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REVIEW ARTICLE

Indices and Parameters in the Diagnosis and The Management of COVID-19: A Comprehensive Review

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ABSTRACT
Coronavirus outbreak has challenged the medical, public health infrastructure and economic status of nearly all countries across the World. The main issue of concern with SARS-CoV-2 has been the high infectivity rate and the high mortality rate especially, observed during the wave 2 of COVID-19. The symptoms associated with SARS-CoV-2 are often misleading with influenza and another respiratory tract seasonal viral infection as, majority of the patients report common constitutional symptoms. Hence, correct diagnosis for COVID-19 may play a key role in early detection, management and curtailment in the transmission rate.Therefore, apart from limiting this outbreak, efforts need to be made to plan comprehensive and stringent measures to develop diagnostic tools to prevent future outbreaks of this zoonotic disease. The present manuscript provides a detailed description of various indices and parameters which are currently being used for easier, rapid, accurate diagnosis, medical managementand prognosis assessment of COVID-19 patients in various stages of the disease.
Keywords: COVID-19, Diagnostic tools, Indices, Parameters.

INTRODUCTION
A new worldwide public health crisis has emerged with the spread of novel coronavirus or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 2019.
Suspected cases of pneumonia had emerged in Wuhan city of China in December 2019[1]. Later, this causative agent was recognized as a new coronavirus (SARS-CoV-2) and the disease was named by WHO as COVID-19.Fromthen, the virus has spread infectious disease across 210 countries and territories. It has been suspected that the virushad been transmittedfrom animals(bats) to humans but, the exact origin is still standscontroversial.[2]
Globally, till February 2022, around 43.21 crores cases of COVID-19 including 59.49 lakhs deaths have been reported to WHO. India has reported 4.29crores cases till date[3]. Fortunately, a total of 176 crores vaccine doses have been administered[4].3.8 million adolescents(15-18years) have been vaccinated in the new COVID-19 vaccination programme[5]. Still, the future outcome of infectious virus and its variants standscrypted andunpredictable.
A unique feature of coronaviruses lies intheir remarkable ability to mutate rapidly and adapt to a new host. Based on their zoonotic origin, viruses spread rapidly from one person to another[6].Coronavirusesgain entry into cells, through angiotensin-converting enzyme-2 (ACE-

2) receptor or a protein known as dipeptidyl peptidase IV (DPP-4) and later replicate within the cells (figure 1)[7].

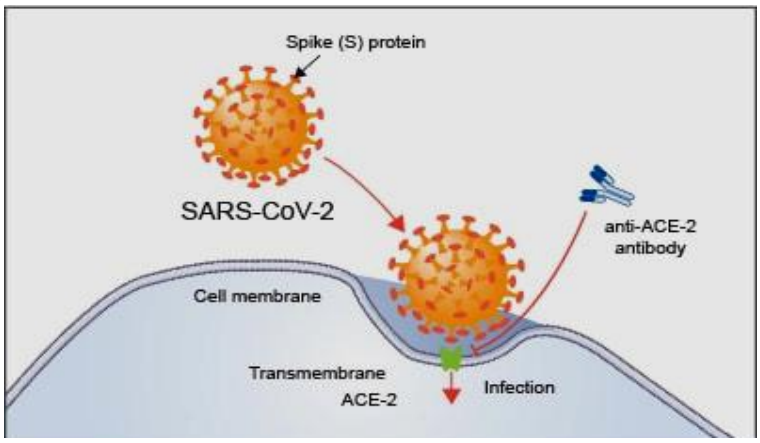


Figure 1: ACE-2 – The entry receptor for SARS-CoV-2

The main issue of concern with SARS-CoV-2 has been the high infectivity rate and the high mortality rate especially, observed during wave 2 of COVID-19.Coronavirus outbreak has since then challenged the medical, public health infrastructure and economic statusof nearly all countries across the World. Therefore, apart from limiting this outbreak, efforts need to be made to plan comprehensive and stringent measures to develop diagnostic tools to prevent future outbreaks of this zoonotic disease.

The symptomsassociated with SARS-CoV-2 are often misleading with influenza & other respiratory tractseasonal viral infections, as majority of the patients reported common constitutional symptoms.Hence, correctdiagnosis for COVID-19 may play akey role in early detection, management and curtailment inthetransmissionrate.COVID-19 should also be a diagnostic consideration in patients who present with extrapulmonary complications associated with SARS-CoV-2 infection, such as cardiac symptoms, ischemic stroke, thromboembolic events, and inflammatory complications[8].

The diagnosis of COVID-19 disease is mainly made by the gold standard RT-PCR (Real Time–Polymerase Chain Reaction) (quantitative PCR) tests, which besides detecting the presence of the virus, also quantifies the viral load.However, this technique is time-consuming and relatively expensive[9]. Therefore, finding easy, cheaper and rapid tests for early diagnosis has been a crucial issue and new platforms for early detection of aforesaid infection are actively being developed and being brought into general use in many countries.

Present manuscript is intended to provide a road map for diagnostic strategies and to assessthe effectiveness of different inflammatory indices, in terms ofaccessibility, calculation ease and costfortimely diagnosis of COVID-19, so that early life-saving measures could be undertaken to reduce mortality and morbidity rates.

In view of the above facts,a detailed description of various indices and parameters which are currently being used for easy, accurate diagnosis and medical management of COVID-19 patients in various stages of the disease is as follows:

RT- PCR (CT VALUE)

Critical Threshold value (Ct) refers to the significant value that arises as a result of RT-PCR tests done for the detection of SARS-CoV-2. Ct value obtained by RT-PCR serves as an indicator for the viral load in an infected individual[10].

MEANING OF CT VALUE

Ct value indicates the number of cycles after which the virus is recognized in the RNA extracted from the swab of patients hence,it would help to infer the magnitude of infection.InRT-PCR test, RNA is extracted from naso/oropharyngeal swab or BAL (Bronchoalveolarlavage) of the patient and is converted into DNA, which later undergoes a process of amplification. The amplification process involves several cycles before the detectable amount of virus is produced. The test takes around 4-6 hours to produce measurable results.

IMPORTANCE OF CT VALUE

As per ICMR guidelines, the Ct value of the RT-PCR test is the number of times a fluorescence of the PCR product is detectable over and above the background signal. Lesser the cycles more will be the viral load of a patient.

Thus, the Ct value and the viral load are said to be inversely proportional. The lower the Ct value, the higher the viral load because the virus can be detected just after fewer cycles[11].

CT VALUE AND SEVERITY OF DISEASE

It has been observed that the patient may have a low Ct value, having a high viral load, but may still be asymptomatic, suggesting that Ct value does not necessarily correlate with severity of disease symptoms but may correlate with the infectivity of the cases[12].

According to ICMR guidelines, a patient may be considered as Covid-positive if the Ct value lies below 35[13].

Table 1: Interpretations of Ct value

Ct Values	Reaction	Response
< 29	Strong positive	High viral load
30-35	Positive	Moderate viral load
36-40	Negative	Minimal viral load

The diagnosis and treatment plan can be madeon the basis ofthe Ct value obtained on RT-PCR. However, many factors influence RT-PCR test results, such as the method of sample collection, the time from infection to the samplecollection and to analysis, the technical competence of the person performing the test, the thermal cycle maintained during sampletransportation, calibration of the equipment, and the analytical skills of the interpreters[14].

IGM AND IGG NEUTRALISING ANTIBODY TITERS

Serological tests involving IgM and IgG antibodies detection against SARS-CoV-2 have diagnostic value, as these antibodies arise from the second week from the onset of COVID-19 symptoms. Soon after the disease progresses, firstly the IgM level rises from the fourth day of infection followed by IgG antibody which appears after the eighth day ofdiseaseonset. IgM & IgG antibody assay provides quick diagnostic values as compared to RT-PCR,fewer false positive or false negative results are seenand additionally provides an estimate of strength and duration of humoral immunity induced as a result of COVID-19[15].

However, the presence of immunoglobulins (i.e IgG, IgM& IgA) together may show the maximum occurrence of neutralization activity against SARS-CoV-2 which is usually observed in the recovery phase of COVID-19 infection.

Antibodytiters may be expected to reduce with time and the patient may become susceptible again to infection after the suppression of the immune response.

IgM, the largest antibody, is the first-line defence of humoral immune system.Soon after the onset of infection, IgM titer remains negligible from the 0-3rd day which then starts rising

from day 4 onwards probably,due to the effect of T-cell dependent humoral response. Finally, these antibodies may persist in blood for 20 days or more[16].

Table 2: Cut-off value of IgM (neutralising antibodies)

Value	Interpretation
<0.9	Negative
0.9-1.1	Equivocal
>1.1	Positive

-Positive interpretation showsa recent COVID-19infection or antibodies developed due to vaccination (active immunisation).

-Negative interpretationindicates the absence ofthe development of antibodies againstcoronavirus. It may occur if tested too early, too late after COVID or immediately after COVID vaccination[17].

Later on,IgM levels may start diminishing with theproduction of IgG antibodies(class switching) whichare supposed to provide long term immunity against the coronavirus infection[18].

IgG antibodiesare formed almost 10–14 days after infection following antigen presentation to T cells and isotype switching from IgM-IgG, reaches peak around day 25 and remains high for many weeks after acute infection signifies the secondary immune response[19]. These observations conform to the fact that IgM antibody is produced as a primary immune response and IgG antibody productionsignifies secondary immune response (figure 2).

Table3: Cut-off values of IgG (neutralising antibodies)

Value	Interpretation
<0.9	Negative
0.9-1.1	Equivocal
>1.1	Positive

A **positive** test indicates that coronavirus infection has occurred at some point in the past, or antibodies have developed due to vaccination with one of the current SARS-CoV-2 vaccines. It also suggests the absence of current infection or that the patient is in the convalescent or recovery phase of the disease[17].

A **negative** test result means that the antibodies in response to coronavirus or due to vaccine are not present in the body

An **equivocal result** suggests that it should be tested again on a second sample taken 1-2 weeks later.

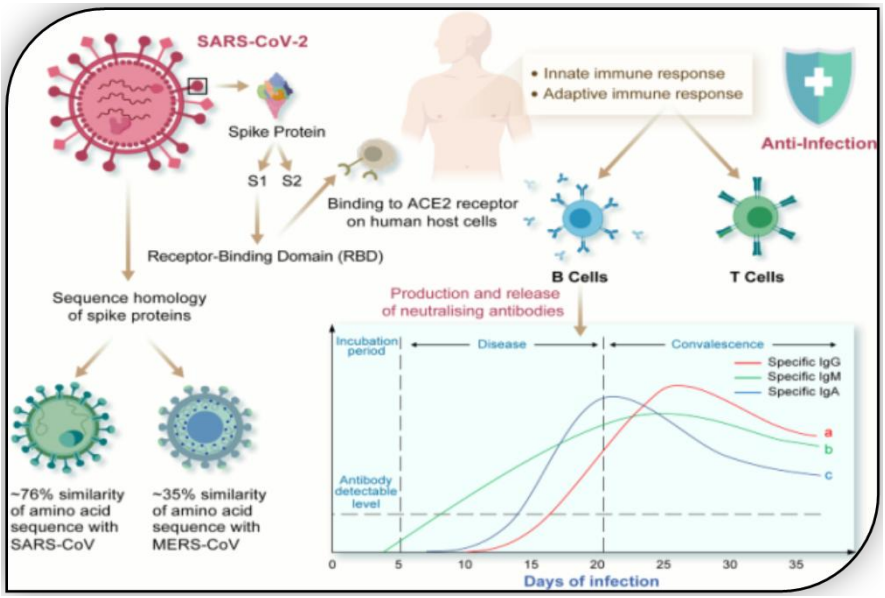


Figure 2: Showing onset and persistence of neutralizing antibodies (IgM &IgG)

Lastly, quantification oftheseneutralizing antibodies and determination of their persistence may play a significant role in determining thephase of the disease and theclinical severity.

CT SCAN

One of the main diagnostic techniques for coronavirus disease includes a chest computed tomography (CT) scan. The chest imaging observations of COVID-19 were first published in January 2020[20]. Coronavirus disease can be diagnosed, detected, and prognosis evaluated by performing a chest CT scan.

A high-resolution CT chest imaging plays an essential role in the early detection of disease, as well as in monitoring and managing the course of disease. Furthermore, lung CT-Scan findings can be used to assess the severity of the disease, thus, assisting clinicians in making appropriatediagnosis and ensuring effective management[21].

Chest scanning is not suggestive as a screening tool for asymptomatic or mildlysick patients but, indicated in subjects having moderate to severe respiratory dysfunctioni.e., 2nd and 3rdstages of COVID-19or in any probable cases where the RT-PCR test shows negative results[22]. CT scan results can be obtainedfaster than RT-PCR findings, which is an advantagewith CT scans. However, there is no documentation so far, as to which method is superior to the other.

The majority of the CT imaging finding of patients admitted for suspected cases of COVID-19 shows bilateral lung involvement, ground-glass opacities, vascular enlargement, lower lobe involvement, and posterior inclination, detection of which may further aid in the diagnosis and staging of COVID-19, hence increasing the chances of improvement of clinical outcome by timely diagnosis and treatment of these complications in COVID-19 patients[23].

Based on the area of the lungs involved, a scoring system has been introduced to assess the involvement of the lungs. Each of the 5 lung lobes can be scored as 0 to 5[24].

Table 4: Chest CT severity scores

Involvement	Score
No involvement	0
<5%	1
<25%	2
26-49%	3
50-75%	4
>75%	5

The total CT score is calculated as the sum of the individual lobar scores and ranges from 0 (no involvement) to 25 (maximum involvement).

Sometimes, interpreting chest CT scans can be difficult, especially during influenza season. Few studies have suggested thatperipheral distribution of ground-glass opacities is a more typical feature of COVID-19 related pneumonia[25], while others have found these features to be ineffective in distinguishing COVID-19 pneumonia from influenza-relatedpneumonia[26].

On the other hand, CT scans have certain drawbacks such as reliance on the radiologist's skill and the requirement to sterilize the instrument after each use in patients suspected of having COVID-19[27]. In addition, the diagnostic accuracy of chest CT is influenced by a number of other parameters, including the study population, COVID-19 prevalence, COVID-19 stage, disease severity at the time of imaging, and coexisting lung morbidities[28].

Therefore, it is important to correlate and review the findings of chest CT scanalong with patient history, clinical symptoms, and results of the RT-PCR test. Based on these limitations, chest CT scan should not be considered as an independent diagnostic tool for the diagnosis of COVID-19, however, it may be used as an additional tool to stratify the COVID patients into different grades viz, mild, moderate and severe.

Hence, it is recommended that a final decision regarding the COVID-19 staging be made considering both CT scan and RT-PCR findings, as neither of the two diagnostic modalities are 100% percent accurate on their own. However, correlating the findings of both the testing modalities may remarkably increase the accuracy in diagnosis and staging of COVID-19 infection.

D-DIMER TEST

After a blood clot is destroyed by fibrinolysis, D-dimer, a fibrin degradation product, a tiny protein fragment is seen in the blood. As it comprises two D segments of the fibrin protein connected by a cross-link, this protein is known as D-dimer[29].

D-dimer levels in the blood can be detected for up to eight hours after it is formed until the kidney eliminates it. Normally, the levels of D-dimer remain low whereas higher levels of D-dimer indicate the presence of a major clot[30].

D-dimer test has become crucial in the COVID-19 pandemic because,it's high levels have been linked to illness severity and mortality patterns due to coagulopathy seen as a complication in stage 3/severe cases of COVID-19. For a person diagnosed with COVID-19 or recovering from it, a D-dimer test has been found to provide insight of the details as to what extent COVID-19 has affected patient's health.

MECHANISM OF D-DIMER PRODUCTION

D-dimer is the degradative product formed by crosslinking of fibrin (by factor XIII).

Upon activation ofthe intrinsic or extrinsic pathway of the coagulation cascade, thrombin formation causescleavage of fibrinogen into fibrinopeptide A and B, resulting in the formation of soluble monomeric fibrin, which associate and form fibrin polymers. The D domains of these fibrin polymers are cross-linked by activated factor XIII, producing an insoluble cross-linked fibrin clot.

Due to the parallel activation of the fibrinolytic system to maintain a proper balance between coagulation and fibrinolysis, plasmin, the end product of the fibrinolytic system, break down insoluble polymers of fibrin, leading totheformation of degradative products of fibrin i.e. (FDPs). If the polymers are crosslinked between two D domains of the fibrinopeptides, D-dimer(hence the name) is produced[31].

Several studies have suggested that the levels of D-dimer may increase rapidly in cases of COVID-19 and are linked with the severity of the disease in a proportionate manner.

NORMAL RANGE

D-Dimer quantitative: <500 ng/ml

-Increased levels of D-dimer can help to identify patients at higher risk of COVID-19 complications (signifying the hypercoagulable state) [32].

In a nutshell, it can be inferred thatraised level of D dimer indicates the presence of clots in the body, in COVID-19 patientssimilar to other hypercoagulable states. Therefore, D-dimer along with other markers are currently being used as a useful index for staging, and as a guidelinefor treatment of COVID-19patients. Thus, D-dimer test can measure the severity & predict complications associated with COVID-19 at an early stage.Hence, if interpreted judiciously may help in a marked reduction in morbidity and mortality in COVID-19 patients.

NEUTROPHIL TO LYMPHOCYTE RATIO (NLR)

Different hematological parameters of the human immune system have been identified to fight the disease[33]. Indicators of these parameters may serve as markers in COVID-19 also, such as total blood count (CBC), TLC and DLC. Neutrophils increase in bacterial infection

whereas lymphocyte, depletion is seen in viremia. Examining these two clinical conditions can be helpful in testing of COVID-19 infection too. Neutrophil to Lymphocyte ratio (NLR) in peripheral blood has been lately studied as systemic inflammation marker in COVID-19. Various studies have previously shown that it is a valid predictor in variety of clinical scenarios such as lung, cardiovascular and kidney diseases[34].

Recent systematic reviews and meta-analysis by Feng et al regarding immune inflammation parameters in COVID-19 infection have concluded that NLR is associated with the progression of infection can also is being used by clinicians to identify the patients with increased risk of deteriorating health at initial stage[35]. In addition, a series of studies have suggested that NLR is a reliable predictor of occurrence of adverse sequelae of COVID-19 and that higher NLR is associated with higher mortality rates in various populations studied so far[36, 37].

NLR ratio can be calculated by using the simple formula:

$$NLR = \frac{\text{Absolute number of Neutrophils}}{\text{Asolute number of Lymphocytes}}$$

In critical patients with severe COVID-19, the lymphocytes count decreases progressively, while the number of neutrophils increases moderately. This may be due to excess inflammation and suppression of the immune system caused by SARS-CoV-2 infection. Neutrophils are generally considered to be anti-inflammatory cells with antimicrobial properties (acting as chemotactic agents), which are released by viral inflammatory factors, such as interleukin-6, interleukin-8 and interleukin-10 etc.[38]. On the other hand, systemic inflammation caused by SARS-CoV-2 severely depresses the immune system, leading to a decrease in CD3 + T cells, CD4 + T cells and CD8 + T cells. In addition, T cells infected with SARS-CoV-2 may also elicit cytopathic effects in T cells[39, 40] resulting in hematological manifestations associated with COVID-19. So, NLR can be used as a warning signal of COVID-19 rapid deterioration and may provide some ground for early detection of serious COVID-19. This may allow for the development and evaluation of successive new treatment modalities by various researchers at the earliest possible. Therefore, NLR an inexpensive hematological marker, may be determined from a simple peripheral blood smear / cell count, the findings of which may be utilized to predict the course and progression of disease in COVID-19

PLATELET COUNT AND PLATELET INDICES

Some studies have found platelet counts as predictors of COVID-19 mortality[41] while others could not establish its role in determining COVID-19 severity.

Mean platelet volume (MPV) and platelet distribution width (PDW) are widely used in clinical practice around the world. High MPV and increased PDW have been found in sepsis[42]. However, the role of these parameters in COVID-19 has not been investigated much. MPV defines the average size of flowing platelets and is a possible indicator of platelet activation and function. Inflammatory cytokines are known to cause the release of large platelets from the bone marrow by stimulating thrombopoiesis[43]. As COVID-19 has also been seen to be a hypercoagulable state especially, in severe cases, platelet indices might be a predictor of severity in COVID-19.

Few studies have found an association between thrombocytopenia and COVID-19 severity and related mortality. Mortality has been reported to increase with the decrease in platelet count [44, 45]. Besides this, platelet indices, MPV and PDW, have been found to be high in severe COVID-19 patients. According to a study, every 1 unit increased MPV increased mortality by 1.76 times[46]. Three theories related to platelet count and compositions have been proposed in COVID-19. Firstly, like other viruses of corona family, thrombocytopenia may be caused by bone marrow infection. Secondly, the destruction of platelets by the immune

system may have taken place and thirdly, the consumption of platelets due to aggregation in the lungs might occur[47]. In general, new platelet production increases as platelet count decreases. The population of young platelets is more pronounced than older platelets in blood. These changes may explain the increase in platelet indices, MPV and PDW in COVID-19 patients.

Normal ranges of MPV and PWD:

MPV (fl)	7.5-12.0
PWD (%)	9-17

C- REACTIVE PROTEIN (CRP)

CRP is a commonly available biomarker of inflammation that is generated by liver in response to cytokines like interleukin-6 (IL-6) and was first reported by Tillet and Francis[48]. COVID-19 patients have been found to have higher CRP levels especially, more so, in severe forms of COVID-19[49].

The normal concentration of CRP in blood is less than 10 mg/l; nevertheless, it rises rapidly within 6 to 8 hours and peaks 48 hours after the onset of the disease[50]. It has a half-life of around 19 hours[51] and it's concentration diminishes as the inflammatory stages of illness fade away and the recovery phase ensues. CRP binds preferably to phosphocholine, which is abundantly produced on the surface of injured cells[52]. This binding activates the immune system's classical complement pathway and stimulates phagocytic activity to eliminate pathogens and damaged cells from the body. CRP concentration declines when inflammation or tissue damage is resolved, making it a helpful measure for monitoring disease prognosis[50].

A cytokine reaction storm (CRS) can be triggered during the COVID-19 phase, which is linked to high COVID-19 mortality[53]. Hepatocytes are stimulated to synthesize CRP by cytokines such as IL-6, IL-10 and TNF-α (figure-3). CRP, the biomarker most clearly linked to the course of COVID-19, is markedly raised during the early stages of inflammation[54]. CRP has been shown to be an independent outcome predictor and discriminator of illness severity[55, 56], implying that CRP's diagnostic value for COVID-19 could be beneficial in improving clinical outcomes.

Table5: Interpretation of CRP:

CRP levels (mg/l)	Interpretation
<1	Low risk
1-3	Moderate risk
>3	High risk

CRP levels have been found to be greater in thrombotic events after COVID-19 infection in a multicenter retrospective investigation[57]. Obesity and metabolic syndrome have also been linked to chronic systemic inflammation in COVID-19, including atherosclerosis and hypertension where, CRP levels have been found to be in high risk range[58]. Alamdari et al.[59] have found that lymphopenia, hypomagnesemia, elevated CRP, and raised creatinine levels on admission were associated with a greater risk of mortality in COVID-19 patients in an observational analysis of older Iranian patients with a higher BMI. Likewise, CRP was found to have a positive connection in a group of metabolically sick individuals who were obese and infected with COVID-19[60].

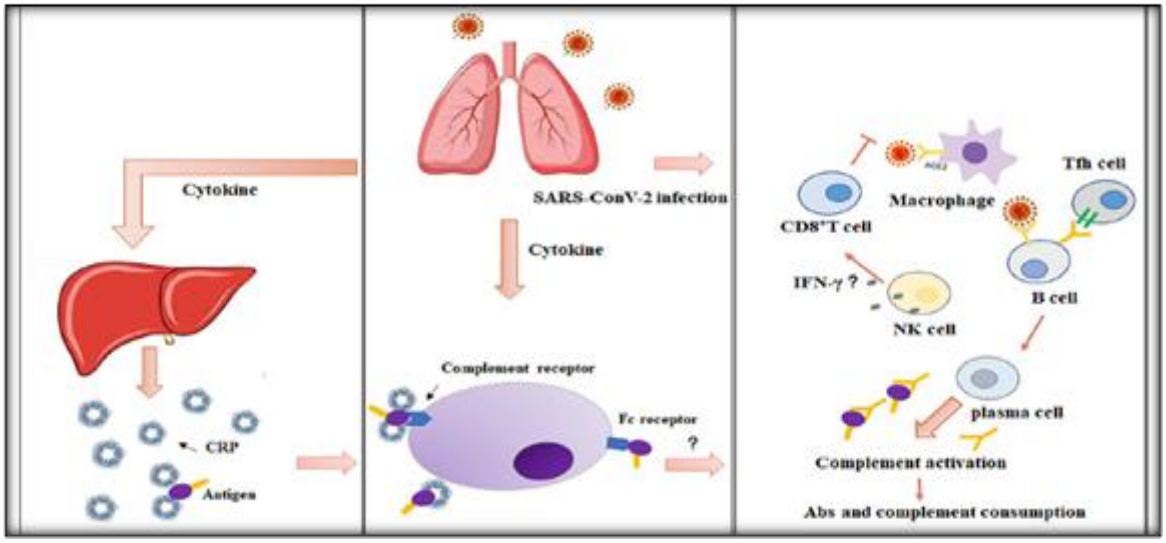


Figure 3: Immune regulatory mechanism of CRP in the pathogenesis of COVID-19

Existing evidence thus, suggests that CRP, an inflammatory marker, is strongly linked to the severity and prognosis of excessive inflammatory reactions, and that it can thus, be used to measure the severity of COVID-19 and assess the prognosis in these patients.

EPIDEMIOLOGICAL PARAMETERS (METRICS)/ COMMUNITY BASED PARAMETERS

As seen in 1st and 2nd waves of COVID-19 much havoc caused by the disease in terms of morbidity and mortality, the health care providers and government and non-government authorities across various countries have been working incessantly to curtail the spread of pandemic by ensuing various measures. But, considering the practical difficulties and feasibility of individual contact tracing and testing of whole population it has been advocated by epidemiologists from various countries thatcertain epidemiological parameters like R number, doubling time etc. if calculated and implemented effectively may come as a major rescue measure to contain the spread of COVID-19 pandemic. A detailed description of these epidemiological or community-based parameters is as follows:

R NUMBER (REPRODUCTION NUMBER/ R RATE / RATIO):

R number defines the average number of secondary cases generated by one primary case thus, referring to the number of people an infected person may infect on an average.

R number holds good to determine the spread of all infectious diseases in general and in no way restricted only to COVID-19, only. It heralds the rapidity with which a pandemic may spread[61].

Parameter	Threshold value	Spread
R number	<1	Slow spread
	>1	Epidemic phase (Exponential rise with each round)

Note:- The larger the R number faster the rate of spread.

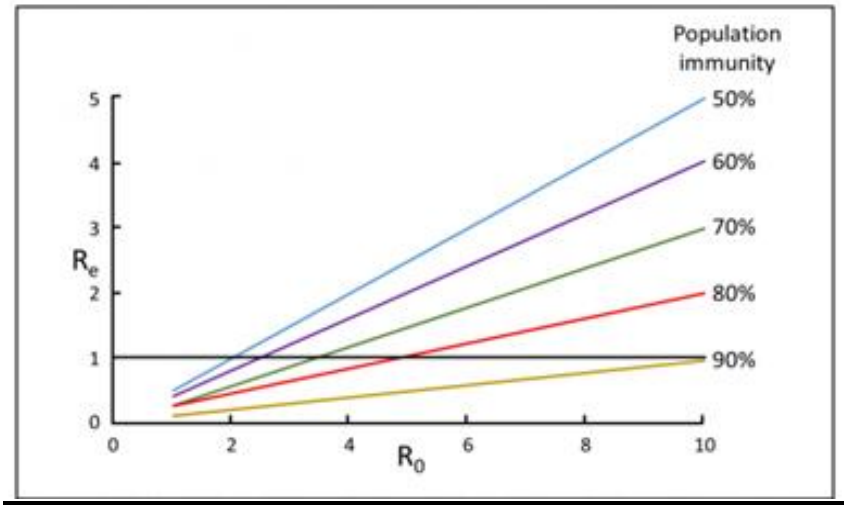


Figure 4- A plot between Re and R_0

TYPES

(I). R_0& Re / Rt

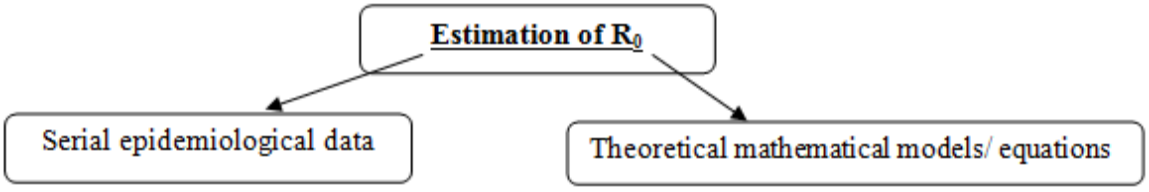
R_0: Stands for Basic reproduction number/ Basic reproduction rate/ ratio.

- Assumption: Everybody in population is susceptible to infection assuming zero immunity in a population.
- R_0<1 (vaning infection) R_0>1 (Fast spread).
- Dependent variables: period of infectivity, human behaviour (contact rate, hygiene practices etc.) and the biological character of the pathogen influences R_0 value.
- R_0 holds good for the initial part of the pandemic and predicts the extent of immunity required to achieve herd immunity[62].

Re (Effective Reproduction member) or Rt (Reproduction number as a function of time):-

- Valid at any time during an epidemic.
- Assumption: Some proportion of the population may be immunized either by natural infection or vaccination.
- Dependent variables: people with active infection, number of contacts, human behavior like social distancing, hygiene maintenance etc.
- Useful for testing the effectiveness of vaccination[63]

CALCULATION OF R_0 AND RE/R_T



E.g. by cumulative incidence data

It is the no of cases at a given time

R_0- Reproduction no.

SI: serial interval

t- prediction time

E.g. It= (Ro) t /SI

ADVANTAGES OF MEASUREMENT OF RE/RT

- Calculated over time
- When an outbreak progress

- Inclusion of immune status acquired by population
- It's a real time measurement taking into account truly susceptible/ vulnerable individuals from the population rather than the whole population.

(II). R (THE GROWTH RATE)

In the calculation of R scale no time scale is involved. R only tells that the epidemic is advancing or not, but can't deduce the pace of advancement of community infection/ epidemic. Whereas r signifies how cases change over time. The growth rate, r gives a good idea for real time situation i.e. it can be worked out to determine that how many cases may rise per day[64].

RELATIONSHIP BETWEEN 'R' AND 'R'

$R= e^{rT}$

Where R= Reproduction number

r= Growth rate

T= mean generation time

ADVANTAGES OF EPIDEMIOLOGICAL PARAMETERS CALCULATION IN AN EPIDEMIC/ PANDEMIC

1. Due to time and resources constraints each individual of a population cannot be assessed for infectivity so, these parameters give information about the infection spread in the community as a whole.
2. These parameters once calculated may serve as important tools for formulating various community guidelines to limit the progression of pandemic.
3. Transmission dynamics better understood by these parameters may help in formulating proper and timely measures to limit transmission viz; social distancing, lockdown, quarantine etc. if implemented in a time appropriate manner may help in limiting the spread of pandemic.

LIMITATIONS

Certain considerations must be made while interpreting these epidemiological metrices in assessing the gravity and extent of infection due to outbreaks. These constraints are as follows:

Epidemiological indices are only indicative and not exact depicters as they are subjected to influence by numerous external factors viz; human behavior, biological nature of causative organism, social norms and beliefs & practices amongst various ethnic groups[65].

CONCLUSION

Thus, this review article summarizes the clinical implications of calculating and determining different blood indices in patients with COVID-19. The importance of determination of these parameters and indices across various stages cannot be undermined, as they may serve as useful tests both independently or as adjuncts to RT-PCR, NAT or other antigen detection rapid tests in the determination of clinical stage, severity and prognosis of disease in COVID-19. As a result of which, proper risk stratification of patients with COVID-19 could be achieved, which could not only help in decreasing the mortality rates in COVID-19 but, also help alleviate various morbidities (both short term and long term) consequent to COVD-19 thus, improving the quality-of-life post COVID-19 in these patients.

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