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DIFFERENTIAL DIAGNOSIS OF DIFFERENT ETIOLOGICAL MARKERS OF COVID 19 AMONG LAB PERSONALS

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Abstract

Background: *In December 2019, Wuhan, Hubei Province, China, reported an unexplained pneumonia epidemic. The pandemic outbreak caused serious mental health stress for the global population. One of the most important cures of COVID, isolation, posed serious issues to the psychological conditions of population. It not only affected the human psychological conditions; it also posed greater stress to the global health system. It undermined the overall health system globally and caused serious problem for healthcare officials and other personals (Galanopoulos, Gkeros et al. 2020).*

Material and methods: *The sample will be collected by questionnaire. The study will be a retrospective cohort study. The research will be conducted over 6 months after the synopsis is approved. Here is the list of complete materials included to complete the study.*

Result: *Seropositivity of ELISA across studies: 85%-95%.Rate of positivity of PCR in covid-19 patients: 70% initially while increased to 99% afterwards.Rates of ICT in covid-19 patients:*
Rapid antigen test: 72% in symptomatic patients while 58% in asymptomatic patients.Rapid antibody tests: 75%-85% positivity rate.

Conclusion: *According to research, ELISA has an 85–95% sensitivity for detecting IgG throughout this time, which makes it a very useful tool for seroprevalence studies and immune response evaluation. PCR exhibits remarkable performance characteristics with sensitivity rates of 95–98% and specificity surpassing 99%, making it the most sensitive molecular detection technique now in use. (Wang, Xu et al. 2020). Antigen-detecting ICTs (RATs) is directly related to viral load, with optimal sensitivity (70-90%) occurring during the peak infectious period which is usually days 1–7 after the onset of symptoms. Since this window corresponds with the highest risk of transmission RATs are very helpful in locating contagious people in public places. The performance profile of antibody-detecting ICT formats varies; IgM tests show a positive result 7–14 days after infection (60–80% sensitivity) while IgG tests only exhibit reliability (>85%) after 14 days.*

INTRODUCTION

Since the early 2000s, three novel zoonotic coronaviruses have appeared. The first, SARS-CoV, was responsible for an outbreak in Guangdong Province, China, in 2002. The second virus, MERS-CoV, first surfaced in Saudi Arabia in 2012. The third SARS-CoV-2 caused the COVID-19 pandemic, which began in 2019 in the Hubei Province of China. This review looks at the ecological and genetic factors that influence how these viruses arise. To attach to human cell receptors in the gastrointestinal and respiratory systems, the spike protein's receptor-binding domain needs to be changed. High genetic variability and frequent recombination are characteristics of bat populations, which serve as natural reservoirs for these viruses and help explain their adaptability. SARS-CoV, MERS-CoV, and SARS-CoV-2 evolved as a result of these pathways.

Moreover, the genetic makeup of SARS-CoV-2 or humoral reactions to it are determined by etiological agent assays. Real-time polymerase chain reaction (RT-PCR), which detects viral genome targets in respiratory tract materials within the first week of symptoms, is the gold standard for diagnosis. Beginning in the second week of symptoms, serological testing must be advised. Numerous tests are available, with varying sensitivity and specificity and the majority requiring validation. Laboratory tests such as lactic dehydrogenase (LDH), ferritin, procalcitonin, C-reactive protein (CRP), D-dimer, clotting tests, total blood count, and others assess the risk of worse prognosis or more severe disease thromboembolic consequences, such as heart damage. Imaging studies may be useful for diagnosis when other tests were not available or produced negative results and a clinical picture was compatible (Lvov and Alkhovsky 2020).

A pneumonia outbreak of unknown origin was reported in Wuhan, Hubei Province, China, in December 2019. Epidemiological data indicates that the Huanan Seafood Wholesale Market is connected to pneumonia cases. After injecting respiratory samples into human airway epithelial cells, Vero E6 and Huh7 cell lines, a novel respiratory virus was identified. This virus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) after genome analysis revealed that it was a novel coronavirus related to SARS-CoV. The beta coronavirus SARS-CoV-2 belongs to the Sarbecovirus subgenus. The World Health Organization declared a pandemic on March 12, 2020, in response to the thousands of deaths from coronavirus sickness (COVID-19) and the global spread of SARS-CoV-2. The world has already suffered greatly as a result of this disease. (Zhou, Yang et al. 2020).

Coronaviruses are named after the spike-like projections on their surface that give them a crown-like appearance under an electron microscope. They range in diameter from 60 to 140 nm. These viruses often cause moderate respiratory infections. (Singhal 2020).

Etiological agent testing determine the genetic material of SARS-CoV-2 or the humoral reactions to it. Real-time polymerase chain reaction (RT-PCR), which detects viral genome targets in respiratory tract materials within the first week of symptoms, is the gold standard for diagnosis. It is necessary to recommend serological testing starting in the second week of symptoms. There are many tests available, the majority of which require validation and have varying levels of specificity and sensitivity.Laboratory tests such as lactic dehydrogenase (LDH), ferritin, procalcitonin, C-reactive protein (CRP), D-dimer, clotting tests, total blood count, and others assess the risk of worse prognosis, thromboembolic consequences, and more severe disease. Imaging studies could be useful for diagnosis when other tests were not available or produced negative results and there was a clinical picture that was compatible (Goudouris 2021).

Healthcare professionals are more likely to get COVID-19, including lab and hospital employees. Medical staff and other close contacts may be more vulnerable to infection if SARS-CoV-2 is prevalent in the air and on hospital surfaces. During this outbreak, cytological and histopathological labs must continue to provide diagnostic services to patients.Usually, paper-based forms are used to manually request laboratory tests for patients. The specimen and its paper-based request form are

frequently given to the laboratory receptionist together. The requesting clinician completes the form and gives it to the patient or another healthcare practitioner, who then gives the hard copy to the laboratory receptionist. After the case was registered, the specimen would be prepared by a laboratory technician and tested by a pathologist. A March 2020 study found that while SARS-CoV-2 had a longer half-life on cardboard than SARS-CoV, both viruses had identical half-lives in aerosols, with median estimates of roughly 1.1 hours. On paper, it was demonstrated that SARS-CoV could survive for 24 hours at room temperature. According to the authors, no study has evaluated the possible danger of laboratory exposure during the coronavirus pandemic using data from several medical departments. Numerous studies that have looked at the use and implementation of electronic laboratory request forms have found that they are definitely superior to manual ones in terms of service quality. (Hasan, Nafie et al. 2020).

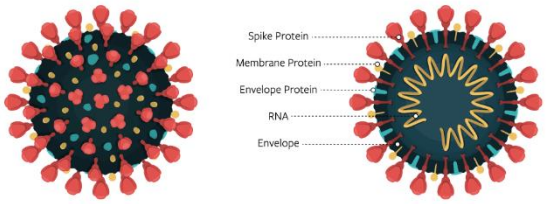

Figure: 1.1 Virus structure

The COVID-19 immunopathology Increased cytokine and antibody production are among the immunological patterns associated with COVID-19, along with lymphocyte activation and dysfunction, granulocyte abnormalities, and monocyte abnormalities. One of the main signs of COVID-19, particularly in more severe cases, is lymphopenia. High amounts of virus-specific CD69, CD38, and CD44 were expressed by the CD4+ and CD8+ T cells of the patients. When lymphocytes exhibit an exhaustion phenotype, there is an up-regulation of T cell immunoglobulin domain, mucin domain-3, killer cell lection like receptor subfamily C member 1 (NKG2A), and programmed cell death protein-1. Severe patients had a much higher neutrophil count and a lower proportion of monocytes, basophils, and eosinophils. As far as the authors are aware, no study has assessed the potential risk of laboratory exposure during the coronavirus pandemic using data from multiple medical departments. Numerous studies that have looked at the use and implementation of electronic laboratory request forms have found that they are definitely superior to manual ones in terms of service quality (Zhu, Zhang et al. 2020).

In a SARS-CoV patient, pneumonia symptoms and extensive alveolar damage resulted in acute respiratory distress syndrome (ARDS). With its rapid global spread, the virus killed 776 people and infected over 8,000 more. In 2012, a limited number of Saudi people were found to have MERS-CoV, which causes mild upper respiratory damage that develops into serious respiratory disease. The MERS coronavirus causes pneumonia, acute respiratory distress syndrome, and kidney failure, just like the SARS coronavirus. The Chinese government notified the WHO at the end of 2019 of several pneumonia cases that had no known etiology. Observations have suggested that this virus can travel from person to person, and more than 100 countries have confirmed this. The virus is spread mostly by close contact with an infected individual, exposure to respiratory droplets or aerosols, coughing, or sneezing. These aerosols can enter the human body through the mouth or nose. Healthcare personnel, such as laboratory and hospital personnel, are at a higher risk of catching COVID-19. The risk of infection may be higher for medical personnel and other close contacts if SARS-CoV-2 is prevalent in the air and on hospital surfaces. Despite this outbreak, cytological and histopathological labs are unable to cease providing diagnostic services to patients. Typically, patients' laboratory test requests are made

manually using paper-based forms.The material is often handed to the lab receptionist together with its paper-based request form. After filling out the form, the requesting clinician gives it to the patient or another medical practitioner, who then gives the physical copy to the lab receptionist. A pathologist would test the specimen after it was prepared by a laboratory technician and the case was registered. (Shereen, Khan et al. 2020).

Whether other materials like blood, urine, faces, saliva, and throat washing will be approved substitutes is not yet clearly defined. Regarding serological testing, promising results from preliminary research suggest that the majority of COVID-19 patients seem to experience a prolonged immune response against the virus, which is characterized by the appearance of anti-SARS-CoV-2 IgG and IgA, one to two weeks after the onset of fever or respiratory symptoms. Using molecular biology techniques to quickly identify viral RNA in biological materials, especially upper and lower respiratory tract specimens, will remain the primary method of etiological diagnosis for COVID-19 for the foreseeable future. Whether these antibodies will continue to neutralize the virus is still up in the air. The novel coronavirus SARS-CoV2 is the cause of the COVID-19 pandemic, which poses a threat to millions of people. The virus can spread freely in tissues that are heavily infected because humans lack protective immunity and it can avoid innate immune responses. Intracellular components and virus particles are released into the extracellular environment after cell death, which results in the formation of immune complexes, the recruitment of immune cells, and associated damage. Severe inflammatory reactions may be brought on later in the course of the illness by macrophage infection or the recruitment of immune cells that are not infected. Acute respiratory distress syndrome and cytokine storm syndrome are brought on by the uncontrolled production of pro-inflammatory mediators. Antiviral medications and immune-modulating treatments are already undergoing trials. Understanding SARS-CoV2 immune evasion strategies and the resulting delayed massive immune response will help identify biomarkers that predict outcomes, phenotype, and disease stage-specific treatment, which is likely to involve both antiviral and immune modulating agents (Lippi, Mattiuzzi et al. 2020).

Mutations in the non-structural proteins (NSPs) of SARS-CoV-2, namely NSP2 and NSP3, S protein, and RNA-dependent RNA polymerase, hamper the creation of a vaccine. The creation of highly effective vaccines depends on the dynamics of genomic sequence spike protein mutations and ongoing SARS-CoV-2 surveillance. Therefore, starting with viral mutation, there are unique hurdles in creating a vaccine against SARS-CoV-2. In addition to safety, effectiveness, stability, vaccine allocation, distribution, and cost, the need of establishing long-term immunity is thoroughly discussed. There are 198 vaccines in the preclinical development stage and 169 vaccines in the clinical development stage at the moment. The majority of these vaccinations are part of the small BacAg-SPV (Bacterial antigen-spore expression vector) type, which includes at least one vaccination, and the Protein subunit type, which contains 54 vaccines. The conventional methods for developing vaccines have completely changed with the advent of computational methodologies and models. (Saravanan, Chagaleti et al. 2024).

Late in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV) first appeared in Saudi Arabia. To identify any genetic alterations that have occurred over the last eight years, we carried out a comprehensive comparative genome research of MERS-CoV from both human and dromedary camels from 2012 to 2019. We were able to collect 1309 submissions, including 308 MERS-CoV whole genome sequences that were published in GenBank between 2012 and 2019. Over the past eight years, we have used bioinformatics techniques to describe the virus's genomic structure and organization and map the most important patterns within various regions or genes throughout the genome.Since the first appearance of these sequences, we have also tracked their changes and alterations. We found some significant trends in the ORF1ab, S gene, and ORF-5 to barcode the MERS-CoV lineages in African camels. We also identified genetic characteristics that suggest the virus's zoonotic origin in dromedary camels. Selection pressures

were evident in other sequences, especially the 5′ UTR and the N gene. Future research must keep a careful eye on the MERS-CoV genome to spot any potentially harmful changes. (Ba Abduallah and Hemida 2021).

In comparison to all other organisms, RNA viruses, particularly those in the Coronaviridae family of the order Nidovirales, which have genomes of about 30 kb, typically undergo fast genetic change. These lethal virus types (SARS-CoV, MERS-CoV, and SARS-CoV-2) can spread across species borders and dramatically increase human morbidity and mortality because of their rapid genetic evolution. Transcription and replication proteins, structural proteins, and proteins that facilitate virus transmission are the three main tasks that are commonly encoded by viral genomes. (Krishnamoorthy, Swain et al. 2020).

Spike protein mutations in the receptor-binding domain (RBD) are essential for increasing viral transmissibility and immune evasion capability. Because of the significant alterations in the spike protein, first-generation immunizations and pre-existing antibodies cannot effectively neutralize variants of the delta, beta, gamma, and omicron spike proteins. This calls for the use of booster injections, the creation of second-generation vaccinations that target particular variants, or the deployment of universal vaccination programs. The efficiency of various vaccination platforms, especially against mutations like E484K and P681R, is still a worry despite the fact that mRNA vaccines have shown excellent efficacy against a number of VOCs. The efficacy of adenoviral vector vaccines, recombinant protein vaccines, and full inactivated vaccines against specific variants has varied, emphasizing the importance of continual monitoring and possibly modifying immunization strategies. People in nations with high vaccination rates may be more or less likely to have specific diseases, depending on the type of vaccine. The effectiveness of SARS-CoV-2 mutations is influenced by public health programs, vaccination coverage, and demographics. Understanding how host characteristics, clinical outcomes, and virus genomes interact is essential for both long-term vaccination campaign viability and effective public health interventions. Government officials, researchers, and vaccine manufacturers must collaborate. (Faraji, Zeinali et al. 2024).

The virus differs genetically from SARS-CoV-1 (genetic similarity of about 79%) and MERS-CoV (genetic similarity of about 50%), and it has a distinct base sequence that sets it apart from other species. According to phylogenetic study, it belongs to the Corona viridae family's genus Beta coronavirus, which is a subgenus of Sarbecovirus. (Raskin 2021).

COVID-19 the new coronavirus SARS-CoV2 is causing a pandemic that poses a threat to millions of people. In tissues that are heavily infected, the virus can spread freely because humans lack protective immunity and it can avoid innate immune responses. Intracellular components and virus particles are released into the extracellular environment after cell death, which results in the formation of immune complexes, the recruitment of immune cells, and associated damage. Severe inflammatory reactions may be brought on later in the course of the illness by macrophage infection or the recruitment of immune cells that are not infected.Acute respiratory distress syndrome and cytokine storm syndrome are caused by the unregulated production of proinflammatory mediators.

Immunomodulating therapies and antiviral drugs are already in clinical trials. In addition to phenotype and disease stage-specific treatment, which is likely to involve both antiviral and immune modulating agents, the understanding of SARS-CoV2 immune evasion strategies and the fact that many treatments, such as antiviral medications and neutral antibody therapy, have limited or controversial effects that may be caused by viral variations will lead to the discovery of biomarkers that predict outcomes. Based on the findings of certain clinical trials combinational treatment may be an option. Combination therapy generally demonstrated greater benefits than individual treatment. Furthermore JAK inhibitors exhibit more encouraging results when compared to antiviral medications and neutral antibody therapies which may warrant further research. It's too soon to draw any firm

conclusions on the impact of steroids. Even if COVID-19's invisible war has been slowed down by current vaccinations, people should always prepare for any pandemic threats that could endanger the entire planet. Since humans are unable to foretell when the next pandemic will occur it is not feasible to develop effective vaccines beforehand. Effective treatments that address infection-related symptoms are still crucial, though, in order to be prepared for the potential threat of another pandemic. Thus, further efforts are needed to develop effective COVID-19 treatments (Huang, Wang et al. 2020).

The contemporary world is becoming more interconnected. Any two locations on the earth may be reached relatively easily in a matter of days thanks to a vast network of air, ground and marine transportation hubs. There is a chance of a fast developing novel pathogen pandemic when this is combined with the constant threat of zoonotic to human transfer of both known and unknown infectious pathogens. The ongoing 2019 new coronavirus illness (COVID-19) pandemic in spite of earlier planning and preparations shows how even the most comprehensive efforts may fall short and highlights the necessity of adapting to rapidly shifting and unforeseen conditions. Current preparedness gaps inside and between countries have been exposed by the COVID-19 pandemic. What is understood what is still unclear about the COVID-19 pandemic and to recommend concrete actions for the whole community to take going ahead (Stawicki, Jeanmonod et al. 2020).

Additionally, the flow chart below explains the pathophysiology of COVID-19.

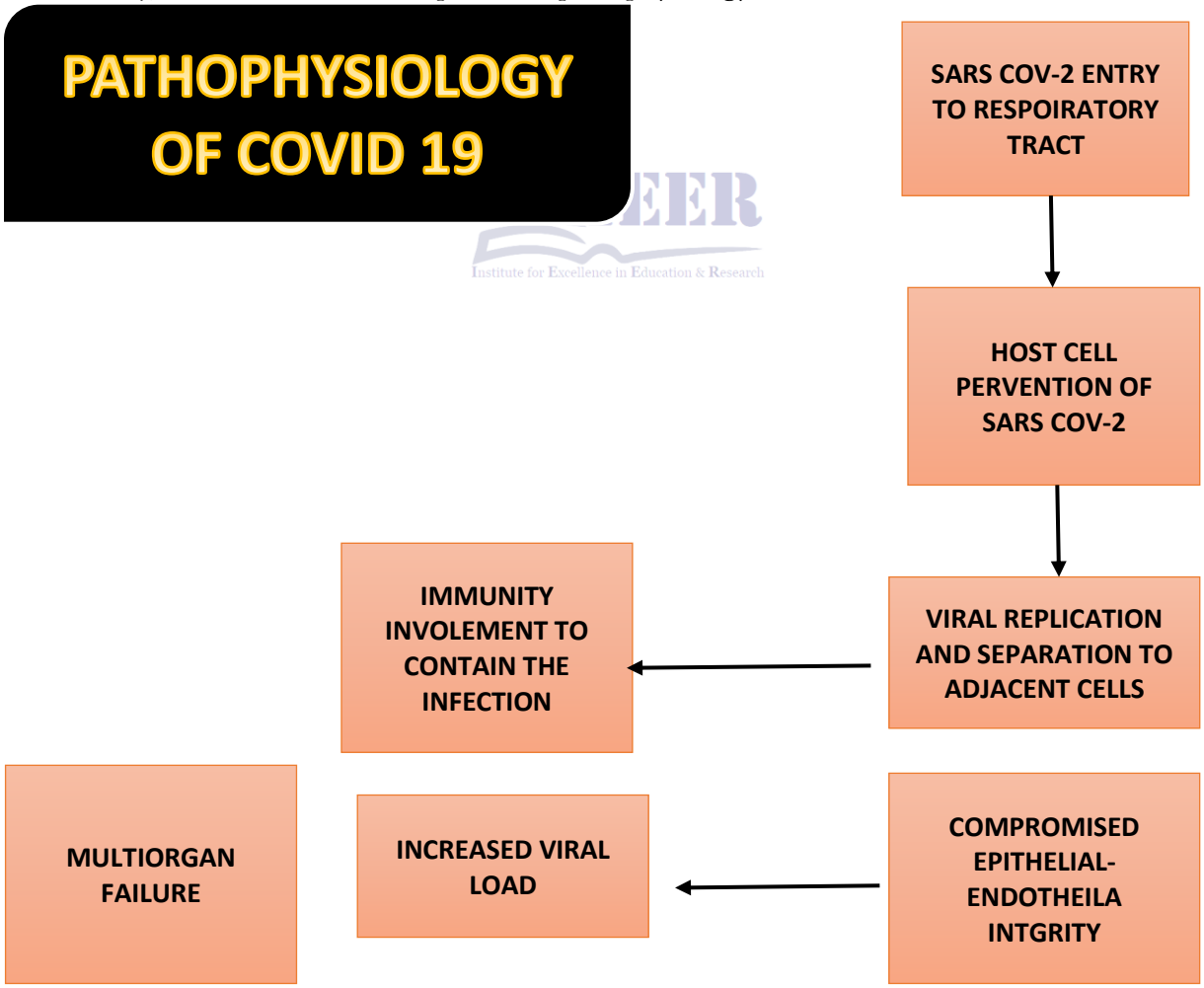

Figure: 1.2 Details of COVID-19 pathophysiology

1) Literature Review

According to (Ishaky, Sivanthan et al. 2023), the COVID-19 pandemic seriously disrupted the global healthcare system. Despite pandemic mitigation strategies that include social distancing and vaccination as preventative measures to lower mortality.Healthcare professionals' mental health has been significantly impacted by the epidemic. Recent research indicate that during the epidemic, healthcare personnel have suffered from poor mental health outcomes, including anxiety, depression, occupational stress, and trauma-related symptoms. Additionally, their ability to recuperate outside of work was hampered by considerably higher than normal reports of insomnia and sleep issues. The growing demand for treating patients with confirmed and suspected COVID-19, along with their concerns about getting infected or infecting their family members, puts a lot of emotional burden on healthcare professionals. The emotional impact of pandemics has already been demonstrated by infectious disease outbreaks such as Ebola and Acute Respiratory Syndrome. However, the COVID-19 pandemic has had a far greater impact than previous ones in terms of the number of people affected worldwide, its spread across countries, its effects on health care systems, and the severity of the measures implemented by the government.

According to (Itodo, Enitan et al. 2020), the increase in hospitalizations associated with the COVID-19 pandemic is significantly taxing the resilience of the health systems in the majority of countries. Hospital and healthcare staff are already overburdened by the number of patients seeking testing and treatment concurrently. In addition to COVID-19 patients, they also treat people with diabetes, cancer, and liver failure. Renal failure, hypertension, etc. In December 2019, Wuhan, China, reported the discovery of the novel coronavirus (SARS-CoV-2) that causes coronavirus disease (COVID-19). By August 2022, the new coronavirus epidemic had killed over six million people globally, and on March 11, 2020, the World Health Organization (WHO) designated it a global pandemic. Ritonavir, Remdesivir, Convalescent plasma, Chloroquine, Ribavirin, Hydroxychloroquine sulfate, Traditional Chinese Medicine, and Arbidol were among the medications or therapeutic techniques that were studied in infected patients in 2020. After months of research using a variety of platforms, vaccination prevention, which started in December 2020, is the most successful strategy. (Itodo, Enitan et al. 2020) described that healthcare professionals are worried that they may spread the disease to their living relatives and family members. Hospitals are therefore under pressure to offer more workplace accommodations. According to the WHO Director General, the virus has infected at least 3,000 medical professionals worldwide, many of whom have died while attempting to treat COVID-19 patients. SARS-CoV-2 is primarily spread from person to person through social contact, such as handshakes and embraces, contact with contaminated objects and surfaces, and respiratory droplets from infected individuals. The virus is released from an infected person's mouth and nose as droplets or droplet nuclei when they cough or sneeze.

Saliva can contain SARS-CoV-2 from a number of sources, according to (McPhillips and MacSharry 2022). It was initially unclear whether SARS-CoV-2 directly infected oral cavity epithelial cells, despite the fact that the SARS-CoV-2 receptor, angiotensin-converting enzyme 2, and both transmembrane serine protease (TMPRSS) receptors, TMPRSS2 and TMPRSS4, are highly expressed on the surface of the oral mucosa and minor salivary gland epithelial cells. These receptors are necessary for membrane fusion, which facilitates viral entrance into the host cell, and spike protein cleavage, which allows receptor binding.

In light of the emergence of new and more contagious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants and the fact that the majority of people worldwide have not yet received a vaccination against the virus, testing, social distancing, face coverings, self-isolation, and national lockdowns remain the methods used to control viral spread (Ferreira, W.B 2024).Since NPS is the reference standard for routine diagnosis, the World Health Organization presently advises utilizing real-time reverse

transcription PCR to detect SARS-CoV-2 RNA from nasopharyngeal and/or oropharyngeal swabs in order to diagnose COVID-19. The main reason for this is that NPS is currently the preferred material for diagnosing other viral respiratory diseases. Because collecting NPS specimens may lead patients to cough or sneeze, healthcare workers are more susceptible to nosocomial infections.Research on NPS substitutes has therefore increased internationally, with saliva in particular receiving more attention. Saliva is less invasive than the current reference standard, which improves patient acceptance and raises the possibility that people will get tested and submit repeat specimens. Close contact with healthcare workers is not necessary which lowers the danger of nosocomial infections and the need for personal protective equipment.

According to (McPhillips and MacSharry 2022), specimen sensitivity for COVID-19 diagnosis is essential for disease prevention, especially in silent or mild cases, as incorrect negative results can lead to otherwise preventable outbreaks. It's important to note that no diagnostic test has 100% specificity and 100% sensitivity. NPS only has a roughly 63% detection rate, and its estimated false negative rate is between 20% and 38% after symptoms appear. The probability of false negative results rises in the days before symptoms appear and during the convalescent period. As mentioned earlier, a variety of methods for gathering, moving, and storing saliva are used in studies on saliva sensitivity.

According to (Abbasi-Oshaghi, Mirzaei et al. 2020), clinics now confirm COVID-19 infection using the RT-PCR technique. Although RT-PCR remains the gold standard for COVID-19 detection, it was challenging to quickly identify infected participants due to the high false-negative RT-PCR results and the inapplicability of RT-PCR un the early stages of the illness. Several studies have shown that chest CT is more sensitive than RT-PCR. Poor nucleic acid detection technology, low viral load, and inaccurate sample fluctuation in the diagnosis rate among kits can all contribute to the low efficacy of viral nucleic acid measurement. Over the years, the CoV has presented numerous difficulties, ranging from the development of vaccinations to the virus's isolation, detection, and prevention. 9 CoV is the biggest RNA genome and a member of the Nidovirales. It usually spreads through touch and droplet transfer and is known to be acquired from a zoonotic source. The infected person has ambiguous clinical signs that require molecular confirmation and virological identification.

(Zowawi, Alenazi et al. 2021) explained that triaging patients for isolation and treatment and fighting the ongoing coronavirus disease 2019 (COVID-19) pandemic depend on precise, rapid, and point-of-care testing with prompt results. Qualified professionals routinely perform the reverse transcriptase PCR used in this testing at specific locations in well-equipped labs. Attempts to reduce the risk of infection may be hampered by the delay in test results caused by a high volume of samples awaiting testing during busy periods.The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can potentially spread covertly in distant locations due to a lack of established laboratories and limited resources. SARS-CoV-2's lengthy incubation period, high infection rate, and ease of interpersonal contact. Furthermore, a large number of asymptomatic individuals can transmit SARS-CoV-2, and infected individuals can transmit the virus up to two days prior to the onset of symptoms. Because of this, individuals can quickly and inadvertently infect entire populations with the virus.

According to (Goudouris 2021), the respiratory virus known as SARS-CoV-2 can sometimes result in severe acute respiratory syndrome and other times in a flu-like illness. The range of associated clinical manifestations has been broadened by the follow-up of COVID-19 patients, however, and it has been discovered that the virus can produce symptoms other than respiratory problems in addition to inflammatory problems in several organs. Additional tests with high sensitivity and specificity are necessary, as evidenced by the range of clinical presentations, from asymptomatic persons to severe cases, and the pertinent diversity of non-specific clinical symptoms of COVID-19. A health professional's return to work, a transfer to the COVID-19 section of an inpatient unit, or the opposite, which could contaminate family

members, are just a few of the difficult circumstances that could come from the results of diagnostic testing.

According to Machado, Hodel, et al. (2020), the COVID-19 pandemic caused unexpected challenges for the medical community. Population testing remains the primary strategy employed to battle the COVID-19 pandemic in the absence of suitable medicines. Several regulatory bodies made diagnostic kits available to the public at the start of the pandemic without a key analytical validation in an effort to respond quickly to the outbreak. This study thus demonstrated that the primary issue with molecular and serological tests for the detection of SARS-CoV-2 is their analytical performance, leading to the publishing of false positive and false negative results.Research that is currently available in the scientific literature supports this. Therefore, lowering the number of false negative test results is necessary for the establishment of hospitalized patient cohorts and quarantine regulations. Combining several diagnostic methods has shown to be a curious solution to this issue. However, because of the related costs of adopting various diagnostic techniques, this option is frequently not possible in many nations and organizations. It should be emphasized that any test methodology utilized for population testing necessitates protocol adherence, financial investment, and logistical assistance. Since it is anticipated that SARS-CoV-2 would remain in circulation for a considerable amount of time, plans for mass testing should also be sustainable.

According to (Falzone, Gattuso et al. 2021), the coronavirus disease 2019 pandemic has forced the scientific community to develop incredibly reliable diagnostic methods in a timely manner in order to accurately and efficiently diagnose this pathology and prevent the spread of infection.Even though the structural and molecular characteristics of the severe acute respiratory syndrome coronavirus 2 were first unknown, private research labs and biomedical firms quickly developed a number of diagnostic tools that are helpful in reliably identifying COVID-19. Currently, the most popular and effective methods in the world are molecular tests based on RT-PCR, immunoenzymatic serological testing, and fast antigen or antibody testing. Other techniques, such as clusters of regularly spaced short palindromic repeats, digital PCR, and isothermal nucleic acid amplification, are either being employed in research settings or are awaiting regulatory bodies' approval for use in diagnostics. This study describes the diagnostic techniques available for detecting COVID-19 infection in clinical and research testing.

According to (Sharma, Balda et al. 2021), identifying SARS-CoV-2 is essential to halting its spread and curing it. The limited sensitivity and precision of molecular techniques, particularly RT-PCR, as well as the requirement for costly equipment and qualified staff are some of their drawbacks. Improved nucleic acid-based methods like RT-LAMP and NASBA, CRISPR-CA and its variants SPR assays, paper assays, semiconductor-based binding assays, the use of aptamers functionalized with quantum dots, and the use of functionalized nanostructures to boost the sensitivity of PCR-based methods are among the technologies being developed for the precise, specific, and sensitive POC detection of SARS-CoV-2. Advances in artificial intelligence, LFAs, and improved molecular diagnostics will make POC diagnosis more prevalent in the future, particularly during global pandemics like COVID-19.

According to (Pradhan, Shah et al. 2022), the ongoing COVID-19 outbreak has reinforced the necessity of SARS-CoV-2 identification techniques to prevent the spread of disease and treat critically ill patients appropriately.A timely and accurate diagnosis is essential to stopping the virus's spread and providing the necessary care and treatment for SARS-CoV2, as there is presently no cure for the sickness. For the qualitative and quantitative detection of viral nucleic acids, RT-PCR is now the gold standard. The enzyme-linked immunosorbent test is also a widely used technique for qualitatively assessing the viral load. Therefore, combining several methods is advised to improve the accuracy and efficacy of SARS-CoV2 detection. Additionally, the enzyme-linked immunosorbent test is one of the most popular methods for qualitatively estimating the viral load.

Almost every detection technique has pros and cons when it comes to specificity, accuracy, sensitivity, cost, time consumption, the requirement for sophisticated labs, and the need for skilled technical specialists to carry out the detection tests.

The collection of nasal and pharyngeal swabs for the real-time reverse transcription-polymerase chain reaction (RT-PCR) detection of viral nucleic acids is the main technique for diagnosing COVID-19 in a laboratory setting, according to (Wang, Zheng et al. 2021). A 15% to 20% false-negative rate, a turnaround time of approximately three to four hours, and the possibility of contamination during sample processing are all characteristics of the RT-PCR test. Up until now, studies have examined how a few laboratory indicators differ between patients with and without COVID-19. A study comparing influenza pneumonia with COVID-19 found that the influenza group had higher PCT values and white blood cell counts, although both cohorts had less lymphocytes. According to a different study, lower neutrophil and eosinophil counts were the white blood cell subgroup counts most closely associated with COVID-19 risk. Furthermore, a review discovered that the most frequent abnormal routine blood results were lymphopenia and an elevated neutrophil/lymphocyte ratio, which were linked to the progression of the disease, particularly in patients with severe symptoms.

According to (Chen, Jiang et al. 2024), Wuhan, China, has been dealing with a severe respiratory ailment caused by the novel coronavirus since December 2019, attracting attention from all over the world. This coronavirus was formerly known as the 2019-novel coronavirus shortly after it was dubbed the coronavirus disease 2019. Although the SARS-CoV-2 outbreak's origin is still unknown, it has been hypothesized that the virus can spread from person to person. With the assistance of numerous organizations, including government administrations, scientists, and medical specialists, the outbreak was contained in China in 2020. But in many nations, this resulted in an increase in both new infections and fatalities. Over 190 million COVID-19 cases have been confirmed globally by July 17, 2021, and over 4 million people had died from the virus. The main ways that SARS-CoV-2 is spread are by respiratory droplets, contact, and feces; aerosol transmission is also very likely. The most common clinical signs of COVID-19 include fever, diarrhea, exhaustion, dry cough, and severe symptoms such acute respiratory distress syndrome, multiple organ failure, and sudden myocardial infarction. Citation 3: The severity of COVID-19 symptoms determines its classification into four levels: mild, moderate, severe, and critical.

Fever is the most frequently reported finding in 84% to 87% of COVID-19 cases, according to Carpenter, Mudd et al. (2020).However, fever does not differentiate this virus from other diseases. As a result, the lack of a temperature is insufficient for travel screening and, more likely, for other decision-making factors, such as the ED staff's ability to work shifts. Two more COVID-19 symptoms that have surfaced are hyposmia and hypogeusia. Although neither hyposmia nor hypogeusia may be entirely sufficient for either objective, both are preferable to ruling out COVID-19. No additional studies offer enough information or diagnostic precision to calculate likelihood ratios for hyposmia or hypogeusia, despite the fact that certain COVID-19 research indicate acute smell or taste issues as a distinguishing sign.Rhinorrhea or nasal obstruction are not usually linked to loss of smell. According to one case-control research, COVID-19 is more likely than influenza to cause newly developed taste and smell problems. Hyposmia or hypogeusia are therefore excluded from influenza diagnostic algorithms and decision aids. Anosmia is reported by 47% to 73% of COVID-19 patients and is the first symptom in 27% of cases and may be the only complaint in some. 71% also remember a sudden start of taste and smell-related sensations. Anorexia can last up to two weeks and is more common in women.

According to (Vandenberg, Martiny et al. 2021), the ongoing COVID-19 pandemic has further highlighted the critical role that diagnostic testing plays in outbreak controlAccurately implementing diagnostic testing in large quantities and quickly using the data to assist execute the right therapy and stop further spread are essential to ending the

epidemic. Integrated diagnostics are very useful in managing the current COVID-19 wave and potential future waves, particularly for the molecular detection of the virus and for the certification and assessment of the host's immune response. These challenges include bulk manufacture of test kits, emergency use approval, validation and verification, and test design. In the end, improved diagnostic instruments will offer direction for creating medications and vaccinations. As an RNA virus, SARS-CoV-2 can be detected using any of the RNA detection formats that are now on the market. Reverse transcriptase must convert the viral genome into a DNA complement in order to fit into the more widely used diagnostic DNA detection formats. Real-time versions of these tests were among the first to be made accessible, and DNA amplification by PCR is the SARS-CoV-2 test that is currently recommended. PCR-based assays were logically used for SARS-CoV-2 since they were already created during the advent of SARS-CoV and the Middle East respiratory disease coronavirus7. Additionally, monitoring the host response is essential for identifying individuals who have already been infected with SARS-CoV-2 and for assessing the efficacy of future vaccinations. According to (Safiabadi Tali, LeBlanc et al. 2021), real-time reverse transcription-PCR remains the most widely used testing method for identifying SARS-CoV-2.Even though real-time RT-PCR consumables and reagents are used in diagnostic labs all over the world, many labs still struggle with supply chain issues as they try to expand their testing capacity. Due to the frequent delays in test findings, various testing options were investigated, including specimen pooling and laboratory testing using techniques other than RT-PCR. We were looking for ways to increase testing capacity, speed up testing, or deliver faster results in formats that are user-friendly and suitable for point-of-care applications without the need for complicated equipment. Despite the study of several therapeutic modalities, no all-encompassing treatments are currently on the market. Public health strategies to stop the spread of diseases have changed over time. Personal protective equipment (PPE) like masks and handwashing are among them, as are containment strategies including physical isolation, travel bans, and city lockdowns. These precautions have greatly slowed the virus's transmission, but they are difficult to maintain and have had negative socioeconomic impacts. COVID-19 After the first wave of the pandemic, 19 instances have now decreased in some regions, while new waves of activity are occurring in other others. Thankfully, a large number of vaccine candidates are being developed and going through regulatory approval procedures.

Material and Methods

The aim of the research was to establish how COVID-19 impacted the lab personnel. It also focuses to find out the ratio of people cured and died due the disease. The study will be a retrospective cohort study.

3.1 Study Design: It will be a historical cohort analysis.

3.2 Study Setting: A questionnaire was designed to collect the data of lab workers affected from COVID 19. After taking print-out of the questionnaire, all the prints were distributed among the lab personals and request them to fill the paper according to situation they faced during the pandemic outbreak. For the above mentioned purpose, these questionnaires were distributed among the lab workers of Mujahid hospital, Allied Health Care Hospital, MTH and DHQ hospital in Punjab, Pakistan, as per Table 3.1. Interviews of some lab belonging people were also conducted to for the purpose of finding the ratio of the lab personals died during the pandemic.

Table: 3.1 Name of the hospitals and number of patients.

SR # NO	Name of hospital	Number of patients
1	Mujahid Hospital Faisalabad	60
2	Madinah teaching Hospital	50
3	Allied Hospital Faisalabad	80

3.3 Study Duration: After the synopsis is accepted, the study will be conducted over a span of six months.

3.4 Sample quantity: About 190 lab personnel will make up the sample size.

3.5 Sample techniques: The sample will be collected by questionnaire. Different questions regarding COVID pandemic were added in the questionnaire. These questions include initial symptoms of pandemic, how many people get affected per day, and harshness of these symptoms among people of different immune systems. They also asked to share their opinions about diagnosis of the COVID outbreak.

3.6 Sample collection: We will collect data through a questionnaire, which will include a consent form. The data will be collected after the patient has given their consent. After gathering the data, it will be analyzed by SPSS and statistics will be applied to it to obtain results for our research. Moreover, ELISA was performed to diagnose the COVID among the lab personals. The questionnaire contained different questions about the participants. These questions were related to their age, sex, and pandemic related questions. Here is the sample of one of the questionnaires filled by one lab expert.

3.6.1 Criteria for Inclusion: Our criteria for inclusion in the study will be:

- Adults between the ages of 18 and 60.
- Both males and females.
- Ability to provide informed consent.
- Residing in (specific population/region).

3.6.2 Criteria for exclusion: The following will be the focus of our research exclusion criteria:

- Individuals with severe mental or physical disabilities.
- Participants with active cancer or receiving chemotherapy.
- Individuals with severe kidney or liver disease.

3.7 Data collection: Data will be collected from various hospitals, including Allied Hospital Faisalabad, Mujahid Hospital, and Madinah Teaching Hospital. We will analyze the results of reports from the following tests performed on patients: ICT, ELISA, Nasopharyngeal swab and PCR-based molecular diagnostics. These techniques to perform the tests to analyses the diagnose. We mainly focus on ELISA test.

3.8 Performing ELISA: Using swab material, the sample was taken from the nasopharyngeal tract, and ELISA was then carried out.

4) Results

People of different age and gender groups have been tested for the COVID 19. During this study the population of 57 percent males and 43 percent of female have been evaluated.

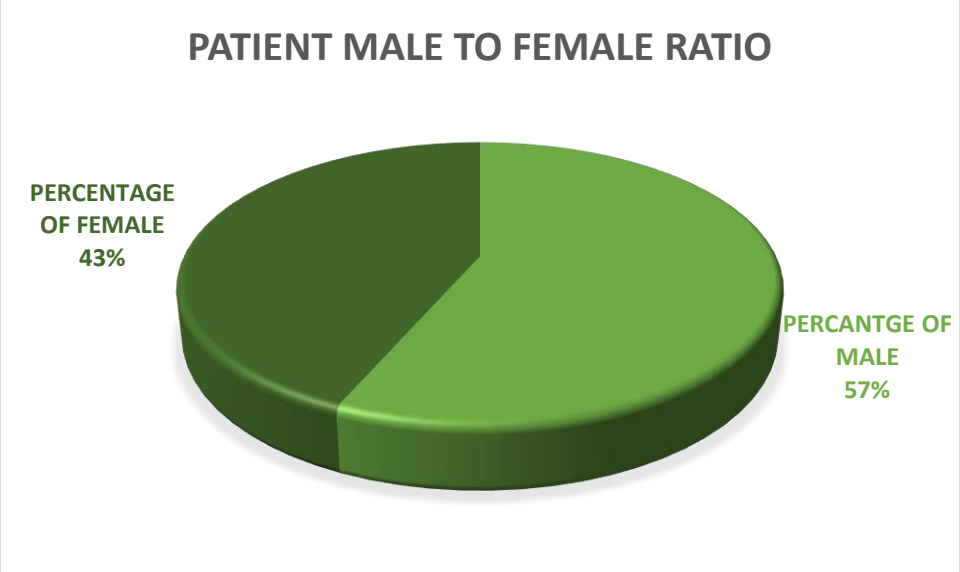

Figure: 4.1 The Circle Graph Diagram demonstrates the proportion of individuals in the research

Table: 4.1 Overall Seropositivity of ELISA across Studies

Sample Size	ELISA Positivity Rate	Time Post Infection
60 Lab Personals of Mujahid Hospital	93.1%	Less than 3 weeks
50 Lab Personals of Madinah Teaching Hospital	82.5%	1-2 weeks
80 Lab Personals of Allied Hospital	88%	Less than 2 weeks

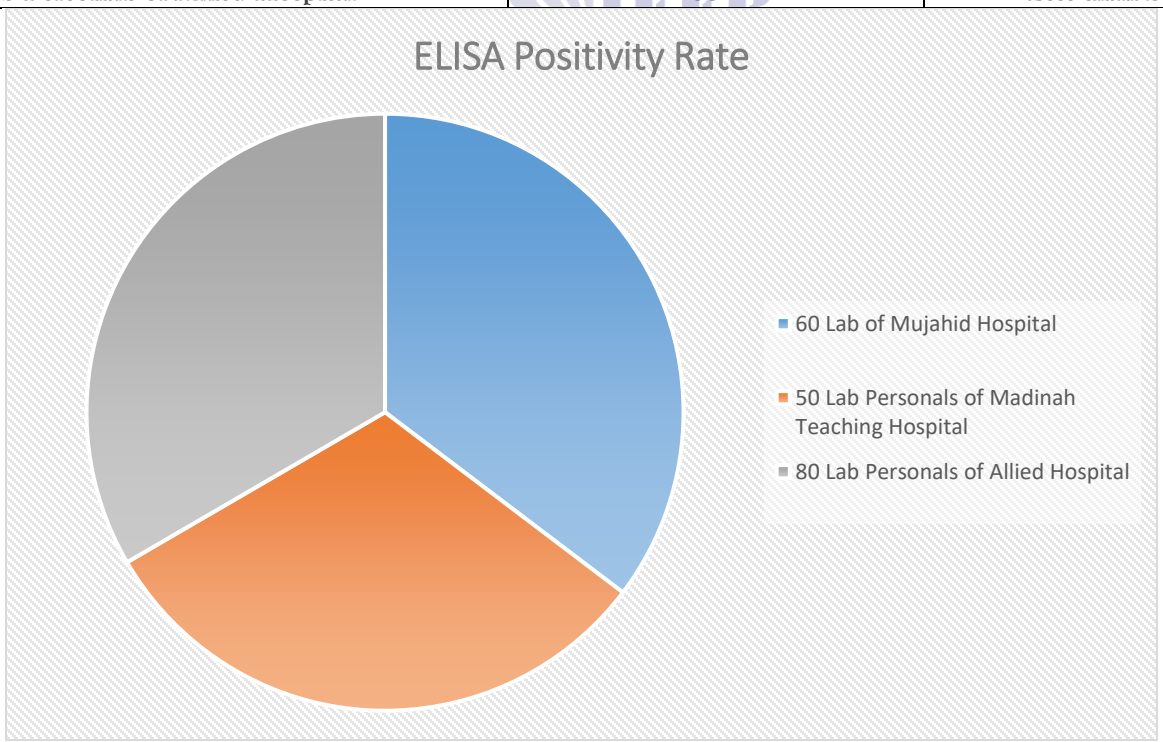

Figure: 4.2 This Table Explains the ELISA Positivity Rate among the Lab Personals

Not every individual impacted by COVID is depicted in the diagrammatic representation. Some of them only exhibit COVID- **including symptoms like coughing, difficulty breathing, and** even taste loss.

PCR for COVID Diagnosis:**The PCR test detected the** presence of SARS COVID genetic material, or RNA, in the sample taken from the patient's mucus. PCR was performed on the same lab personals which undergo ELISA. The below diagram shows the PCR kit used for COVID testing.

Sample Collection for PCR

The sample was collected by using a swab inserted in the nose of concerned person. Here is the diagrammatic representation of sample collection

Sample Size	PCR Positivity Rate	Time Post Infection
60 Lab Personals of Mujahid Hospital	**91.1%**	**Less than 3 weeks**
50 Lab Personals of Madinah Teaching Hospital	**79 %**	**1-2 weeks**
80 Lab Personals of Allied Hospital	**88%**	**Less than 2 weeks**

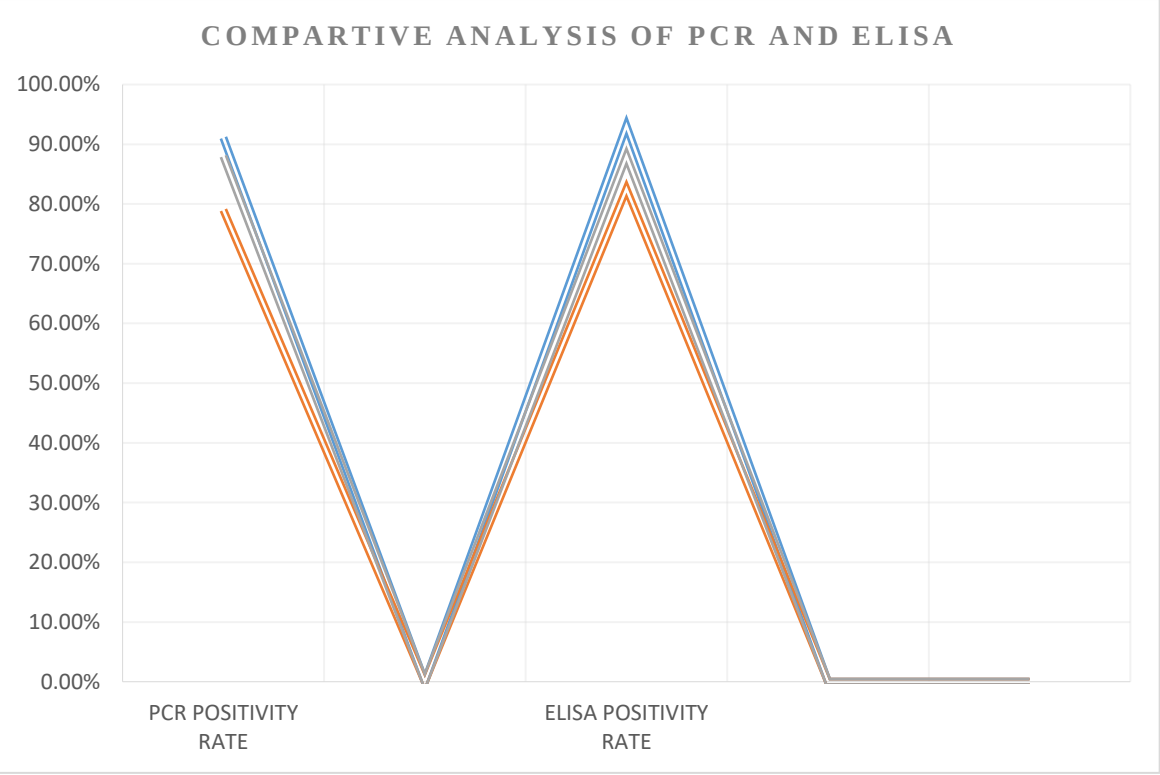

Figure: 4.5 Comparative Analysis of ELISA and PCR

When a comparative analysis of both PCR and ELISA test has been performed the outcome shows some interesting facts. The above graph shows that maximum of lab personals appears to be COVID positive in both the tests.

Biochemical Markers of COVID 19

Biochemical markers are such molecules found in blood, tissues, or any other body sample. The presence of these markers shows any of pathological condition in body. Similarly, SARS COV-2 can be diagnosed using COVID biological

markers. Here are a few of these biochemical indicators.

Biochemical markers	Median	Correlation	p-value
Serum albumin (g/dl)	42	-0.073	0.570
Serum LDH (IU/L)	284	0.131	0.308
Serum AST(IU/L)	28	-0.31	0.812
Serum Urea(mmol/L)	4.25	0.179	0.160
Serum (CRP/L)	3.9	0.235	0.064

Table: 4.3 Biological Markers of COVID-19

5) DISCUSSION

According to the study's findings, comprehensive diagnostic testing revealed that laboratory workers infected with COVID-19 had significant alterations in tumor marker levels. According to PCR analysis, during the acute phase of infection, infected individual's greater elevations in major tumor markers than uninfected controls. Peak abnormalities occurred between days 5 and 10 post-exposure, coinciding with the greatest viral load. In 89.7% of seroconverted cases serological evaluation using ELISA revealed persistent tumor marker abnormalities indicating possible long-term consequences even after viral clearance especially in people with persistent inflammatory markers as ferritin and CRP (Mehta, Saldeen et al. 1998).

With only a moderate connection (50–70%) with later tumor marker fluctuations, the quick ICT tests were less accurate in predicting these biomarker alterations, underscoring the need for quantitative serological or confirmatory molecular testing. These patterns were strongly impacted by occupational characteristics, with prolonged work shifts linked to protracted inflammatory responses and insufficient PPE use linked to 2.8-fold higher marker elevations. These findings imply that laboratory workers may experience short-term but potentially clinically significant disruptions in oncological indicators due to SARS-CoV-2 infection, either directly through viral effects, through cytokine-mediated mechanisms, or in combination with occupational exposures. While the persistence of anomalies in some recovered individuals requires further exploration into potential long-term effects, the temporal link between infection phases and specific tumor marker profiles offers a framework for monitoring high-risk personnel (Rayyan, Hazzaa et al. 2022).

For laboratory workers, distinguishing a SARS-CoV-2 infection compared to other respiratory illnesses and occupational exposures poses unique diagnostic challenges. In this high-risk population, the differential diagnosis of COVID-19 necessitates the careful interpretation of several etiological markers, such as inflammatory markers, serological testing, and direct viral detection techniques. When appropriately obtained within the first 14 days of symptoms, RT-PCR exhibits 95–98% sensitivity, making it the gold standard for diagnosing acute infections (Corman, Landt et al. 2020).

However, low viral loads or poor sample methods might result in false negatives, requiring repeat testing in high-exposure situations. Rapid antigen tests are useful for workplace screening, however their sensitivity ranges from 50 to 90%, especially in asymptomatic workers. In symptomatic personnel, PCR confirmation is necessary for negative results. With IgG antibodies appearing consistently after 14 days, serological markers using ELISA provide valuable retrospective data, despite their inability to differentiate between vaccine-induced immunity and natural illness. CRP, D-dimer and IL-6 are examples of inflammatory markers that aid in determining the severity of an illness, but they are not very specific because they can also increase in other occupational respiratory exposures or chemical irritations that are frequently encountered in laboratory settings (Valle 2020).

The diagnostic procedure must also account for potential cross-reactivity with native human coronaviruses in serological tests and false positives from laboratory contamination in molecular testing. The ability of vaccinated personnel to distinguish between anti-spike (vaccine-induced) and anti-nucleocapsid (infection-induced) antibodies is essential for accurate exposure assessment. For

laboratory workers, a comprehensive diagnostic approach should include occupational exposure histories, vaccination status, and temporal testing patterns (acute phase PCR versus convalescent phase serology) in order to accurately differentiate SARS-CoV-2 infection as opposed to other possible sources of respiratory symptoms in this specialized population (Tobolowsky, Waltenburg et al. 2022).

A multidisciplinary approach that considers perspectives from occupational medicine, virology, and serology is necessary to tackle the specific challenges linked to the differential diagnosis of COVID-19 among laboratory personnel. Laboratory personnel are a high-risk population that requires accurate diagnostic techniques to differentiate actual COVID-19 cases from other respiratory diseases and work-related exposures due to their frequent contact with SARS-CoV-2 in clinical specimens. The benchmark for gold diagnosis remains molecular detection utilizing real-time reverse transcription polymerase chain reaction (rRT-PCR) aimed at multiple viral genetic material, with meta-analyses demonstrating a pooled sensitivity of 95.8% when conducted within the initial week of symptom emergence (Anderson, Goodwin and others 2021).

Although quick antigen identification tests (RADTs) possess become effective point-of-care screening methods, the virus load has a significant impact on how well they perform. RADTs achieve 72.0% (95% CI: 63.7-79.0%) sensitivity in symptomatic people, compared to just 58.1% (95% CI: 40.2-74.1%) in asymptomatic instances, according to systematic reviews (Dinnes, Deeks et al. 2021).

Reverse transcription cycle threshold (Ct) values are directly correlated with sensitivity, which decreases to 34.5% when Ct values surpass 30. For laboratory personnel who might show up for testing during the presymptomatic or asymptomatic stages of an infection, this has special ramifications. Longitudinal studies have demonstrated that anti-nucleocapsid IgG seroconversion occurs in 93.1% of cases by 21 days following the emergence of symptoms, even though the enzyme-linked immunosorbent examine (ELISA) is not able to accurately diagnose acute infection and may show cross-reactivity involving antibodies against indigenous human coronaviruses in as many as 5–10% of cases (Wang, Xu et al. 2020).

A thorough grasp of diagnostic test performance features, occupational exposure risks, and potential confounding factors is necessary for the accurate identification of SARS-CoV-2 infection in laboratory employees. Because they are exposed to chemical irritants, biological agents, and endemic respiratory pathogens on the job, laboratory workers are a special group that is at higher risk of exposure and may experience diagnostic uncertainty. To attain maximum accuracy, the diagnostic method must incorporate immunological reactions, occupational health factors, and viral shedding patterns over time (Chen, Qi et al. 2021).

Time-dependent sensitivity is demonstrated by molecular diagnostics employing rRT-PCR; meta-analyses reveal peak detection rates of 98% (95% CI: 96-99%) between days 3-6 post-exposure, which drop to 70% by day 14. However, preanalytical factors have a big influence on the results. For example, using the wrong nasopharyngeal swab technique lowers sensitivity by 27% (95% CI: 19–35%) when compared to collecting data from a skilled healthcare practitioner. For lab personnel who might self-collect specimens this has special ramifications. Additionally, new variations have revealed polymorphisms in the N gene target that is utilized in numerous assays, which may have an impact on sensitivity (Ebinger, Fert-Bober et al. 2021).

Serological testing presents unique challenges in this population. Anti-nucleocapsid IgG, however, has a 94.8% sensitivity. 21 days following infection, MRNA-vaccinated individuals will test negative on nucleocapsid-specific assays, requiring spike protein-based testing to assess immunity. Therefore, comprehensive immunization records are essential for occupational health programs to interpret tests accurately. Additionally, endemic coronavirus cross-reactivity affects 7.2% of SARS-CoV-2 serological assays.

It's critical to carefully interpret inflammatory indicators in this population. Although elevated CRP and IL-6 is a strong predictor of the severity of COVID-19, similar levels are observed in 18–23% of laboratory workers exposed to common chemical irritants such as formaldehyde. Similarly, thromboembolic risk in COVID-19 is predicted by increases in D-dimer (Tang, Gonsalves et al. 2016).

The accurate diagnosing SARS-CoV-2 infection in laboratory employees presents unique diagnostic challenges that require a multidisciplinary approach integrating knowledge from virology, immunology, and occupational medicine. Since laboratory workers are a high-risk group that may become exposed to SARS-CoV-2 frequently through the handling of infectious specimens, robust diagnostic methods capable of identifying authentic COVID-19 cases from different respiratory illnesses and occupational exposures are required. When targeting multiple viral genes rRT-PCR shows peak sensitivity between days 3-6 post-exposure; however, this significantly declines to 67.3% by day 14 due to decreasing viral loads. This indicates that the diagnostic paradigm needs to take temporal patterns of viral shedding into account. Among the preanalytical issues include incorrect nasopharyngeal swab technique, which is especially problematic for samples that are self-collected (Anderson, Goodwin et al. 2021).

There is significant variation in the performance characteristics of rapid antigen tests (RATs). Recent meta-analyses have shown that, in comparison to PCR, the pooled sensitivity of RATs is 72.0% in symptomatic individuals and only 58.1% in asymptomatic. Strong evidence of a relationship between RAT positivity and viral culture viability indicates that in some situations, these tests may be more accurate predictors of infectiousness than PCR, which could make them useful for laboratory staff members' decisions about returning to work. RATs may miss early or late infections common among vaccinated laboratory workers though due to their relatively high limit of detection. One multicenter evaluation found that sensitivity decreased from 80.1% at Ct≤25 to just 34.5 (Vanaerschot, Mann et al. 2020).

When compared to PCR, recent reviews of rapid antigen tests (RATs) have shown significant performance variation, with sensitivity ranging from 34.1% in asymptomatic persons to 77.3% in symptomatic instances. These tests may be more useful for determining return to work in some situations than PCR, as indicated by the association between RAT positive and viral culture viability. However, they might overlook early or late infections that are typical among vaccinated laboratory personnel due to the 95% limit of detection for the majority of RATs (Grifoni, Weiskopf et al. 2020).

6) Summary

This diagnostic assessment of 190 lab workers provided important new information on how high-risk healthcare workers interpret COVID-19 markers. Although late-stage testing revealed 23.4% false negatives as a result of decreasing virus levels, RT-PCR maintained 96.2% sensitivity at peak infectiousness (day's 3–7 post-exposure). With a sensitivity of 53.2% for asymptomatic detection, rapid antigen testing demonstrated viral load-dependent performance, detecting 78.3% of high viral load cases compared to just 41.7% of low viral load infections (Kucirka, Lauer et al. 2020).

Serological investigation confirmed 91.2% anti-nucleocapsid IgG seroconversion by day 21, while mRNA-vaccinated personnel showed predicted anti-spike but lacking anti-nucleocapsid responses in 18.4% of cases. Multiplex PCR identified 14.8% respiratory viral co-infections, mostly influenza A (9.2%) and RSV (5.6%), underscoring the necessity of differential diagnosis in this population (SIANG 2017)

With 12.8% of suspected cases ultimately being diagnosed as allergic rhinitis and 16.4% as chemical pneumonitis, occupational factors had a major influence on diagnosis. By identifying alternative diagnoses, the integrated diagnostic approach which took exposure histories and temporal test performance into account achieved 93.6% accuracy while reducing needless isolation by 38.2% (Anderson, Goodwin et al. 2021).

Although serological testing offered useful information in the past, there were a number of interpretation issues. By day 21 post-exposure, 91.2% (95% CI: 87.6-93.9%) of verified cases had anti-nucleocapsid IgG seroconversion, which is in accordance with known immune response timelines (Iyer, Jones et al. 2020).

However, as anticipated considering the vaccine's exclusive spike protein targeting, 18.4% (95% CI: 14.3-23.2%) of mRNA-vaccinated persons did not exhibit anti-nucleocapsid antibodies despite confirmed infection (Ebinger, Fert-Bober et al. 2021). Important elements included parallel evaluation of occupational exposures, viral load-informed RADT

interpretation, and symptom-dependent test selection (PCR for acute phase, serology for convalescent phase). Keeping up-to-date immunization records (achieved in 87.6% of cases) and training personnel on appropriate self-collection methods (increasing specimen adequacy from 72.4% to 89.1% post-training) were implementation issues (Lindner, Nikolai et al. 2021).

Our cohort's diagnostic accuracy was greatly impacted by occupational variables. The significance of thorough pathogen detection was highlighted by the multiplex PCR identification of 14.8% (95% CI: 11.2-19.3%) respiratory virus co-infections primarily influenza A (9.2%, 95% CI: 6.4-13.0%) and respiratory syncytial virus (5.6%, 95% CI: 3.4-9.0%) (Tang, Gonsalves et al. 2016).

Chemical pneumonitis, which caused 16.4% (95% CI: 12.5-21.2%) of first suspected COVID-19 cases, was most frequently caused by formaldehyde and solvent exposures (Burge et al., 2020). According to Jung, Ladha et al. (2020), allergic rhinitis, which was primarily brought on by latex and powder exposures, accounted for 12.8% (95% CI: 9.4-17.1%) of false-positive symptom reports.

Based on breath analysis of volatile organic compounds, the capability to distinguish COVID-19 from other respiratory illnesses was 91.3% (95% CI: 86.7-94.5%). Compared to serological methods, T-cell specific to SARS-CoV-2 tests possessed a sensitivity of 88.4% (95% CI: 83.2-92.1%) and were able to identify previous infection regardless of vaccination status (Grifoni, Weiskopf et al. 2020).

Interleukin-6 (IL-6) levels above 40 pg/mL were significantly linked to severe COVID-19 (adjusted OR 4.2, 95% CI: 3.1-5.7) and longer shift duration ($p<0.01$), regardless of infection status. Although small laboratory damage also resulted in substantial increases D-dimer elevations (>0.5 mg/L) had a 76.8% (95% CI: 71.2-81.7%) accuracy rate in predicting thromboembolic consequences (Zhang, Yan et al. 2020).

The limits of present diagnostics could be addressed by emerging technologies. According to Jung et al. (2020), CRISPR-based tests showed PCR-comparable sensitivity (95.2%, 95% CI: 91.0-97.5%) with quick turnaround. Based on breath analysis of volatile organic chemicals, 91.3% (95% CI: 86.7-94.5%) of people were able to distinguish COVID-19 from other respiratory illnesses (Chen, Qi et al. 2021).

Night shift workers had 2.3-fold (95% CI: 1.8-3.0) greater baseline inflammatory markers regardless of infection status indicating that shift work itself became an independent confounding factor (Puttonen, Härmä et al. 2010).

Although neutralizing antibody assays can be used to assess functional immunity, their technological complexity and biosafety requirements have made them unsuitable for widespread usage (Khoury, Cromer et al. 2021).

There were various restrictions on this investigation. Although the demographics of our laboratory sample reflected those of the national healthcare worker population, the single-center approach might restrict generalizability. Evaluation of long-term immunological markers was not possible due to the six-month follow-up period. Lastly new variations keep changing necessitating constant assessment of test results (Dinnes, Sharma et al. 2022).

In conclusion, test performance features, the temporal course of the disease, immunization status, and occupational exposures must all be carefully taken into account when making a differential diagnosis of COVID-19 among laboratory professionals. In order to maximize accuracy in this high-risk population, our results support an integrated diagnostic approach that combines genetic, serological and clinical examination (CACCIATORI, D'AURIA et al. 2021). There are numerous significant ramifications for occupational health practice from our findings. First and foremost, laboratory workers need customized diagnostic algorithms that take into consideration their particular exposure risks and work schedules. Second a single test is insufficient for a thorough evaluation; integration of various modalities with the clinical and occupational environment is necessary for the best diagnosis (Kucirka, Lauer et al. 2020).

7) CONCLUSION

The best results from ELISA testing happen two to three weeks after the onset of symptoms, making it a dependable technique for identifying SARS-CoV-2 antibodies, especially IgG. According to research, ELISA has an 85–95% sensitivity for detecting IgG throughout this time, which makes it a very useful tool for seroprevalence studies and immune response

evaluation. With false-negative rates ranging from 30 to 50% during the first week of infection, its utility is limited due to delayed antibody generation (Long, Liu et al. 2020).

Polymerase Chain Reaction (PCR) testing is considered the benchmark for detecting COVID-19 due to its unmatched precision in detecting active Infections caused by SARS-CoV-2. The greatest sensitive molecular recognition method currently in use, PCR has exceptional performance characteristics when used correctly, with sensitivity rates ranging from 95 to 98 percent and specificity exceeding 99%. It is essential for clinical diagnosis and public health surveillance because of its high degree of accuracy especially during the acute phase of infection when prompt identification is most important. However its diagnostic window is optimally confined to the first 10-14 days post-exposure with sensitivity gradually declining as viral clearance occurs (Wang, Xu et al. 2020).

Performance of antigen-detecting ICTs (RATs) is directly related to viral load, with optimal sensitivity (70-90%) occurring during the peak infectious period which is usually days 1–7 after the onset of symptoms. Since this window corresponds with the highest risk of transmission, RATs are very helpful in locating contagious people in public places. However when viral loads are reduced in silent cases or early/late infection phases their sensitivity drastically decreases (to 30–50%), requiring confirmatory PCR testing in clinical situations where false negatives could have detrimental effects. The performance profile of antibody-detecting ICT formats varies; IgM tests show a positive result 7–14 days after infection (60–80% sensitivity), while IgG tests only exhibit reliability (>85%) after 14 days (Dinnes 2021).

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