400mg
- Casirivimab and Imdevimab 600mg +600mg
- Sotrovimab 500mg (also active against Omicron)(Table 2).

Preventive Strategy :

Simple things that people can follow to prevent spread of COVID-19 like Namaste, Physical distancing, Take off Shoes, chappals before entering house, Hand wash, Wear mask when out of home, follow a healthy diet to boost immunity, Meditation, Yoga, Exercise, Good sleep. No addiction. Sanskar, respect and care of seniors, passionate environment at home. Work From Home. Tele consultation. Appropriate measures for Airborne Infection Control at Clinics and Hospitals. PPE kit, N95 masks during procedures.

Some actions are also required in the Country level also, WHO recommends acceleration of vaccination against COVID-19 and Booster/ Precautionary Doses for eligible groups, measures to increase the adherence of all individuals to protective measures, social measures to prevent crowding and people gathering in confined spaces , activating and prioritizing the case investigation and contact tracing for any COVID-19 cases, including Omicron; enhancing testing (and sequencing) and making it available freely to people with symptoms.

COVID Vaccination :

Vaccines which have mainly been available in India to fight against COVID, these are COVAXIN,

COVISHIELD & SPUTNIK V.

Covaxin was India’s first indigenous, whole-virion, inactivated vaccine developed by Bharat Biotech in collaboration with the Indian Medical Research Council (ICMR) and the National Institute of Virology (NIV). In July 2021, Bharat Biotech reported the vaccine to be 78% effective against symptomatic cases, 93% effective against severe COVID-19 infection and 65% effective against the Delta variant. **Covishield** on the other hand is the Indian modification of the Oxford–AstraZeneca COVID-19 vaccine in which instead of Chimpanzee Adeno virus Human Adeno virus is used. Currently these 3 vaccines are in use, however emergency use authorization has been given for 3 more vaccines which are Moderna, Johnson & Johnson, Zydus Cadila Zycova-D (3 doses, for 12 years and above)

First phase of vaccination was started on 16th January, 2021. Till now 157 crore doses have been given. UTTAR PRADESH VACCINATION (UPDATED on 17/1/2022)- Till now 22 crore doses have been given, Of which 8.59 crore are fully vaccinated. 13.7 crore have been given 1st dose .51,37,027 doses to children of age 15-18 and 3,87,596 precautionary doses were also given .

Booster/ Precautionary Dose :

Bharat Biotech said a study conducted at EMORY University demonstrated that subjects who received a booster dose of Covaxin six months after getting a primary two dose series have witnessed neutralising of the SARS-Cov 2 Omicron, Delta variants. Currently the booster dose of vaccination for Health Care Workers and high risk group has started in view of protection against the emerging new variants²⁷. COVID-19 Vaccination of children in the age-group of 15-18 years to be started from 3rd January, 2022, vaccination option

Table 2 — Showing Comparison of Different Treatment Options in the Treatment of Nonsevere COVID-19 Disease

	Nirmatrelvir-ritonavir	Sotrovimab	Remdesivir	Molnupiravir
Efficacy (prevention of hospitalization or death)	Relative risk reduction: 88%	Relative risk reduction: 85%	Relative risk reduction: 87%	Relative risk reduction: 30%
Advantages	Highly efficacious Oral regimen Safe in pregnancy	Highly efficacious Safe in pregnancy Few/no drug interactions	Highly efficacious Studied in pregnancy Few/no drug interactions	Oral regimen Not anticipated to have drug interactions
Disadvantages	Drug-drug interactions	Requires IV infusion followed by 1-h observation	Requires IV infusion on 3 consecutive days	Low efficacy Concern: mutagenicity Not recommended in pregnancy/child

is "Covaxin" only. Health Care Workers (HCWs) & Front Line Workers (FLWs) or persons aged 60 years and above with comorbidities who have received two doses of COVID-19 vaccine after completion of 9 months another dose of COVID-19 vaccine provided from 10th January, 2022.

Conclusion :

India as always has stood against the unprecedented challenges caused by the spread of COVID-19 infections, with both government and non-governmental cooperation. After the first and second COVID-19 wave the third wave has emerged with new variant with high transmission rate and reduced efficiency of treatments and vaccines. Vaccination including additional Booster / Precautionary Dose along with the COVID appropriate behaviours, if we are able to maintain physical distance, wear mask properly, wash our hands, and prevent crowd from gathering then we will not allow the virus to spread, rather this will also curtail the spread of infectious disease including Tuberculosis. The Public has now become wiser and aware on how to be healthy and have a check on their vitals via Pulse Oximeter for Oxygen saturation, Prone Position to maintain the Oxygen levels, Eating Healthy Diet to improve their Immunity. People now understand the importance of Social Distancing and other preventive measures prescribed by the Government with a good attitude. So together lets fight this war, this too shall pass.

REFERENCES

- Kant S — The Covid-19 Pandemic: Impact on primary and secondary healthcare in India. *The National Medical Journal of India* 2020; **33(4)**: 193.
- Kant S — COVID-19 impact on health care workers. *Journal of the Indian Medical Association* 2020; **118(9)**.
- Kant S, Tyagi R — The impact of COVID-19 on tuberculosis: challenges and opportunities. *Therapeutic Advances in Infectious Disease* 2021; **8**: 20499361211016973.
- Bajpai J, Kant S, Verma AK, Kar A — Chronic Obstructive Pulmonary Disease and COVID-19- A Double Trouble. *J Clin of Diagn Res* 2021; **15(11)**: OI01-OI03. <https://www.doi.org/10.7860/JCDR/2021/46660/15648>.
- Gowrisankar A, Priyanka TM, Banerjee S — Omicron: a mysterious variant of concern. *The European Physical Journal Plus* 2022; **137(1)**: 1-8.
- COVID C, Team R — SARS-CoV-2 B. 1.1. 529 (Omicron) Variant—United States, December 1–8, 2021. *Morbidity and Mortality Weekly Report* 2021; **70(50)**: 1731.
- Christie B — Covid-19: Early studies give hope omicron is milder than other variants.
- Lung tissue study sheds light on fast Omicron spread. CIDRAP. Archived from the original on 16 December 2021. Retrieved 25 December 2021
- The Issue Is: Congresswoman Barbara Lee and conservative commentator Michael Knowles." (2021).
- Richwine LR — MS-233: Papers of Theta Chi.
- Advisory on Purposive Testing Strategy for COVID-19 in India (Version VII, dated 10th January, 2022).
- Jyoti B, Surya K, Akshyaya P, Verma AK — Remdesivir – *Current evidence & perspective in management of COVID-19 infection* 2021; **10(5)**: 1808-13.
- Vora A, Arora VK, Behera D, Tripathy SK — White paper on Ivermectin as a potential therapy for COVID-19. *Indian J Tuberc* 2020; **67(3)**: 448-51. doi: 10.1016/j.ijtb.2020.07.031.
- Kant S, Rastogi H, Bajpai J, Aggarwal KK — Ivermectin—a potent weapon in the anti-COVID-19 armamentarium. *Indian Journal of Clinical Practice* 2020; 31(5).
- Singh A, Kumar H, Gupta P, Verma AK, Jain A, Kant S, *et al* — Assessment of knowledge, attitude, and practices towards hydroxy chloroquine pre-exposure prophylaxis among health care professionals. *Indian Journal of Community Health* 2020; 32(4).
- Thanesekaraan V, Samaria JK, Kant S, Koul P, Mishra N, Tampi PS, *et al* — Consensus statement on: Favipiravir as an empirical therapy for influenza-like illness during COVID-19 pandemic. *Journal of the Indian Medical Association* 2020; 118(9).
- Kant S, Rastogi H, Arora VK, Ghoshal AG, *et al* — Ivermectin as a Chemo-prophylaxis Agent against Covid-19: A consensus statement. *JIMA* 2020; 118(12).
- Bajpai J, Pradhan A, Singh A, Kant S — Hydroxychloroquine and COVID-19- A narrative review. *Indian J of tub.* 2020;67: S147-S154.
- Kant S — COVID Management and Prophylaxis among Rural, Hilly and Tribal Population of India; *J Indian Medical Assoc* 2021; **119(9)**: 63-9.
- Marik PE, Kory P — Ivermectin, a reanalysis of the data. *American Journal of Therapeutics* 2021; 28(5): e579.
- Cruciani M, Pati I, Masiello F, Malena M, Pupella S, De Angelis V — Ivermectin for prophylaxis and treatment of COVID-19: a systematic review and meta-analysis. *Diagnostics* 2021; **11(9)**: 1645.
- Morgenstern J, Redondo JN, Olavarria A, Rondon I, Roca S, De Leon A, *et al* — Ivermectin as a SARS-CoV-2 Pre-Exposure Prophylaxis Method in Healthcare Workers: A Propensity Score-Matched Retrospective Cohort Study. *Cureus* 2021; **26**: 13(8).
- Ahmed S, Karim MM, Ross AG, Hossain MS, Clemens JD, Sumiya MK, Phru CS, Rahman M, Zaman K, Somani J, Yasmin R. A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. *International Journal of Infectious Diseases* 2021; **103**: 214-6.
- Bryant A, Lawrie TA, Dowsell T, Fordham EJ, Scott M, Hill SR, *et al* — Ivermectin for prevention and treatment of COVID-19 infection: a systematic review, meta-analysis and trial sequential analysis to inform clinical guidelines.
- Alam M, RM P — Ivermectin as pre-exposure prophylaxis for COVID 19 among healthcare providers in a selected tertiary hospital in Dhaka an observational study. *Eur J Med Health Sci* 2020; **2**: 1-5
- www.covid19treatmentguidelines.nih.gov
- Croda J, Ranzani OT — Booster doses for inactivated COVID-19 vaccines: if, when, and for whom. *The Lancet Infectious Diseases* 2021; Dec 8.