Usefulness of Complete Blood Count in Predicting COVID-19 Severities

Monika Sukhija, Vasant Wagh*, Sanchit Sukhija

Department of Community Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Wardha, Maharashtra, India

ABSTRACT

Background: COVID-19 or coronavirus disease 2019 is the evolving pandemic that has grabbed the whole earth and havoc can be seen around the world. Since its inception, it has spread to every nook and corner of the world affecting almost each and every individual mostly in negative way. Long COVID-19 is slowly emerging as parallel medical emergency and patients are experiencing wide range of symptoms even after being testing negative for the COVID-19.

Summary: Biomarkers are the readings of the various enzymes, proteins and various other fluid levels which are available to predict the severity of the COVID-19 disease in severe to critical patients. These are widely range of biochemical which can be found everywhere for example blood. Blood count can reveal several parameters and their ideal status.

Conclusion: Close monitoring of severely ill patient can only help the biomarkers to work in predicting the severity of the COVID-19. Specific algorithm can be made to employ for certain group of patient which in turn can alert the health care professionals at right time.

Key words: COVID-19, Biomarkers, Hepatologic, Blood count, CRP, D dimer

INTRODUCTION

Coronavirus disease 2019 or COVID-19 is the constantly evolving disease which is initially thought to be a generic pneumonia. The coronaviridae family of the viruses has bestowed another of its virus members which is named as novel coronavirus which is the latest among the vial lineage. The virus has caused havoc of extremely large extent. Since its inception in Wuhan city of Hubei province in China [1]. It has grappled the whole world due its high transmissibility and ability to make severe to fatal clinical complications. Till November 28, 2021, 261,316,240 infections of COVID-19 has been reported from all across the globe and 5,198,584 people met the unfortunate fatal clinical outcome caused due to COVID-19 related complications [2]. Vaccination has been approved for certain section of people by specific vaccine makers who were certified by the respective drug controlling agencies. Till now 7,601,136,000 jabs has been administered all over the world [3]. The mutations in the novel coronavirus is dangerous yet a normal routine among the viruses as they mutate themselves to survive and evade the antibodies and also to increase their longevity. Recent mutation in novel coronavirus reportedly from southern part of the African continent has made the whole world nervous which can be seen from the response at the different bourses post news break around the world. The new variant which is already classified as variant of concern is named as omicron, reportedly multiple times more infectious than previously infecting delta variant [4]. Therefore as the pandemic is here to stay, we should mainly focus on severely ill patient as they can be saved and case fatality rate can be lowered. The biomarkers can be used at the disposal of the health care professional to stratify the patients according to the severity of the disease so that they can be given preferential treatment in case of critically ill patients. Long COVID-19 is slowly emerging as parallel medical emergency and patients are experiencing wide range of symptoms even after being testing negative for the COVID-19 [5]. Some of the biomarkers are able to predict the severe symptoms during the follow up of patients. It also highlights the necessity of the follow ups.

LITERATURE REVIEW

Epidemiology of COVID-19

Few had thought that the nominal flu which propagated to pneumonia would cause destruction of such a massive scale. That unknown flu later named COVID-19 or

coronavirus disease 2019 which is caused by the new member of the coronaviridae family, known as novel coronavirus. Soon, after it's discovering in China, it spread to entire world, in a rapid pace. All the health care authorities were taken aback by the speed of the virus of spreading and made them to think on various options through which it can be brought under control. Other members of the coronaviridae family such as SARS-COV-1 and MERS-COV also caused some destruction but it was limited to certain geographical extent. In case of novel coronavirus causing COVID-19, it did not paid any heed to the geographical boundaries and spread itself over entire globe [6]. Even remotest tribes on the earth which have extremely limited contact with the outer world also came infection umbrella of COVID-19. The viral strain of the novel coronavirus is extremely infective and highly unpredictable. Previously thought symptoms of cough and cold were expanded periodically and ranges from fever, diarrhoea, dyspnoea, headache and nausea to dysosmia, bran fogging and so on. But it is not limited to these mentioned symptoms and it is highly variable according to the patient and its clinical history. The symptoms may starts appearing from 4th day to sixth or seventh day and the incubation period is generally from 2 days to 14 days depending upon various factors like viral load, patients age, clinical history and so on. The Viral load can be one of the game changing aspect as more is the viral load, more complicated it becomes to manage the patient clinically. Virus detection can be done through various tests like Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), antigen test, antibodies detection test, x-ray test through ground glass opacity test and son. RT-PCR is considered as the golden standard for the detection of the novel coronavirus. The person not showing any symptoms may be positive and person showing similar symptoms may test negative for COVID-19 depending upon the situation. Continuous monitoring of oneself is needed if one suspicious of its medical condition. Generally the infection cases are classified as mild cases, moderate cases, severe cases and critical cases. Mild cases are those cases which shown initial symptoms like normal cough with light fever. These people are advised to get enough rest along with dosage of medications treating the symptoms. Generally if the treatment is started early enough, then these sections of patients are cured at home itself. But proper consultation by the prescribed doctor is necessary to take any action. Moderate cases are those cases which have multiple symptoms but these too can be treated at home with one medical personnel clinically watching the patient's condition round the clock. If patient's condition deteriorates, then hospitalization of the patient becomes inevitable [7]. Diarrhoea, along with dyspnea and other symptoms can be seen. Severe patients are those patients who have high viral load and they can experience symptoms such as breathing difficulties, dropped oxygen levels in blood, dizziness and so on. These patients need urgent medical attention and may arise the need of sophisticated medical equipment's. Last type of patients that is critically ill patients with COVID-19 needs highly sophisticate medical care along with essential surgeries if

needed to save the patients' lives. The fatality rate from the last two groups is extremely high and covers majority of the case fatalities associated with COVID-19.

Comorbidity and COVID-19

After more than a year has been passed and several conclusions can be made which are backed by the empirical evidence for the behaviour of the novel coronavirus. It is seeing from various studies that certain section of the population comprises majority of the part of the case fatalities and these section needs highly sophisticated medical attention like intensive care unit, oxygen support system and mechanical ventilator and so on. Round the clock monitoring is needed to ensure the patients stable health. These sections of patients are called vulnerable section of population which comprises elderly, pregnant women, comorbid patients and so on. All these patients are undergoing immunosuppressive state and their immune system response is being consumed by their current anatomical state. Comorbidities like Pre-existing diseases such as cardiovascular diseases, live ailments, renal failure, diabetes mellitus are some of the diseases which are found all over the world [8]. These types of chronic disease make the immune system response of the patient extremely weak and novel coronavirus exploits the loop hole and easily take the control of the cells in such bodies. The rapid multiplication of the virus and spread from one part of the body to another part happen due to no or less checks and balance by immune system response. Therefore chance of patients slipping into multi organ failure is high. Also certain medications which are currently used in dealing with several and critical patient of COVID-19 may cross with the medications which patient is already taking and create other complications. Therefore clinical management of the patient becomes extremely difficult. Although the chance of the novel coronavirus infecting people are almost equal for every section of population but the severity of the symptoms and chance of producing fatal clinical outcome is high in the above mentioned vulnerable section of population. The severity of the disease increase in such patient. In such patients certain medical and bio chemical reaction takes place after patient experience such symptoms which are critical in nature. If these reactions are observed and noted down, then the chance of survival of the said patient due to early intervention becomes high [9].

Biomarkers in COVID-19

Certain biochemical reaction and medical parameters can show us when a patient is slipping into severe condition. After observing many patients, various researched zeroed down few biomarkers which are extremely effective in averting the patient into slipping into critical medical condition from where the survival chance of the patient goes down. Some of these biomarkers as they are said can be made use of to predict the severity of the disease or the onset of the critical symptoms. These biomarkers can range from immune, hematologic to

biochemical biomarkers which can show abnormalities while the severe symptoms are round the corner [10]. Hematologic biomarkers include White blood corpuscles count, neutrophil, lymphocyte, eosinophil, platelet count, haemoglobin. Biochemical markers includes Alanine Aminotransferase (ALT), Aspartate aminotransferase (AST), bilirubin, creatinine, blood urea nitrogen, lactate dehydrogenase, creating kinase, myoglobin, cardiac troponin, creatinine kinase MB. Coagulation biomarker includes d dimer and prothrombin time and inflammatory biomarkers includes Erythrocyte Sedimentation Rate (ESR), serum ferritin, CRP, PCT, Interleukin (IL) 2R, 6, 8 and 10. All these fluctuate between certain ranges and if the biomarker goes beyond the comfortable range, then it can be said that it is indicating towards the deterioration of the patient's condition. Various studies have already highlighted the abnormalities in these biomarkers in patients of severe category of COVID-19 and it is found that patients which unfortunately met with fatal clinical outcome. Therefore these biomarkers can prove important in identifying the patients slipping into critical medical condition. These can also help in preventing the majority of the case fatalities as proper medications for particular symptoms can be proactively administered at right time.

Blood count in predicting COVID-19 severity

Blood count is also is a one of the most important biomarker which ca predicts or indicates the onset of the severe medical condition of the patients. Blood count includes detailed blood profile of the patient and the related fluctuations in the important parameters. Radboud University suggests that blood count of the patient while in hospital and also at the time of hospitalization can reveal certain inferences which can help the health care professionals to take the decision of the person's course of treatment. The clinical picture of the future of the clinical condition of the said patient can be somewhat defogged and educated prediction can be done accordingly. Haemocytometer or the analysis of full blood count of the patient is done to assess the changes that components of the blood are undergoing. Various cells in the blood can change their structure and shape and invite certain abnormalities which can be extremely fatal. White Blood Cells (WBC) were found to be reduced in number in some of the severely ill COVID-19 patients. Similarly Lymphocyte count is also found to be reduced in some patients who produced severe clinical symptoms [11]. The increase in WBC is further categorized in severe and deceased patients of COVID-19. In a study, it is found that the WBC levels were increase to lesser extent in severe patient than the deceased one. The increase in severe patient was found to be 0.41×10^9/L against the increase of 4.15×10^9/L Weighted Mean Difference (WMD) [12]. The increase in deceased patients is markedly higher and can be regularly checked for, in order to prevent more case fatalities. A significant increase in count of WBC can indicate the rapid deterioration in the health of the patient concerned. Neutrophils are the driving force behind the increase in the WBC's, according to the study. Lymphocyte count on

decrease is another biomarker and predictor of the worsening clinical condition of the patient. The chance of survival of the patients depends upon how quickly the damaged lymphocytes can be replaced. Neutrophil to Lymphocyte Ratio (NLR) have found to be closely associated with the patients clinical outcome. It is a potential marker for inflammatory response which is generally seen among COVID-19 patients and in general. COVID-19 has its deadly nature is due to severe inflammatory response all across the body. Therefore NLR can be checked for its rise as rise can indicate the elevated levels of inflammation in the infection person's body. A marked difference between the NLR figure can be seen from various studied between non-severe and severe COVID-19 patients [13]. Non-severe COVID-19 patients saw comparatively less value of NLR than severe COVID-19 patients with weighted mean difference of -2.48. Both the role of lymphocyte and neutrophil can be confirmed from the analysis of NLR figure of the COVID-19 patients with varying severity of the disease. Not only COVID-19 but other inflammatory disease and aliments can also be anticipated by the health care professionals by looking at abnormalities in NLR values. The NLR which is of greater value than there is associated with more than 4 is closely linked with developing the severe symptoms as compared to the NLR vales which are below three. The haemoglobin levels are another biomarker to identify the upcoming severe state of medical illness. Haemoglobin is the important component as it carries the oxygen without which proper functioning of the various organs will not be possible. There are considerable amount decrees in the haemoglobin the blood count among severe patients than non-severe patients and among deceased patients than survived patients. A meta-analysis from 8 studies confirms the haemoglobin as the biomarker as the indicator of the severity of the COVID-19 infection. Other biomarkers and predictors of the severe COVID-19 conditions are decreased platelets count and eosinophil count which can anticipate the oncoming severe and critical condition. The stoutest connection among two biomarkers was predictably CRP and IL-6 (R=0.65 p ≤ 0.00001) as CRP fabrication is propelled directly by IL-6 [14].

Viruses of the coronavirus lineage have history of affecting brain function and cause life threatening injuries to the brain. The virus is closely linked with the impact on the central nervous system which can alter the response by the innate immune system of the body towards body leading to unhindered proliferation of the virus. Various studies have also shown that novel coronavirus can reproduce itself in the brain cells also which is also a cause of concern. Also Angiotensin Converting Enzyme 2 (ACE 2) receptors which acts as the entry point for the novel coronavirus are also present ion the cerebrovascular endothelium. The increased oxidative stress, degeneration of the brain cells, neural inflammation can lead to severe brain injury and patient may slip into critical condition. Anosmia, Dysosmia, altered perception of smell and taste has been closely associated with viral infection reaching brain. Although

these stated abnormalities are not life threatening but if the viral load increases further then it can cause permanent dame leading to wide spectrum of medical criticality [15]. Certain proteins and enzymes levels changes considerably when there is neurode generation, injury in brain cell etc. which can be identified from the protein analysis from the blood assays of the concerned patients. Certain biomarkers such as Neuro Filament Light Polypeptide (NfL), Glial Fibrillary Acidic Protein (GFAP), increases Cerebrospinal Fluid (CSF) was found to be increased in patient having brain injury. Tau proteins were among the highly elevated figures among the patients having brain injury by COVID-19 infection. Also the inflammatory proteins were found to be elevated in such patients.

DISCUSSION

Long COVID-19 is the condition in which the symptoms of the novel coronavirus causing coronavirus disease 2019 persists for long time even after the getting recovered and testing negative for the same. The symptoms which persist for long includes occasional and recurring fever, cough and cold, headache, extremely fatigue, weakened muscles, sleep apnoea, occasional dyspnoea, and occasional diarrhoea. Some severe after effects can have critical impact on patients as various other ailments may crop depending upon the person. Long COVID-19 can have detrimental impact on the infected person. Earlier, it was thought that the adverse effects on the infected persons life is only up to testing negative for COVID-19. Certainly it is a false notion and one has to be extremely cautious regarding the long term impact of the COVID-19. Some unalterable clinical impact has been observed among patients but needs more comprehensive analysis of its permanent nature [16]. A summary of report of follow up of 384 patients for average of 54 days post COVID-19 infection. There is a marked feature of the patients studied which is high prevalence of comorbidities among the followed up people. Hypertension was prevalent among 41% of the patients and diabetes mellitus was prevalent among 27.2% of the followed up patients. In case of biomarkers, D dimer and CRP levels were up by 30.1 and 9.5% among the followed up population. Although the study was limited to the patients which are in the prolong exposure of the Intensive Care Unit (ICU) and took long period to tested negative for COVID-19 [17].

CONCLUSION

COVID-19 is not going anywhere and is here to stay for considerable amount of time and which can deduced from the new variant of concern of the novel coronavirus which is recently named as omicron. It is supposedly many times more transmissible than the delta variant which wreaking havoc before the omicron variant. In case of severity of the COVID-19, after more than a year, certain pattern can be drawn in order to predict the severity of the disease which can then use to prevent the patients from meeting to fatal clinical outcome. The biomarkers are really helpful in finding the oncoming disease severity. Therefore, multifaceted researches backed by bigger cohorts will aid further confirm the theory devised and aid health care professionals in projecting panning out of disease in patients with COVID-19 beforehand. By analysing these biomarkers the patients can be categorized easily and the treatment course can be change dynamically and quickly according to the need of the patient. Severely ill patients need to be monitored constantly and algorithm can be developing to alert the health care professionals to look at the patient when the marker reaches a certain threshold. Long COVID-19 is slowly becoming the menace and it needs to be checked upon. Follow up of severely and critically ill survived patients must be done at regular intervals in order to take stock of the situation. Some patients are obtaining fatal clinical outcome even after testing negative for COVID-19. Therefore Biomarkers can aid in identifying such patients beforehand.

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