COVID-19-OUT BREAK OF DISASTER

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Abstract:-
Corona virus a deadly disease (2019) since December 2019 covid caused a global outbreak of illness related to respiration which is known as corona virus disease. Covid-19 is a group of single stranded viral genome (RNA) world health origination declared covid -19 as pandemic outbreak. There are various varieties of this deadly disease. But mostly six are very dangerous for the human. Corona virus belong to family “Corona Virdae” which can cause a lot of human as well as animal disease. In this given paper a lot of information unintended consequences of covid-19 mitigation measures and other complex health issues were considered and all possible information about corona virus were discussed.

Keywords:- Covid-19, Corona, Pandemic, Respiration, Various, deadly, Diseases, Dangerous.

Introduction:-
The Covid-19 pandemic in march 2020,WHO declared covid a pandemic and called for governments to take some fast step to decrease bind prevent its spreading speed. This leads to various measures like, (hygiene, lockdowns, school closures, travel restrictions, and lot) were taken to save lives. It was firstly reported in wuhan china (2019) . Near November 2020 cases reached to millions and more spreading like a fire in forest. (SARS Cov) was the first (MERS-COV) was the second and (n Cov) is the 3rd type of this pandemic to infect humans in large scale with in last 2 decades¹²

Microbiology:-
Corona viruses are RNA virus having extensive range of hosts and affect multiple system. Covid-19 possess an unsegmented single stranded RNA genome of about 30kb enclosed in a 5 cap and 3’ poly (A) tail³. These viruses are encircled with envelope containing. Nucleocapsid in helical symmetry⁴. It form a crown like appearance when seen under microscope⁵ mostly spherical in its shape with a covering of glycoprotein. Corona virus cause major health issues in human beings. It is also very harmful to animals. It can cause serious infection in respiratory tract and damage to the kidneys in chicken⁶.
Replications of Corona viruses:-

Corona virus not only inject humans, it infection mammals, livestock and other animals, and are therefore not only a danger for public but animals health too. Coronavirus mainly express and replicate its Genomic RNA into cells via 2 spike protein subunits, which have different functions. The S1 and S2 subunits

S1 subunit------ACE2 attachment through receptor domain

S2 subunit------Fusion peptide and transmembrane domain

Cleavage occur (along the border of s1 and s 2 subunits) so infection depend on the proteases availability. After reaching cells, virus release its RNA with 7 genes. Genes one by encodes i.e. 1 gene encodes 20 RF which translate 2 polypeptides in returns. There polypeptides have 16 units. There 16 units/Proteins form double membrane vesicles, and this is the target side of viral replication and transcription7-9.

Body immune response:-

Interferons play key role in immune response. Virus infected cell start secreting interferons molecules that start binding to cell receptor and triggers JAK/STAT pathway and activate many antiviral genes and then get transcribed into the RNA and proteins this result in the suppression of viral spread10.

Spread and transmission:-

Firstly wuhan in city of china lot of patients with pneumonia has reported with unknown factor common cases have a common source i.e. sea food. It was known to be spreaded via sea food market. After that reports revelels, it spread from human to human, than reports revers, it spreads from infectd to healthy person via contact11. But on 31st December china informed and cleared the fact to WHO about the outbreak of this pandemic disease and the virus is known as coronavirus which is similar to bat coronavirus. There was a huge increase in number of cases and it affected other person too without any contact12-13. Transmission via bats are also reported. Ebola virus that is spreaded via bats have 96% similarity with coronavirus. After all the reports and analysis it is informed that virus spread via droplets (blood etc).

Fig:--Corona Virus

Transmission of SARS-COV-214:-

Can occur through direct or indirect contact with infected person, infected secretions or respiratory droplets (Saliva, cough, Sneeze)

Sign and symptoms

Symptoms are as follows: -

a) Dry cough

b) Fever (99% patient)
c) Sore throat
d) Headache
e) Tiredness
f) Loss of taste and smell
g) Diarrhea
h) Respiratory issue
i) Conjunctivitis
j) Rash/ discoloration of fingers
k) Shortness of breath
l) Loss of speech
m) Chest pain
n) Chills
o) Muscle pain

**Diagnosis:**
Patient with anyone of the above mentioned symptoms are kept under medical care for days, when a case is confirmed with tests such as sputum, oropharyngeal swab, blood test, etc. Collected sample sent to lab and then certified by the government testing of coronavirus. Transportation of sample should be done at 4°C. In many cases the WBC count is less, Increase in the level of procalcitonin reveals bacteria infection C.T also act as a useful tool in diagnosing corona presence. Platelets count in corona infection is unaffected. The collection of sample, Testing of sample shows be under government guidelines.

**Prevention:**
It's better to be safe than to be sorry. Following are the precautions or ways to prevent corona.

1. One must always wash hands with hand wash, Soap regularly.
2. Washing reduce chance of transmission.
3. When hands are unwashed avoid, touching the face, nose, eyes and no close contact with the people.
4. Limiting social gatherings there must be a distance of 1m between two people.
5. Occasion like parties, devotion in temples, marriages, should be reduced or banned are limited.
6. Use of face mask should be must hands must be sanitized, musk must be on the face to cover nose and mouth.
7. Don’t use disposal mask twice
8. Use of personal protective equipment is very important for preventing transmission of disease like use of PPE kit. There kit have mask gowns, head gear, goggles, gloves, and are very expensive.
Impact:-

1. On education system
2. Mental health
3. Agriculture
4. Healthcare
5. Sports
6. Tourism

Pharmaceutical Industry: -

In the case of education, Various school, colleges, Universities, are badly affected. Online classes are there but not with that much efficiency, lesson plans have been prepared for good classes work. Like reports, project files, assessment are given to student over online methods. Semester exams are almost impossible to conduct many universities, schools promotes student on there previous performance. Online exams cannot ensure integrity of the exams. Other students from other countries also face lot of problems due to improper transportation. Students miss practicals project submission on time. Lot of loss to education system. Covid disturb the lives of people all over the world, Fear causes so many mental issues to various people around the globe. Corona disturb everyone life in one or another way, which ultimately reduce their balance and disrupt their mental peace and health. Agriculture crushed very badly demands for vegetable fruits and other essential just get crushed very quickly lock down and closure affected the demand of agriculture products due to low demand prices also get low and farmers suffer very badly. Tourism, Sports are affected too in large scale due to corona. Each and everything from small to big get effected by corona very quickly and deeply. Impact of corona just completely change the lives of people arounds the globe very affectively.
Corona virus state wise data of India from 31 MARCH, 2021:-

In India the corona virus cases are spreading like a forest fire taking every thing in its range and affecting more than 75,000 people per day\(^1\).

<table>
<thead>
<tr>
<th>S.No.</th>
<th>State Name</th>
<th>Confirmed Cases</th>
<th>Cured Cases</th>
<th>Deaths</th>
</tr>
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<tbody>
<tr>
<td>1.</td>
<td>Andaman and Nicobar Island</td>
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<td>6.</td>
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<td>318436</td>
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<td>8.</td>
<td>Dadra and Nagar Haveli &amp; Damani and Diu</td>
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<td>13.</td>
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<td>26.</td>
<td>Tamil nadu</td>
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<td>29.</td>
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<td>30.</td>
<td>Lakshadweep</td>
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<td>31.</td>
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<td>32.</td>
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<td>12134</td>
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<td>35.</td>
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<td>301227</td>
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<td>36.</td>
<td>Tripura</td>
<td>33503</td>
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</table>
Vaccines should be manufactured in huge quantities and should be safe and effective. Which can face the unpredictable challenge. Every step of vaccine production should be well analyzed and evaluated. Various effective vaccines for Covid-19 were developed which can produce protection against disease.

**Treatment for Covid-19**^{33-40}:-

Various treatment for patients to receive a new. Potential treatment with no other options are available, FDA issue (EVA) to help patients and public to make new medications and medical products.

1) Remdesivir (Veklury):- It is an antiviral given iv infusion in the hospital on 22,2020, the FDA approved it for treatment of Covid-19 patients (age-12 and older). It is also being studied in combination with other medication. Not all studies have been promising with Remdesivir. Some for 10 days and got mixed result overall. A study of 236 patients with covid-19 in china didn’t worked well. This above research and researchers state that larger studies are needed to confirm better result.

2. Dexamethasone: - It is steroid in nature and used in curing various health issues and giving this medication to patient found that there was a lower death rate at day 28 in 2019. Patients with covid-19 which got dose of dexamethasone.

3. Convalescent plasma: - FDA on 24 march 2020 issued an EIND to treat Covid-19 and than transfused it to a Coronavirus active patient. It is found that antibodies in convalescent plasma can help fight infection. Rarely data from a mayo clinic study of over 55,000 hospitalized patients with Covid-19 who get this treatment. But in future they didn’t get enough evidence to recommend the different doses, different patient, at different timing were given and observed (low quantity result)

4. Monoclonal antibodies: - Antibodies are proteins bind to pathogens and destroy them. MABs are ab. made in lab. Which are higher in fighting infection.

5. Bamlanivimab: - This medication was designed to block the SARS-Cov-2 virus from entering and infection human cells. Eli Lilly reported in an early analysis that this medication can provide mild to moderate response. Three different doses were tested by him higher doses proved good but not them lower doses on the other hand. Then he performed combined study, combination of two MABs there studies are still ongoing and find result not yet available.

Substance like kinase inhibitors, interferons, Kaletra, ivermectin were also used for providing immunity to patient but result was mixed.

Traditional method like use of Curcumin, Xanthorrhizol were also under study to be provide beneficial for curing Covid-19 patient. These two are widely used as a medication and supplement for specific diseases they have various properties like:-

a) Anti-inflammatory

b) Anti-cancer

c) Anti-microbial

d) Anti-hypertensive etc.

The studies show that Xanthorrhized treatment inhibit inflammatory cytokine production in adipose tissue and tumor necrosis factor. This can interrupt various pathway related to RAA system. Herbals agent act useful in treatment of Covid-19 suggestion for the patients is that still not recommended to heal the disease without any specific advice^{41-45}. 
**Repurposed agents**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Adult dose/Administrations</th>
<th>Contraindications</th>
<th>Toxicities</th>
<th>Major drug-drug interactions</th>
<th>Special Populations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chloroquine phosphate</strong>&lt;sup&gt;46-52&lt;/sup&gt;</td>
<td>Blockade of viral entry by inhibiting glycosylation of host receptors, proteolytic processing, and endosomal acidification. Additional immunomodulatory effects through inhibition of cytokine production, autophagy, and lysosomal activity in host cells</td>
<td>500 mg by mouth every 12-24 h × 5-10 d. Available as: 250-mg tablets (salt); 500-mg tablets (salt); 500-mg tablets of chloroquine phosphate (salt) = 300-mg chloroquine base. Dose adjustments: Kidney: Creatinine clearance &lt;10 mL/min administer 50% of dose. Hepatic: No dose adjustments in hepatic impairment recommended; use with caution. Administration: Preferable to avoid crushing. If needed, may be crushed and mixed with jam, pasteurized yogurt or similar foods</td>
<td>Hypersensitivity to chloroquine, 4-aminoquinoline compounds, or any component of formulation. Presence of retinal or visual field changes of any etiology (unless benefit outweighs risk)</td>
<td>Common: Abdominal cramps, anorexia, diarrhea, nausea, vomiting. Major: Cardiovascular effects (including QTc prolongation), hematologic effects (including hemolysis with G6PD deficiency, use if benefit outweighs risks), hypoglycemia, retinal toxicity, neuropsychiatric and central nervous system effects, idiosyncratic adverse drug reactions</td>
<td>CYP2D6 and CYP3A4 substrate</td>
<td>May be used in pregnancy if benefit outweighs risks</td>
</tr>
<tr>
<td><strong>Hydroxychloroquine sulfate</strong>&lt;sup&gt;(Plaquenil/generic)&lt;/sup&gt;&lt;sup&gt;33-38&lt;/sup&gt;</td>
<td>Hydroxychloroquine shares the same mechanism of action as chloroquine</td>
<td>400 mg by mouth every 12 h × 1 d, then 200 mg by mouth every 12 h × 4 d; alternative dosing: 400 mg by mouth daily × 5 d or 200 mg by mouth 3 times/d for 10 d. Available as: 200-mg tablets of hydroxychloroquine sulfate (salt) = 155 mg hydroxychloroquine base. Dose adjustments: No kidney or hepatic dose adjustments recommended; use with caution. Administration: Manufacturer does not recommend crushing tablets; however, some sources suggest that tablets can be crushed and dispersed with water OR compounded into an oral solution</td>
<td>Known hypersensitivity to hydroxychloroquine, 4-aminoquinoline derivative, or any component of the formulation</td>
<td>Adverse drug reactions similar to chloroquine but less common</td>
<td>CYP2D6, CYP3A4, CYP3A5, and CYP2C8 substrate</td>
<td>May be used in pregnancy if benefit outweighs risks</td>
</tr>
<tr>
<td><strong>Lopinavir/ritonavir</strong>&lt;sup&gt;(Kaletra)&lt;/sup&gt;&lt;sup&gt;59-64&lt;/sup&gt;</td>
<td>3CL protease</td>
<td>400 mg/100 mg by mouth every 12 h for up to 14 d. Available as: lopinavir/ritonavir 200-mg/50-mg tablets; lopinavir/ritonavir, 100-50-mg tablets; lopinavir/ritonavir 400-mg/100-mg per 5-mL oral solution (can be given via feeding tubes compatible with ethanol and propylene glycol, contains 42% alcohol). Dose adjustments: No kidney or hepatic dose adjustments</td>
<td>Hypersensitivity to lopinavir/ritonavir or any of its ingredients, including ritonavir. Co-administration with drugs highly dependent on CYP4503A. Co-administration with potent CYP450 3A</td>
<td>Common: gastrointestinal intolerance, nausea, vomiting, diarrhea. Major: Pancreatitis, hepatotoxicity, cardiac conduction abnormalities</td>
<td>CYP3A4 inhibitor and substrate; CYP2D6 substrate; CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19 inducer. P-gp substrate; UGT1A1 inducer</td>
<td>May be used in pregnancy; avoid oral solution if possible due to ethanol content</td>
</tr>
<tr>
<td>Agent</td>
<td>Target</td>
<td>Adult dose/Administrations</td>
<td>Contraindication</td>
<td>Toxicities</td>
<td>Major drug-drug interactions</td>
<td>Special Populations</td>
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<tr>
<td>Umifenovir (Arbidol)</td>
<td>S protein/ACE2, membrane fusion inhibitor</td>
<td>200mg every 8 h by mouth 7-14d. Available as: 50-mg and 100mg tablets, capsules and granules. Dose adjustments: Kidney: no dose adjustment necessary. Hepatic: No specific recommendations available. caution in those with hepatic impairment. Administration: Bioavailability 40%</td>
<td>Known hypersensitivity to umifenovir</td>
<td>Allergic reaction, gastrointestinal upset, elevated transaminases</td>
<td>Metabolized by CYP3A4, monitor with strong inducers/inhibitors</td>
<td>Contraindicated in children &lt;2 y of age (increased sensitivity)</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>RNA polymerase inhibitor</td>
<td>200 mg × 1, 100 mg every 24h IV infusion. Available as: 5-mg/mL via (reconstituted). Dose adjustments: Kidney: No recommended for GFR &lt;30. No kidney/hepatic dose adjustment currently recommended but holding doses may be considered if significant toxicities occur. Administration: 30-min IV infusion</td>
<td>Exclusion criteria based on specific protocols</td>
<td>Elevated transaminases (reversible), kidney injury</td>
<td>Not a significant inducer/inhibitor of CYP enzymes, monitor with strong inducers/inhibitors</td>
<td>Safety in pregnancy unknown, currently recommended to avoid</td>
</tr>
<tr>
<td>Favipiravir</td>
<td>RNA polymerase inhibitor</td>
<td>Doses vary based on indication, limited data available. Available as (not in the US): 200-mg tablet. Dose adjustments: Kidney: no dose adjustment recommended, limited data available. Hepatic: Dose adjustment considered in Child-Pugh C, increased exposures observed in Child-Pugh class A to C. Administration: Tablet can be crushed or mixed with liquid, bioavailability &gt;95%</td>
<td>Exclusion criteria based on specific protocols</td>
<td>Hyperuricemia, diarrhea, elevated transaminases, reduction in neutrophil count</td>
<td>CYP2C8 and aldehyde oxidase inhibitor, metabolized by aldehyde oxidase and xanthine oxidase</td>
<td>Contraindicated during pregnancy, metabolite found in breast milk</td>
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<tr>
<td>Adjunctive therapies</td>
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<tr>
<td>Tocilizumab (Actemra)</td>
<td>IL-6 inhibition- reduction in cytokine storm</td>
<td>400 mg IV or 8 mg/kg × 1-2 doses. Second dose 8-12 h after first dose if inadequate response. Available as: IV infusion injection: 80 mg/4 mL</td>
<td>Known hypersensitivity to tocilizumab or any components of the formulation. Caution in patients</td>
<td>Common: Increase in upper respiratory tract infections(including tuberculosis), nasopharyngitis,</td>
<td>In vitro data suggested that IL-6 reduces mRNA</td>
<td>Safety in pregnancy unknown; may cause harm to the fetus</td>
</tr>
</tbody>
</table>
**Conclusion:**

The quick emerging danger outspread is affecting use in lot of ways. It is a challenging problem for cell the people. Previously only china was experiencing this virus attack and now the whole world is undergoing such deadly virus disease. There must be some medicine, vaccines, Technology,to fight to prevent these deadly pandemic outbreak. Which slowly but completely affect all the social, Physical, Mental, economic, health of country in large scale. This responsibility should also followed by the people of the country by following the rules, Guidelines of the government regarding this alarming problem worldwide.

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