In testing, these independent clinical signs can be interpreted more confidently using biomarkers. Finding out how different biomarkers behave during an illness can help doctors diagnose a serious illness early and later improve their prognosis. Clinical symptoms can be acknowledged more suitably using biological symptoms. This provides target values during progression of disease. From now on, classifying a patient into a soft, sensitive or sensitive condition is highly defined, allowing for early intervention.

LITERATURE REVIEW

Biomarkers and its importance

Biomarkers are often described as measurable biological indicators of where they are acute or genetic disease in the medical field. Biomarkers are the signs of notification that serves as an indication of any normal or abnormal process. It also serves as an indication of a pathological condition or disease. It is also use to visualize how the body responds to a particular type of treatment. The role of biomarker has currently been increasing in medical decisions as well as in every phase of drug development that is from the time of discovery of drug to its evaluations processing and testing. The huge cost and expenditure that go under vain when clinical trials of medications fail has now given rise to the interest of researchers to use biomarkers as the analysing method. The use of biological markers is especially important in our current epidemic because they can help in the development and approval of new, new drugs, especially vaccines. Biomarkers can be used to describe the physiological features of a particular disease and determine appropriate treatment based on phenotypes, as well as genotypes, which, in turn, receive a great deal of attention [2]. It plays an important role in predicting future problems or problems and can be useful as a prediction of COVID-19.

SARS-CoV-2 testing: Current situation

COVID-19 global outbreak and has caused widespread dysfunction around the world. It has become hazardous disease globally and early detection is a major issue for the disease. Everywhere around the globe researchers are trying to invent an innovative COVID-19 diagnostic test, as the currently used RT-PCR method is time consuming and expensive. Thereby scientists have a crucial requirement for definitive biomarkers connected to Coronavirus 2019. The COVID-19 screening devices are designed to be used in conventional research facilities, with the desire to shorten the diagnostic time window and thus make it easier to diagnose patients and their contacts. Effectiveness of these kits is based on certified biomarkers that provide high sensitivity and clear results. Indeed, the negative effects can be devastating, since anonymous infected people may not be isolated and may infect others. Less number of biomarkers is approved for laboratory use; including risk of results produced may be unreliable and not very helpful in making medical decisions [3]. The haematology and general integration tests have been instrumental in identifying useful speculative symptoms and predicting outcome and recovery. In addition, in the course of personal therapy, biomarkers may enable the appropriate treatment options for cases with infection.

Disadvantages of RT-PCR

Testing is difficult to use grossly, requires money and expensive laboratory equipment; trained and skilful lab staff. Currently used polymerase chain reaction tests also suffer from a degree of resistance. This means that other clinical tests should also be considered when considering, the results of reverse transcription polymerase chain reaction tests. Polymerase chain reaction testing has a considerably high level of positive and negative, false positive and false negative results [4]. Hence, it is needed to find methods of improvements in polymerase chain reaction testing. Technically, the polymerase chain reaction process for COVID-19 infected samples has few stages and requires laboratory equipment which turns the process hideous and difficult to perform outside the lab environment. Firstly, RNA material is released from cells and virions are stored. This step requires laboratory equipment and sometimes there may be loss of some RNA material due to colour conversion. Secondly, hot cycling equipment is required to create a temperature change during the RNA amplification process. Third and last difficulty is the learning method used.

Hence, consideration of the onset of symptoms becomes important when interpreting the probability of infection according to the results of polymerase chain reaction tests. It is in findings that the viral load is high on day 3 that is from the starting of symptoms in the samples obtained from the upper respiratory tract and live active virus may be seen within 8 days after arrival of symptoms when tested by viral culture testing. Although the effects of transcription polymerase chain reaction continue to detect the presence of viral RNA properties. The false standard of diagnosis may initially appear to be insignificant, provided the situation of the latest global incidences of the disease. However, pros are really important and may have a significant impact on public health services.

RT-PCR with serum testing

Although reversed transcriptase polymerase chain reaction testing is primary examination in the early stages, testing remains a high level of failure to detect true COVID-19 infection. However, when polymerase chain reaction testing is combined with other clinical molecular tests, the sensitiveness of the COVID-19 test is increased. In addition, polymerase chain reaction testing and serologic tests show a tendency to sensitivity during infection, whereas single tests may mask other failures as the disease advances. In the first stage of infection, the rate of infection with polymerase chain reaction test is low; however, the results of RT-PCR are enhanced when ELISA cell testing is performed in combined form. The integration of this approach has so far being used to

upgrade sensitivity in the initial phases [5]. During the first 5-6 days of symptoms, polymerase chain reaction testing has a lower chance of detection of the virus in nasopharyx sample but when polymerase chain reaction tests and ELISA technique when put together, sensitivity was significantly improved.

Urgent need for validated biomarkers

Biomarkers will play a vital role in:

- Assessment and productivity of future drugs.
- Prevention as well as diagnosis of clinical effects.
- Arrangement of patients for explanation of treatment objectives and identification of individual risk of infection, appropriate preventive interventions [6].

Salivary biomarkers: Salivary immunoglobulin a serves as an important biomarker of the immune system hidden by healthy individuals and cases in various medical situations, in stress and exercise response. It plays vital role among mucosal protective proteins, which is a key player in the first line of defence against foreign particles adhesion and intrusion in oral cavity [7]. The oral mucosa serves as the first defence against foreign intruder and is a potential site for the first cases that trigger COVID-19. IgA antibody is important part of the immune system which has ability to adapt to antibodies to the mucosal surface and have both anti-inflammatory effects [8].

Cardiac biomarkers: Cardiac biomarker is a measurable protein produced in response to certain pathological conditions in the cardiovascular system. In medical practice, these biomarkers are now the most commonly practiced method of diagnosing the presence and progression of heart disease. These biomarkers are essential for diagnosis of various heart conditions [9]. Latest studies shows micro ribonucleic acids have been successfully identified as cardiac biomarkers.

Interleukin-6: This is involved in increasing release of anti-inflammatory mediators. This mechanism has number of pathological processes. Understanding their role in COVID-19 may help simplify the design of novel immunotherapies. Studies have shown that IL-6 levels increase significantly in the COVID-19. However, as many studies have so far observed, it is difficult to exclude if the ascent is important enough to cause visual detection in complex ways [10]. Since a balanced increase in IL-6 is associated with disease gravity, this study may demonstrate the results to be incorrect. In spite of the fact doctors can employ this to diagnose early and early oxygen treatment; the different outcomes make it a bit difficult to determine which IL-6 level is associated with which side effects.

Lactate dehydrogenase: LDH helps in conversion of pyruvate into lactate. LDH secretion is caused by necrosis of cell membranes; this is an indication of viral infection or lung injury. Evidence shows strong linkage of LDH levels to COVID-19 infection progression. The study found higher levels of LDH in ICU patients than non ICU patients. As high levels of LDH continue to ICU patients number of days after admission, LDH it may be a predictable biomarker for serious diseases [11]. A multicentre study that included 1099 samples of infected cases reported strong evidence related to the severity of tissue damage and inflammation with elevated LDH levels. In addition, when LDH levels were associated with CT scans, higher levels indicated the severity of pneumonia. There is growing confidence in using LDH as a biomarker to measure its resilience infection with COVID-19. Another study found that there was a significant increase in LDH rates among patients who deny COVID-19.

C-reactive protein: It is produced in liver and is caused by various inflammatory mediators. Despite the inaccuracies, this is used clinically as a biomarker for various inflammatory conditions; an increase in CRP levels is associated with an increase in the severity of the disease. An observational study found that the risk of developing COVID-19 disease increased in patients with high CRP levels. Both studies suggest that CRP levels are a strong indication of the presence and severity of COVID-19 infection. In addition, research from unpublished observations shows that CRP is one of the first signals of a biomarker within a flexible blood plasma to indicate metabolic disorders; if CRP is approved it will be the most productive biomarker to predict continuous infection with COVID-19.

D-dimer: D-dimer raised levels indicate coagulation activation and fibrinolysis. Preliminary studies linked COVID-19 with haemostatic abnormalities in a single study looking at higher D-dimer levels, the concentration ratio, in non survivors compared with survivors was associated with an increase in mortality among patients. In addition, they found that levels of two or higher at admission were a complete discontinuation of hospital mortality exposure to COVID-19. In addition found that D-dimer levels when received can be used to test patients in critical care. The research showed that average D-dimer levels were higher in ICU patients in comparison to non ICU patient.

Cardiac TPN: There is day by day increment in evidences of high mortality rates among individuals with cardiovascular disease caused by the presence of infection. Some studies investigated that highly sensitive troponin I of the heart can be used to signaller of progressive illness and death [12]. It is a gold standard necrotic biomarker for global heart attack. It is removed almost entirely from the myocardium where there is a myocardial injury regardless of the traumatic method. Elevated levels are associated with severe myocardial injury, ICU admission, hospital mortality, inflammation intensity in COVID-19.

Aspartate aminotransferase: Liver action has also been established as an important diagnostic feature of death in corona patient. Research propose that COVID-19 virus may have direct linkage with cholangiocyte, therefore, liver dysfunction in Corona sufferers may be because of cholangiocyte malfunction and some more causes, such as drug induced liver damage and an inflammatory system caused by inflammation.

DISCUSSION

Biomarkers have wholly established their ability to predict the decline in COVID-19 patient prediction. However, when considering the predictability potential for these biological symptoms, it is interesting to consider whether they are the reason for COVID-19 or the result of the progression of the disease. We still need to learn about the biology of this disease and the flexible response that patients show in their manifestations and recovery. We expect that the process of biomarker detection and validation will also guide the rapid translation strategy to address this global health problem [13]. Quality and productivity are essential to translating basic findings into effective clinical interventions and following this approach alone is an effective response to a proven epidemic. The combined efforts of the scientific community will create high quality information that is clearly accessible and will bring about a better understanding of SARS-CoV-2, which benefits everyone. Reverse transcription polymerase chain reaction has its own pros and cons. The test has its own outcome timings; it is difficult to be performed outside the laboratory environment and is time consuming. It requires highly qualified and trained staff members. The reliability of RT-PCR is still under questionable condition [14]. Henceforth there is serious requirement of some suitable pocket friendly, time effective and reliable method of testing so that false results like false negative and false positive results may get minimized and there may be proper testing. Biomarkers serve to be reliable testing method as compared to reverse transcription polymerase chain reaction. Biomarkers like salivary immunoglobulin's, cardiac protein biomarker, interleukin-6, lactase dehydrogenase or LDH, C-reactive protein, D-dimer, cardiac TPN, aspartate aminotransferase are some of the biomarkers that after studies have shown their positive impact in diagnosis as well as prognosis and has reduced chances of some serious delayed complication that may get unnoticed in initial days of disease.

CONCLUSION

Bringing biomarkers in the testing strategy will be lot more beneficial and effective in every aspect when compared to reverse transcription polymerase chain reaction test or commonly known as RT-PCR. Biomarkers are found to play an important role as they will reduce detection time, be more expensive and reduce the chances of transmission of the virus during the diagnosis. It can also be used to improve RT-PCR test results.

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