

Review Article

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Diagnosis and management of SARS - CoV-2 patients with its cause in COVID hospital as IPD admitted in General ward or Intensive Care Unit

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Abstract

Keywords

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COVID-19,
SARS-CoV-2,
ARDS, and
PUBMED.

SARS-CoV-2 is the causative agent of COVID -19 that is declared a global pandemic by the WHO in 2020.COVID-19 is transmitted by aerosol particle and close contact through the sneezing and coughing. Till date no effective treatment is present for its management. This review is from different article for useful therapeutic for COVID -19.

Aim of study; Diagnosis and management of SARS CoV-2 patients with its cause in COVID hospital as IPD admitted in general ward or intensive care unit

Methods: A systematic review was developed on based of screening of different research article , review article, Guideline and case profile .that all are selected from electronic media from Google and Pub med. After full screening and review from article and downloading from Google, the some therapeutic agents are decided for management of COVID-19 infected patient.

Result: The initial manuscripts identified about 16, included in this review. This study have clinical trial case report, retrospective study, prospective study and observational study. The most commonly reported medicine in this systematic review was HCQ, CQ, Azithromycin, Immunoglobulin and Convalescence Plasma and Ivermectin and Doxycycline.

Conclusion: This studies has considered many study and concluded as HCQ AND Azithromycin, is having tendency to become patient negative for COVID -19 and there is Convalescence plasma and Immunoglobulin is useful in severely COVID -19 infected patient.

Introduction

COVID 19 infection was started from China (Wuhan City). The case had been reported in December 8, 2019, and many patients worked at or live around the local Huanan Seafood whole sale Market and all country of world is affected by this .COVID 19. This is positive single stranded RNA virus. It enter in body through aerosol and air particle which come from the infected patient through sneezing and coughing. Due to remain active at the surface where it fell down, a very long duration and have preserved its infectivity. During coughing and sneezing aerosol can spread to one meter of distance and contact of surface at which virus fell down. So there is only way to prevent the spread of virus is remain isolated because there is no any definite treatment is available till now. The Corona virus COVID -19 is affecting 212 countries and territories around the world. In world Corona virus infected cases are 3318739 and death due to corona 234264 and recovered case are 1048508. In India corona virus cases 35043 and death 1154, recovered cases are 9068 .Severe acute respiratory syndrome corona virus, SARS-CoV-2 is the cause of the corona virus disease, this name of COVID -19 is given by WHO and this pathogens is renamed as revere acute respiratory syndrome corona virus 2(SARS-CoV-2) WHO also declared a global pandemic in 2020. SARS-CoV-2 is a member of the family coronaviridae and order Nidovrale. The family have two subfamily, coronavirinae and Torovirinae. The member of subfamily coronavirinae are subdivided into four genera which are as below.

A – Alpha corona virus; It contained the human corona virus (HCoV)-229 E and HCoV-NL63:

B-Beta corona virus include HCoV-OC43, Sever Acute Respiratory Syndrome human corona virus (SARS-HCoV), HCoV-HKU1 and Middle eastern respiratory syndrome corona virus (MERS –CoV)

C –Gamma corona virus; It include viruse of Whale And Birds.

D – Delta corona virus; It contains viruses of Pig and Bird .

SARS-CoV-2 is the an Enveloped and positive – sense single stranded RNA virus (+ss RNA).Phylogenetically analysis of the SARS-Cov-2 genome indicates that the virus is closely related with 88% identity to two bat derived SARS –like corona viruses collected in 2018 in Eastern China and bat- SL- CoVZC45 and bat –SL –CoVZXC210 and genetically distinct from SARS-Co-V (79% Similarity) and MERS-Co-V. Genome sequences of SARS –CoV-2, RaTG13 and SARS-Co-V, A further study found that virus is more related to Bat Co-V Rat G13, a bat corona virus that was previously detected in *Rhinolophus affinis* from Yunnan Province with 96.2% over all genome sequence identity.

COVID -19 is the disease have tendency to occur person to person transmission in close contact mainly via respiratory droplets, produced when an infected patient coughing and sneezing. Fomite may be a large source of transmission. Infection can be transmitted through droplets of different size, when the droplet particles are 5-10 micro meter in diameter , that are referred as respiratory droplets and when the size are< 5 micrometer in diameter they are referred to as droplets nuclei, Transmission may also occurred through fomite in the immediate environment around the infected person. Therefore transmission of COVID -19virus can occurred by direct contact with infected people and indirect contact with surface in the immediate environment or with object used on the infected person. In COVID -19 air born transmission may be possible in special condition and setting in which procedure or support treatment that generate aerosol are performed i.e Endotracheal, Intubation, Bronchoscopy, Open Suctioning and Nebulization etc. There is no faecal oral transmission except one study .The virus remain alive a very large duration on the surface on which it shed so for prevention it should be clean frequently with sodium hypo chlorite solution.

Table-1 Tabular representation of remain activeness on different surface

S.No.	COVID-19 on surface	Duration of active
1	Aerosol	3 hour
2	Copper	4 hour
3	Cardboard	24 hour
4	Paper	24 hour
5	Plastic	About 2 days to 3 days
6	Stainless steel	About 3 days
7	Door handle	About 3 days

There is virus can alive on very large time on the surface of different material as on steel it remain alive for 3 hour and on card board about 24 hour .

Screening of suspected patients-

1. All symptomatic (ILI) individuals who undertaken international travel in the last 14 days
2. All symptomatic (ILI) contact of laboratory confirmed cases.
3. All symptomatic (ILI) Healthcare personal.
4. All hospitalized patients with severe acute respiratory illness (SARI) (fever ,cough and shortness of breath)
5. Asymptomatic direct and high risk contact is of a confirmed case should be tested once between day 5 and day 10 after contact.
6. All symptomatic contact of laboratory confirmed cases.
7. All symptomatic ILI within hotspot/containment zones.
8. All symptomatic ILI among returnees and migrants within 7 days of illness.
9. No emergency procedure (Including deliveries) should be delayed for lack of test however sample can be sent for testing if indicated as above (1-8) simultaneously.

ILI case is defined as with respiratory infection with fever 38 degree centigrade and cough.

SARI case is defined as one with acute respiratory infection with fever. 38 degree centigrade and cough and requiring hospitalization.

Diagnosis of suspected cases can be done by as

A - RT PCR

1. Nasopharyngeal swab and Oro pharyngeal swab and also Nasal swab and throat swab.
2. Broncho alveolar lavage, Tracheal aspirate and Sputum
3. Faecal matter,
4. Blood

B- Antibody as IGM and IGG.

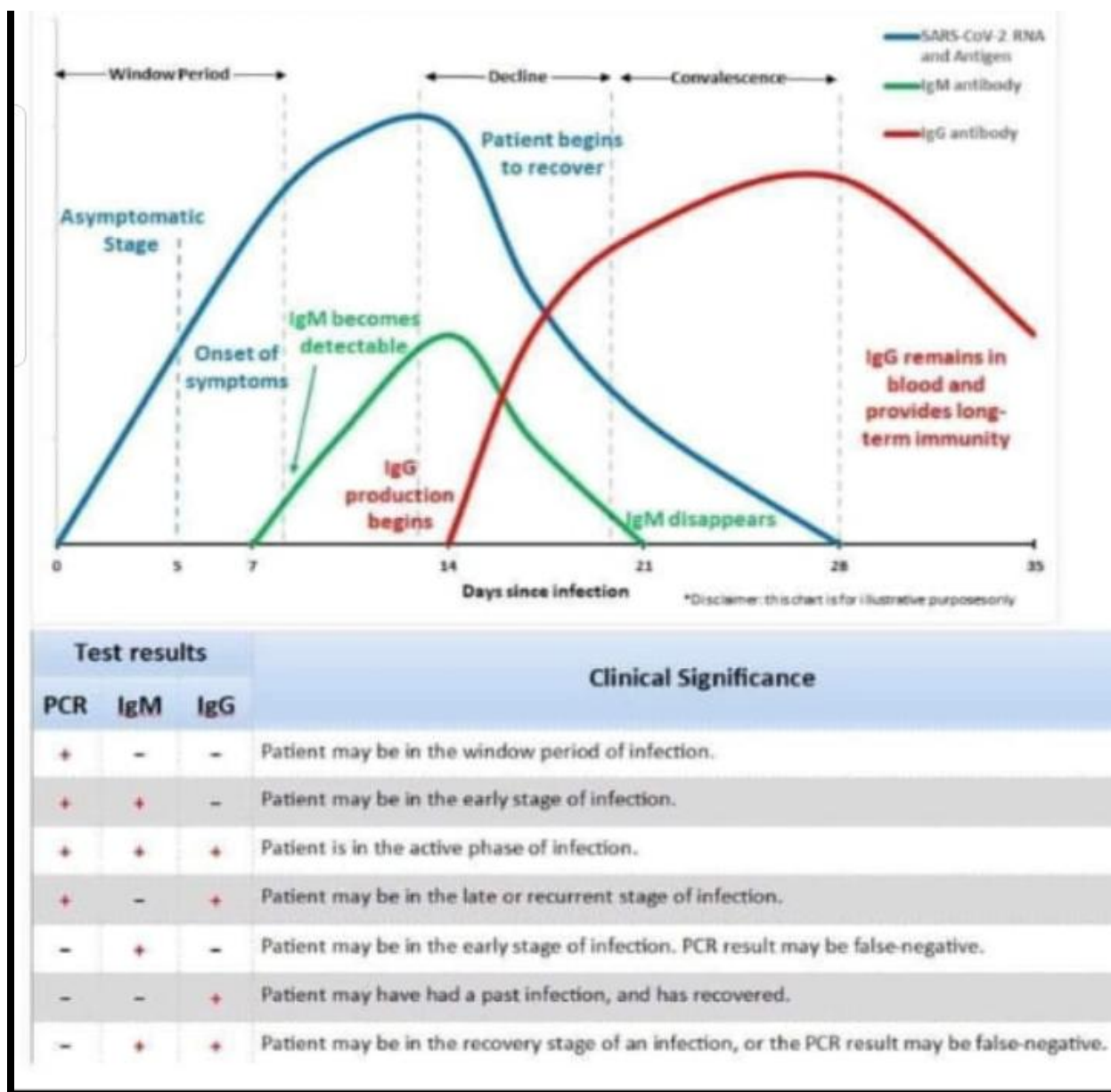
C- Antigens of COVID -19

In the infection of COVID -19 in the patients the first appear the antigen from first day and can be traced by RT-PCR from different site of body as throat swab, nasal swab and nasopharyngeal swab .Antibody is form in the body after some time of patient recovery as IgM is form at 7th day of infection and IgG is form about 14th day of infection .Both antibody is checked by lateral flow method by the blood. ELISA is a common biochemical technique that can detect both antigen and antibody.

Table-2 Tabular representation of corona percentage rate

S.No	Types of specimen	Positive percentage
1	Bronchoalveolar lavage fluid	93%
2	Fibrobronchoscopy brush biopsy	46%
3	Sputum	72%
4	Nasal Swabs	63%
5	Pharyngeal swab	37%
6	Faeces	29%
7	Blood	1%
8	Urine	0%

Graph.1- Graphical representation of appearance of antigens and antibody in COVID- 19 infected patient



This figure shows that sequential appearance of antigen and antibody on basis of duration ; antigen is appear very early ant antibody in which IgM is appear at 7th day and IgG is appear at 14th day. This also depict the stage of infection in the patients.

Patients of COVID – 19 infected patient can be presented as-

1. Uncomplicated illness- having fever cough and sore throat nasal congestion, malaise and headache or patient may be complete asymptomatic.
2. Mild pneumonia -having cough with breathlessness and fast breathing
3. Severe pneumonia – having fever cough breathlessness and respiratory difficulty rate of respiration is. 30, and spo2 is < 90% on room air
4. ARDS - Onset new or worsening respiratory symptoms within one week of known clinical insult. Chest imaging show bilateral opacity not fully explained by effusion, lobar or lung collapse.

ARDS is 3 types as

- A. Mild ARDS – Pao₂/Fio₂ =200 to 300 mm hg and PEEP >5
- B. Moderate ARDS –Pao₂/Fio₂ =100 to 200 mm hg and PEEP >5

C. Severer ARDS –Pao₂/Fio₂ =Pao₂/Fio₂ =<100 mm hg and PEEP > 5
 When Pao₂ is not available then spo₂ /Fio₂ is taken as <315 for ARDS.

Table 3- Tabular representation of news scoring systems to identify the seriousness of patients

Parameter	3	2	1	0	1	2	3
Respiration rate	<8		9-11	12-20		21-24	>25
Spo ₂ scale 1 (%)	<91	92-93	94-95	>96			
Spo ₂ scale 2(%)	<83	84-85	86-87	88-92	93-94 ON OXYGEN	95-96	97 ON OXYGEN
Oxygen or air		oxygen		AIR			
Systolic blood pressure	<90	91-100	101-110	111-217			>220
Pulse (per minute)	<40		41-50	51-90	91-110	111-130	>131
Consciousness				Alert			CVPU
Temp(0°c)	<35		35-36	36.1-38	38.1-39	>39	

There are four triggered level for a clinical alert requiring clinical assessment based on the NEWS.

1. Low score (1-4) This level of patient can be asses by a trained nurse and should decide whether a change to frequency of clinical monitoring and requirement of clinical care.
2. Medium score (5-6) at this level required urgent review by clinician with competencies in the assessment of acute illness and decided the level of critical care.
3. High score (7 or more) is key trigger threshold and should prompt emergency assessment by a clinician team and critical care competent and patient should be managed in higher dependency area.
4. A Single red score (3 in a single parameter) .It is unusual but should be prompt an urgent review by a clinician with competencies in assessment of acute illness and decide the level of critical care.

Because no any effective treatment is present now so for containment of infection it is important to stop infection through self isolation and social distancing in community level is good method for its prevention.

So Government of many country is decided for lockdown and Janta-curfew.

During lockdown the environmental pollution decreased and level of pollutant in environment decreased. India is 21of world most 30 polluted city .All mode of public transport such as Metro Train, buses, Interstate Trains, domestic flights and International flights stopped. Because of above air was unhealthy as 91 micrograms per cubic meter of PM_{2.5} that is dropped to 71 micrograms per cubic meter. Data from the Central pollution control board of India that 71 % decreases in nitrogen dioxide level. On march 25 first day of the lockdown the average PM levels decrease by 22% and nitrogen dioxide which come from burning fossil fuels dropped by 15%. measurements from the European Space Agency, sentinel -5 p satellite show that during late January and early February 2020, level of Nitrogen dioxide (NO₂) over cities and industrial area in ASEA and EUROPE were lower than in the same period in 2019.Two week after nation wise lockdown in the UK.NO₂ pollution in many cities fell as 60% but in USA and other metropolitan areas in north- eastern USA was 30% lower Emission of green house gases in environment is also reduced.

Corona virus Induced lockdown continuously. The water quality of Ganges and Yamuna River has improved significantly in the areas with reduced industrial activities. River Ganges water quality has improved with the increase dissolve oxygen (DO) and reduced nitrate concentration. There has been a 40%-50% improvement in quality of water in River Ganges All river in world has improved the quality of water and also become clean.

In result of lockdown is good for environment .It have low environmental pollution that is very big emerging disaster in future. Society have develop more dreaded result as they feel more disturbances and feeling more depression during lockdown There are no of worker become jobless and shelter less and no of worker are forced to return own home but this indulge to live together with family. There are also domestic violence are increase. Because of above and internal and external loss of business there is loss of GDP during lockdown. There is one aspect of having decrease road traffic accident during this period.

There are no. of therapeutic agents that can be use full in treatment of COVID-19 patients such as

1. Chloroquine
2. Hydroxichloroquine
3. Ramdesvir
4. Lopinavir/ritonavir
5. Arabidol
6. Flavipravir
7. Tocilizumab
8. Immunoglobulin
9. Corticosteroid
10. Convalescent plasma
11. Ivermectin
12. Doxycycline

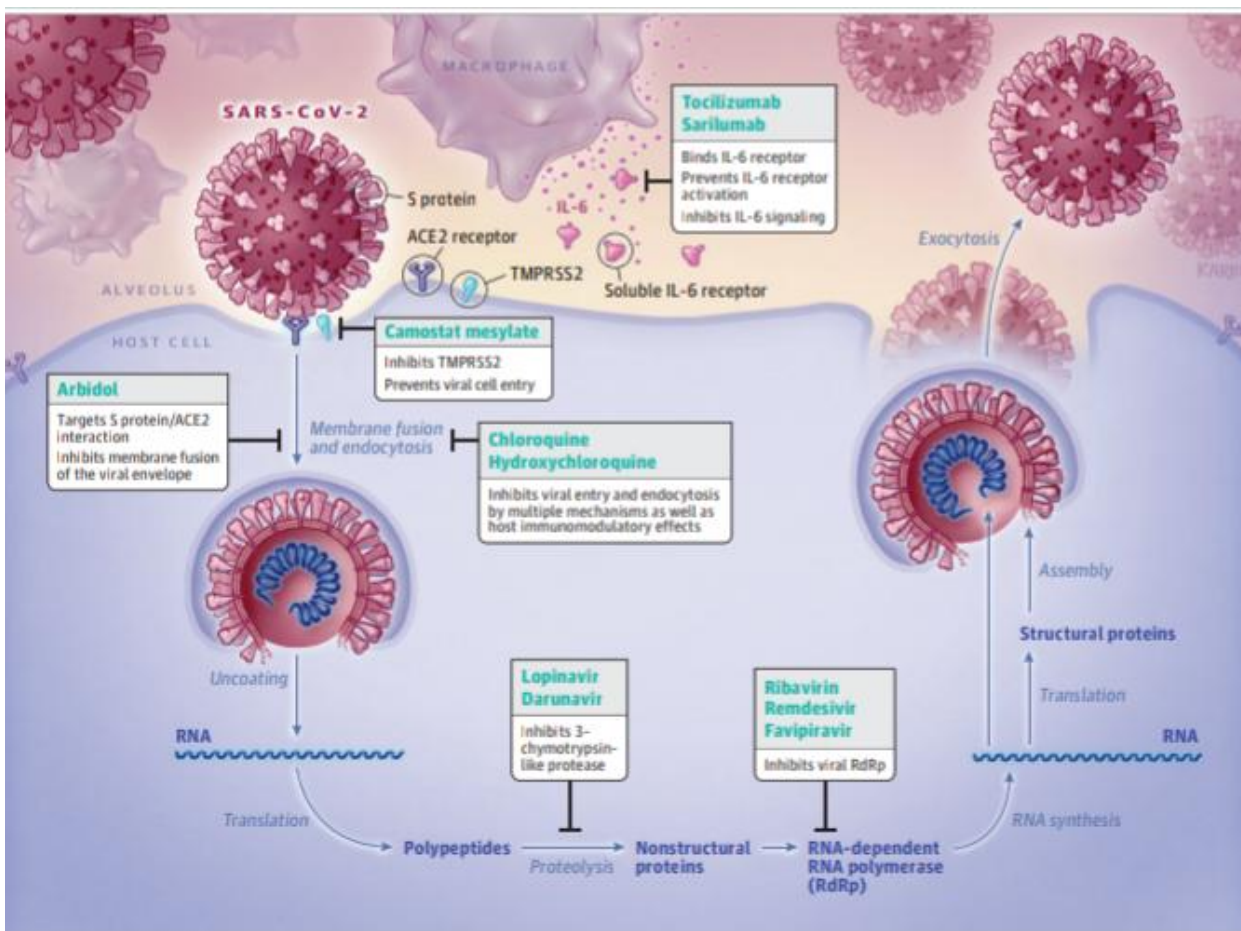
Immunoglobulin and Convalescent plasma can be used as enhance immunity by providing immunoglobulin. Corticosteroids are use for intubated patients or patient or ARDS.

Table-4 Tabular representation of therapeutic agents used in COVID-19 treatment

Agent/dose	Mode of action	Contraindication	Drugs interaction
1.Chloroquine phosphate 500 mg every 12 to 24 hourly for 5 to 10 days	Blockade of viral entry by inhibiting glycosylation of host receptors (ACE), proteolytic processing and endosomal acidification and immunomodulation	Presence of retinal and visual field change and chloroquine hypersensitivity May be used in pregnancy	CYP206AND CYP3A4 Substrate
2.Hydroxychloroquine 400mg every 12 hourly for one day then 200 mg12 hour for 4 day	Same mechanism as chloroquine	Hypersensitivity reaction to it and QT prolonged patients and also retinal disease	CYP2D4 , CTP3A4, CYP3A5AND CYP2C8
3.Lopinavir/Ritonavir, 400/100 mg every 12 hour upto 14 days	3CL protease inhibitor	Hypersensitivity reactions, nausea, vomiting diarrhea hepatotoxicity cardiac conduction abn	CYP3A4 INHITORAND CYP2C8 INDUCER
4.Umifenovir,200 mg every 8 hour by mouth for 7 to 14 days	S Protein /ace 2 memberane. fusion inhibitor	Known hypersensitivity to umefenovir, hetotoxicity allergic reaction gastrointestinal upset	Metabolized by CYP3A4
5.Ramdesivir ,200 mg for 1 day and 100 mg for 5 day every 24 hour	RNA polymerase inhibitor	Elevated.transaminase and kidney injury	No CYP enzymes Reactions
6.Flavipiravir, 200mg based on indications	RNA polymerase inhibitor	Hyperuricimia, Diarrhea Hepatotoxicity	CYP2C8 and aldehyde inhibitor
7.Toclizumab,400mg I/V or 8 mg /kg for 1- 2 dose in 8 to 12 duration interval	IL -6 inhibition –reduction in cytokine storm	Hypersensitivity Rn to tocilizumab, headache Hypertension,Neutropenia and Thrombocytopenia	CYP1A2, CYP2B6 etc may Do low substrate

The mechanism of action and different agent and it adverse effects and it s contraindications.

Figure -1 The schematic diagram of mechanism of action of different therapeutic agent



This figure shows the different stages of virus in infected patient and the therapeutic agent break the cycle and its mechanism of action.

Aims and objective- Diagnosis and management of SARS CoV-2 patients with its cause in COVID hospital as IPD admitted in general ward or intensive care unit

Materials and Methods

Systematic review of the published literature was done for COVID -19 infection and treatment .The Preferred Reporting Items for Systemic Review and Meta-

analysis guide line were is used for the review. Publication selected it. This study included the abstracts, Original article completed and incomplete article pre proof of the accepted article, some guidelines, and original research paper and research study. Google scholar were used and Pub Med were is used for searching the article, The abstract and purpose of the articles found during the literature search were reviewed for COVID -19 infection and its management. Full text of the selected article was downloaded and relevant information about the COVID -19 from all selected article was taken. The data from selected article were studied independently and selected for article.

Results

This article consisted of 16 items downloaded from original article and screen and read properly for management of COVID -19 patients. It consider original paper, review article, case report, pre print media, pre paper and recruiting study retrospective, prospective and observational study for concluding the management .

Discussion

Krishan Mohan Kapoor, and Aanandita Kapoor ; Role of Chloroquine and hydroxychloroquine in treatment of COVID -19 Infection a systematic Literature 1- This study concluded that chloroquine and hydroxychloroquine is promising use in symptomatic patients with supervision.

XiLiu, Huili Chen, Yuqi Shang, Hongqiong Zhu, Gongqi Chen, Yuanii Chen, and Shaoxuan Liu et al: Efficacy of chloroquine and Lopinavir /Ritonavir in mild /general COVID -2019 : A prospective, open label, multicenter randomized controlled clinical study 2- This study concluded that the chloroquine is having role as antiviral as adhesive receptor glycosylation and making acidic autophagy. It also commented on concentrated level of chloroquin.

Awadhesh Kumar Singh, Akriti Singh and Anoop Misra: Chloroquine and Hydroxychloroquine in the treatment of COVID -19 with diabetes: A systematic search and a narrative review with a special reference to INDIA and other developing countries-3 This study concluded that the chloroquine and hydroxychloroquine is low cost and good treatment therapeutic as antiviral agents. It also can be used in diabetes patients having COVID-19 infections.

Sung- Han Kim, Professor, Asan Medical center: Comparison of lopinavir / Ritonavir or Hydroxychloroquine in patient with mild coronavirus disease (COVID-19),- 4 study continued result awaited and there is some role of lopinavir /retonavir in management of COVID -19 mildly infected patients .

Yamini Wang, MD Dinguu Zhang MD, Proff Guanhua, Proff Ronghui, Proff Jianping Zhao: Ramdesvir in adult with sever COVID -19 : A randomized, double blind, placebo-controlled, multicentric tial – There is no clinical

improvement is seen in sever COVID -19 infected patents.

Gilead initiative simple trial, National Institute of Allergy and Infectious disease conducted a phase 2 adaptive randomized double blind placebo control trial and WHO conducted open level multicentric trial 7 All study have the positive efficacy in sever infected patient with COVID -19 .

Yun Xie, Song Cao, Qingyun Li, Erzhen Chen, Hui Dong, and Wenkai Zhang et al : Effect of regular intravenous immunoglobulin therapy on prognosis of sever pneumonia in patient with COVID-19 -8 : This study concluded that the initiation of IVIG as adjuvant treatment for COVID-19 pneumonia within 48 hour of admission to the ICU can reduce the use of mechanical ventilation.

Wenling Wang, Yanli Xu, Ruqin Gao, Roujian Lu , Kai Han and Guizhen Wu: Detection of SARS-cOv-2 in different type of clinical specimen; JAMA 2020 march 11-9 that give the percentage of positive ness of covid-19 in different specimen in which maximum percentage is in bronchoalveolar lavage.

Indian Council Of Medical Research; Revised strategy of COVID 19 Testing in India (version 3, dated 20/03/2020. This guideline for screening of patient and also taking the sample of patient.

James. M. Sanders, Margueurite L., Mongue, Tomasz Z. Jodlowski and James Cutell: Pharmacologic treatments for corona virus Diseases 2019 (COVID-19) –A review; 11 this review give idea about the different type of therapeutic agent used in COVID-19 Infection

Harapan Harapan, Naoya Itoh , Amanda Yufika, Wira Winardi, Synat Keam and Haypheng Te et al: Corona virus disease 2019 (COVID-19: A literature review : Journal of infection and public health, 13(2020)667-673.-12 This article give the evidence of effectiveness of oseltamvir and ramdesvir in severe patient of infected with COVID -19 individually .

Sumaira Omer, Salamat Ali and Zaheer ud Din Babar: Preventive measure and management of COVID -19 In pregnancy : Drugs & Therapy Prospective 13- In this study there is given some idea about treatment of pregnant woman with COVID -19. Lopinavir/ Retinavir 400/100 mg with alfa interferon (5 million in 2ml of sterile water for injection) has shown the improvement in clinical condition and the breast feeding to baby is through breast pump is allow and contact is not allow.

Chenguang Shen et al: Treatment of 5 critically ill patient with COVID-19 With Convalescent plasma:- 14 In this study there convalescent plasma is given to 5 critical patients with all antiviral and supportive treatment .they all improve after giving plasma .

Dr. Kamal Kant Kohli: Medical dialogues; doxycycline and ivermectin combomay be new effective COVID-19 treatment; DR MD TAREK ALAM the Head of Medicine Department at private Bangladesh medical college, use the antiprotozoal Ivermectin and antibiotic Doxycycline give miraculous result in curing the patient with covid -19 patient.

Clinical trial.gov; Hydroxichloroquine, Osaltamvir and Azithromycin for the treatment of COVID -19 infection: An RCT (protect) -16 result is not declared but there is good roll in management of COVID-19 patient positive patients become negative on this therapy .

Conclusion

The all considered the studies concluded that patient first screened for test of COVID -19.The criteria of screening on the basis of history of patients as

Table -5 Tabular Representation of Scoring System on The Basis of History

SL.N.	History	Score
1	Travel history to out of country and COVID-19 area	3
2	Contact history with COVID-19	3
3	Fever	1
4	Dry cough	1
5	Shortness of breathing	1
6	History of similar symptoms in family and friend	1
7	Health care worker with contact history	1

On the basis of above scoring systems the line of action is as below

< 3—Home quarantine or separate space quarantine

4 -8 –Hospital quarantine and test for COVID-19

>9 –Shift to isolation ward

The above suspected patient should be tested through RT PCR from different specimen such as nasopharangeal swab ,throat swab, oropharangeal swa, BAL, tracheal wash and other. Mostly throat swab and nasopharangeal swab is taken .If upper respiratory specimen is negative and patient is clinical

symptomatic then lower respiratory specimen should be taken and send for examination. When the report is found positive for COVID-19 patient should be shifted to COVID -19 dedicated hospital and severity is decided

Table -6 –Tabular representation of COCSS scoring

COVID-19 objective clinical severity score(COCSS)

1. Comorbidities	
Cardiovascular diseases	1
HTN	1
DM	0.5
COPD/Asthma/Active PTB	1
Immunocompromised condition/drugs/ malignancy	0.5
Chronic kidney disease/CLD	0.5
2. Smoking	
Never smoked	0
Reformed	1
Current	2
3. Age	
<49	0
50-64	1
>65	2
4. Fever	
≤38.1	0
≥38.2	2
5. Shortness of breathe	
No	0
Yes (with hemoptysis)	4(6)
6. Systolic Blood pressure(mm hg)	
SBP>90	0
81-90	2
<80	6
7. Pulse rate(per minute)	
61-99	0
100-139	2
<40 or >140	4
8. Respiratory rate(per minute)	
<24	0
24-32	2
33-39	4
>40	7
9. Oxygen saturation at room air(%)	
>93	0
89-92	2
<88	6
10. Auscultation	
Normal auscultation	0
Minimal or focal findings	2
Diffuse wheeze/ronchi/crepts	6

Table -7 – Tabular representation of COCSS assessment of severity of the patients

Score	Disease of severity	Category	Site of treatment
0-7	Mild	A	COVID-19 hospital IPD with general care
8-12	Moderate	B	IPD with vital monitoring
>12	Severe	C	ICU

Management of patient in COVID hospital after deciding the severity of patient as

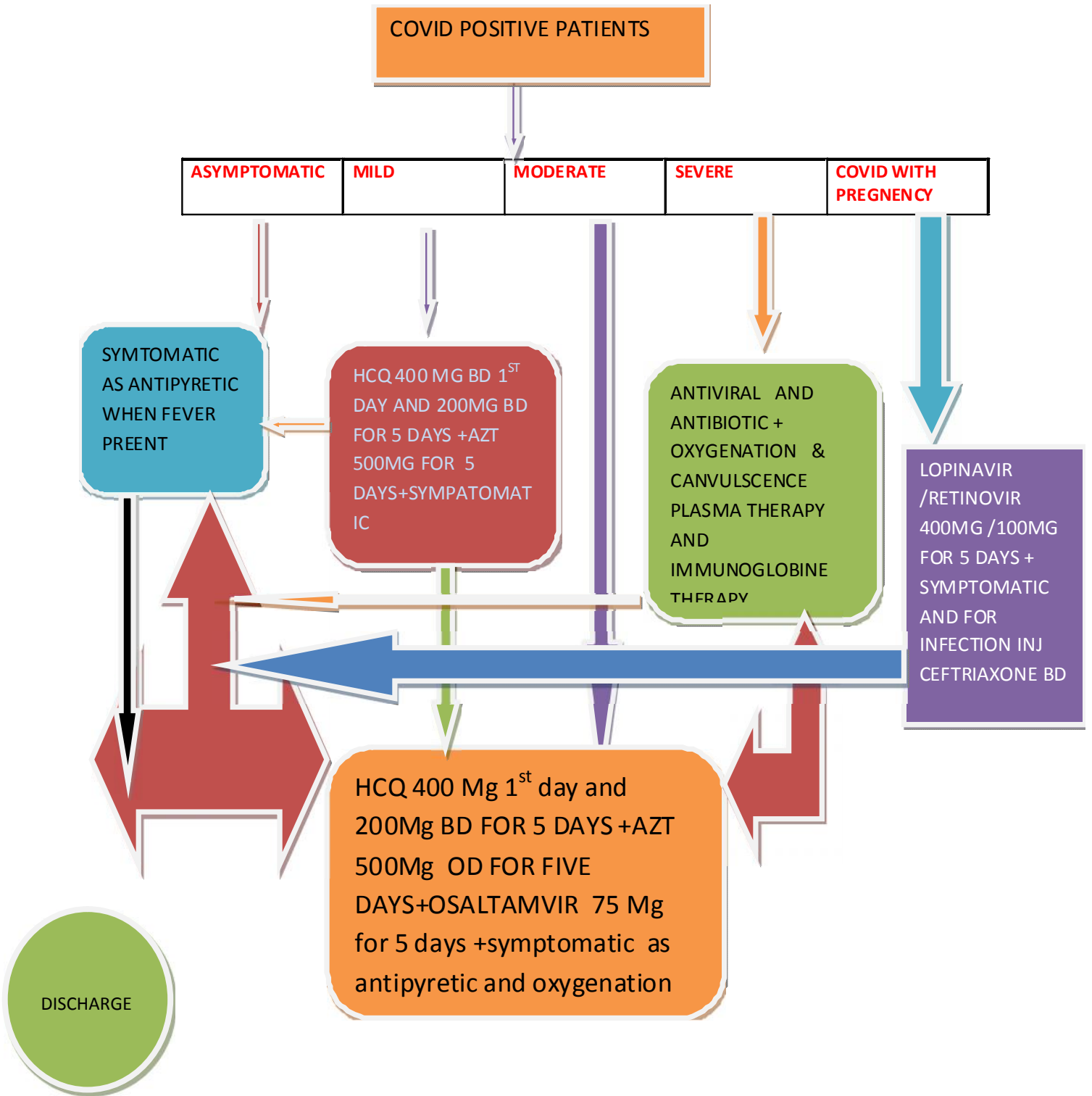
Table -8 – tabular representation of management of COVID patient on the basis of severity grade

Sl.n.	Category	Treatment
1	Asymptomatic	Symptomatic treatment as antipyretic
2	Mild	Hydroxichloroquine + Azithromycin + antipyretic + symptomatic
3	Moderate	Hydroxichloroquine + Azithromycin +Oseltamvir + symptomatic
4	Severe	Immunoglobulin (IVIg)/ Convalescent plasma along with antiviral and symptomatic

If patients is not become negative after full course as above patient can be treated with Ivermectin 600 mg

BD and Doxycycline 100 mg bd for 3 day and repeat the specimen.

Table 9- Line diagram of management of COVID patients



Limitations

This systematic review had limitation including a small sample size of publications and limited data regarding the study.

Declaration of competing interest: N/A

Funding

No funding received

Ethical approval

Not needed

Abbreviation

CQ– Chloroquine, HCQ-Hydroxychloroquine, SARS–CoV-2 Severe acute respiratory syndrome.

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