

Analysis of anti-body development against COVID-19 among persons who had experienced flu-like symptoms in Pagsanjan, Laguna, Philippines

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Abstract

Several studies around the globe are still in process to prevent the transmission of disease-causing virus known as severe acute respiratory syndrome coronavirus 2 (SARS-Cov 2). It is known that flu and Covid-19 disease show similar symptoms that sometimes misinterpreted if not properly tested. SARS-Cov 2 antibody testing may reveal if the flu symptom experienced by a person could be a Covid-19 infection. The development of antibodies against SARS-CoV-2 could depend on age, gender, occupation and vaccination status. This study was conducted to assess the antibody response of Covid-19 in individuals with flu-like symptoms. The study was conducted between January and March 2022 during flu season. The respondents were 50 individuals who experienced flu-like symptoms in Pagsanjan, Laguna. The researchers utilized the descriptive quantitative method and used purposive sampling technique to gather data through questionnaire and antibody test. All consented volunteers underwent testing of antibodies using a rapid chromatographic immunoassay-based qualitative IgG/IgM kit. The data about age, gender, occupation, vaccination status and experienced symptoms were also collected. Frequency, percentage distribution and Chi-square were statistical treatment used in this study. It was found out that among age, gender, occupation and vaccination status, development of antibody against Covid-19 among persons who experienced flu-like symptoms are significantly dependent on occupation and vaccination status.

Keywords: Covid-19, Flu, SARS-Cov-2, Antibody test, IgG and IgM

1. Introduction

The world was startled by a disease-causing virus that could lead to death due to unknown treatment. This was believed to have started in Wuhan, China, and was rapidly found to be a novel coronavirus in December 2019. Several types of research were done to find out the characteristics of the said disease, which was noticed to spread quickly and led to a pandemic. On the 11th day of February 2020, the International Committee on Taxonomy of Viruses, in communication with the World Health Organization, announced the new virus name as severe acute respiratory syndrome coronavirus 2 (SARS-Cov2). This disease-causing virus was announced by the World Health Organization as a new disease named Covid-19.

It was believed that this disease had the same symptoms as the flu. These symptoms appear 2-14 days after infection with the virus, which includes fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, sore throat, congestion or runny nose, nausea or vomiting, and diarrhea. (CDC, n.d.) While the symptoms of loss of taste and smell are rarely found in persons who have the flu.

Several laboratory tests were developed to diagnose an infected person; these are Real-time Polymerase Chain Reaction (RT-PCR), SARS-CoV-2 Rapid Antigen test, and SARS-CoV-2 Rapid Antibody test. (CDC Diagnostic Tests for COVID-19, n.d.) The SARS-CoV-2 rapid antibody test was originally hoped to be sufficient for physical distancing early in pandemics, particularly in March 2020. (West et al., 2021)

This disease created a global impact that overwhelmed the health care system of every country. The health crisis reached every continent in the world and was declared a pandemic. The number of cases reached

more than four hundred forty-four million worldwide as of March 2022. (Worldometers.info) This created panic in every citizen and provoked a sudden change to the global economy including the Philippines.

The Philippines is one of the many countries in the world that suppressed some of the businesses and overwhelmed the health care society. It reaches more than 3 million Covid-19 cases as of March 2022. This country also experienced the agony and shook its citizens that led to lessened movements and created an impact on its economy. International in and out trips are also restricted due to fear of viral transmission. Domestic and tourist transport requires documents for inbound travel to limit movements and prevent further transmission. The government has made amendments to establish minimum health protocols that must be strictly followed.

For some reason, the Philippines is still experiencing a high number of Covid-19 cases. This means, there are still more people in the country that are infected by the virus. Unfortunately, several cases have not been reported due to the inability to test while experiencing the symptoms. Raising awareness among people in the Philippines who have developed antibodies after experiencing flu-like symptoms was the primary focus of the researchers.

Antibody testing, also known as serology testing, has become a tool to determine the state of the population who have been previously infected by Covid-19 but have not declared active cases due to some reasons. There are different types of human antibodies and these are IgG, IgM, IgA, IgD, and IgE. There are also different principles of antibody tests and they fall into two broad categories, laboratory-based, and point-of-care (POC). Laboratory-based includes enzyme-linked immunosorbent assay (ELISA) and chemiluminescence immunoassay (CLIA); and the point-of-care (POC) tests or RATs or Lateral Flow Immunoassay (LFIA) which includes and colloidal gold immunoassay (CGIA) and fluorescence-labeled immunochromatographic assays (FIA). (Use of Rapid Antibody-Based Test Kits (RATs) for Various Use Cases for COVID-19 Section 1. Background, 2020)

Lateral Flow Immunoassay or Rapid Antibody Test is a qualitative test used in determining the presence of immunoglobulin G and immunoglobulin M. It is also used in the detection of antibodies to SARS-Cov-2. The samples used for this diagnostic tool can be plasma, serum, or whole blood. (Black et al., 2021) The use of this rapid antibody test would allow for greater knowledge and understanding of antibody development and its impact on the general population. Also, data from this research would benefit healthcare providers, patients, and local governments. Furthermore, it could be a tool to analyze the presence of antibodies before Covid-19 immunization or vaccination. A possible positive antibody or serology result helps determine whether a person does not require immunization or the less priority in receiving a vaccination.

1.1. Background of the Study

Several studies around the globe are still in process to prevent the transmission of disease-causing virus known as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). This is a disease that affects the upper respiratory system if left untreated could lead to death. Some researchers find ways how to suppress viral transmission.

Different antibodies are formed in a person's body following viral infection. After people recover from infection with a virus, the immune system retains a memory of it. Antibody tests can detect the presence of these antibodies in serum within days to weeks following acute infection. However, antibody testing should not be used to diagnose acute SARS-Cov-2 infections. This testing is used for health care providers who consider that the people have a possible history of Covid-19 disease.

Many patients with flu-like symptoms have not yet been tested for SARS-Cov-2. Since one of the researchers knows laboratory procedures, the researchers came up with the idea of using a rapid antibody test as a tool to detect the possibility of the patients having been infected with Covid-19 disease. As well, researchers believe that performing rapid antibody testing before vaccination against COVID-19 would be a great help before getting a jab against COVID-19.

1.2. Theoretical Framework

One clone act immediately to combat infection while the other is long-lasting, remaining in the immune system for a long time, which results in immunity to that antigen and this theory are called clonal selection theory. This theory was worked together by Australian immunologist Frank Macfarlane Burnet, with input from David W. Talmage. It is the basic operating principle of the adaptive immune response.

Clonal selection is where only one type of antibody—and one type of B cell—responds to the antigenic determinant. This kind of cell then generates a large number of clones, as many as two thousand copies per second. The first time an antigen enters the body and is swept into the lymph node, the antigenic determinants on its surface bind to the few cells that have complementary receptors. The B-cells produced and released this antibody, which are lymphocytes involved in the immune system and called immunoglobulin. The selected cell is activated, grown, divided, and differentiates into two distinct types of cells known as the memory cell and plasma cell. Each plasma cell secretes antibody molecules; each plasma cell requires large amounts of the endoplasmic reticulum; the secreted antibodies circulate in the blood and lymphatic fluid, contributing to the humoral immune response. Each effector cell lasts only 4-5 days before dying off. In the primary immune response, clonal selection produces effector cells and memory cells that may confer lifelong immunity. During the second exposure to the same antigen, memory cells are activated and trigger a faster and more massive reaction. (Fischer, 1964)

Clonal selection theory plays a major role in this study because it shows the process of developing antibodies once the antigen has entered the body. Seroconversion also known as antibody development is the process by which a patient accumulates antigenic-specific antibodies against an epitope, is the first step towards the development of adaptive immunity against pathogens. While this is not a guarantee of protection against future infections, positive seroconversion is an informative measure of past viral infectivity in the population. (Yadav et al., 2021)

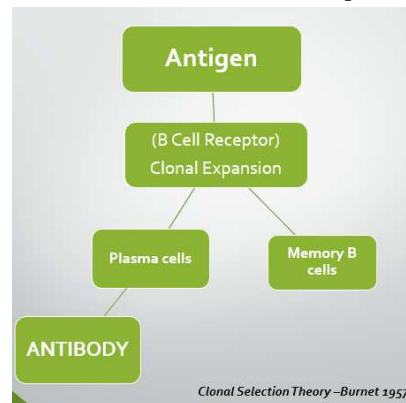


Fig. 1. Clonal selection theory by Macfarlane Burnet

1.3. Conceptual Framework

Through the gathered relevant data and studies, the researcher gave an overview of how the study plan proceeded. For this study, the researchers decided to use the IPO model or the input-output-process model which illustrated in Figure 2. The input box contains relevant data and information's about antibody development. Also, included the information of the respondents, their symptoms, and vaccination status. The is the independent variable or the causes that would trigger the result.

Process approach was utilized to generate the result of the study. In this study, the process included survey and blood test. First, the formulation and validation questionnaires. Then, researchers will seek

permission from the College Administrator of Balian Community College, Local Chief Executive, and Municipal Health Officer of Pagsanjan, Laguna before the distribution of questionnaires and collection of blood samples. When the letters and questionnaires are already approved, the researchers will proceed to distribution and collection questionnaires as well as the collection of blood samples. All the responses and interpreted blood results will be collated. The interpreted results will also be validated by the licensed Medical Technologist and Clinical Pathologist. Collated results and validated blood sample results will be treated statistically using the recommended statistical tool suggested by the statistician. Quantified data will be arranged in tabular form to facilitate analysis and interpretation.

The output box represents the dependent variable which is the result to the study, this was the determined antibody development against Covid-19 among persons who had experienced flu-like symptoms in Pagsanjan, Laguna. The result of the research will be shared with the Local Chief Executive and Municipal Health Officer to help them assess the real number of Covid-19 cases and also a tool to help them to assess the patients before the Covid-19 vaccination.

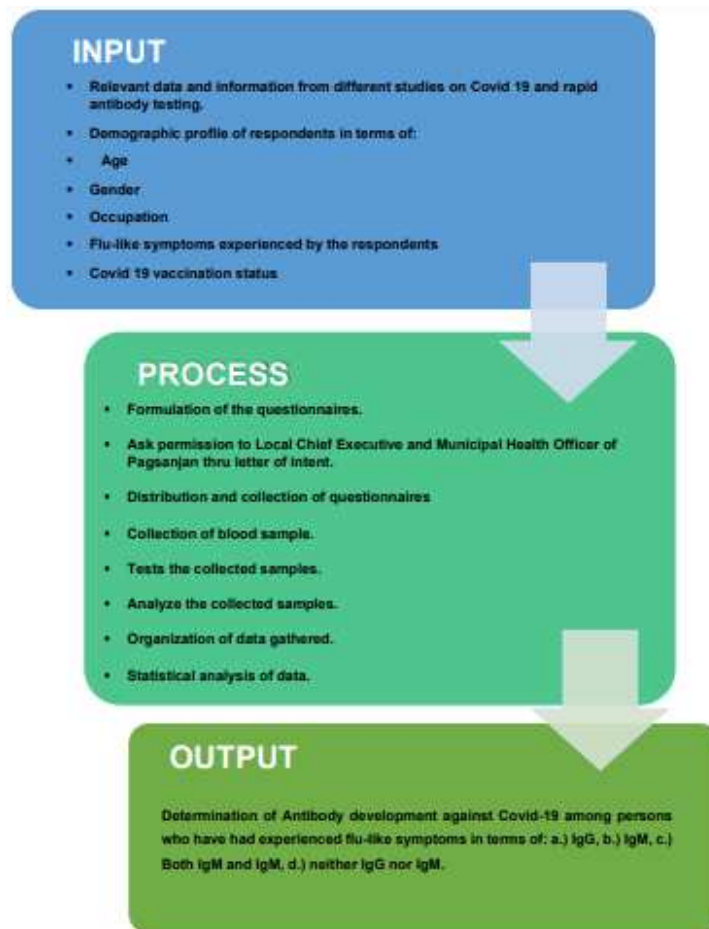


Fig. 2. Research paradigm of the study

1.4. Statement of the Problem

- What is the demographic profile of the respondents in terms of?
 - Age;
 - Gender;
 - Occupation.
- What is/are the flu-like symptoms experienced by the respondents?
- What is the Covid-19 vaccination status of the respondents who had experienced flu-like symptoms?
- What is/are the types of antibody/ies developed among persons who had experienced flu-like symptoms in terms of:
 - IgG;
 - IgM;
 - Both IgG and IgM;
 - Neither IgG nor IgM.
- Does developing antibodies among persons who had experienced flu-like symptoms significantly depend on their demographic profile?
 - Does developing antibodies among persons who have had experienced flu-like symptoms significantly depend on the vaccination status?

1.5. Hypotheses

The hypothesis follows sequential assumptions that offer the closest explanation to a given condition which leaves room for validation through observation. For this study entitled Antibody Development Against Covid-19 Among Persons Who had Experience Flu-like Symptoms. The researchers assumed the following hypothesis:

H_{01} : The developed antibodies among persons who have had experienced flu-like symptoms do not significantly depend on their demographic profile.

H_{02} : The developed antibodies among persons who have had experienced flu-like symptoms do not significantly depend on their Covid-19 vaccination status.

H_{A1} : The developed antibodies among persons who have had experienced flu-like symptoms significantly depend on their demographic profile.

H_{A2} : The developed antibodies among persons who have had experienced flu-like symptoms significantly depend on their Covid-19 vaccination status.

1.6. Significance of the Study

The study was intended to understand the significant dependence of developing antibodies against Covid-19 among persons who had experience flu-like symptoms. Also, to better understand if the flu-like symptoms experienced by the respondents are possibly be Covid-19 infection. The study was beneficial to:

Government – The data from this research will obtain a deep understanding of knowledge and conditions on the possible risk of infection on Covid-19 among persons who had experienced flu-like symptoms. Also, this will help them assess every person before getting a Covid-19 jab.

Medical Institution - Information on this research will help prepare for the potential increase in COVID-19 cases, also in the forecast of possible medical supplies requirements.

Healthcare workers – can also gather reports preliminary conclusions on possible number of undocumented Covid-19 cases, this will help them enhance safety measures against Covid-19 spread.

Community – Some information from this research will provide the awareness that possible flu-like symptoms could be a Covid-19 disease so, they may enhance safety measures on their area.

Future researchers – Data gathered from this study can be used for future studies concerning Covid-19 Antibody development.

1.7. Scope and Limitation of the Study

The study focused on persons who experienced flu-like symptoms for the past 1-3 months. The study is limited to residents of Pagsanjan, Laguna. The scope of the study was limited to 50 respondents who voluntarily participated in the study. Also, 2 box of test kits was used which contains 25 tests per box and abled to maximized the tests for the 50 respondents. This only limited to persons who were not tested for RT-PCR nor antigen test. The experimental test was done at DOH accredited secondary clinical laboratory in Pagsanjan, Laguna, and thru point-of-care testing. This study is limited only to IgG and IgM antibodies and not for the determination of neutralizing antibodies.

1.8. Definition of Terms

Antibody - a protein produced by the body's immune system when it detects harmful substances, called antigens.

Antibody test - a screening for things called antibodies in your blood. Your body makes these when it fights an infection, like COVID-19.

Antigen - a toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies. substance that is capable of stimulating an immune response, specifically activating lymphocytes, which are the body's infection-fighting white blood cells. In general, two main divisions of antigens are recognized: foreign antigens (or heteroantigens) and autoantigens (or self-antigens).

B-lymphocytes- also known as "B cells," a type of white blood cell of the lymphocyte subtype

Convalescent plasma - a way of artificially induced passive immunity by transferring blood plasma from patients who have had a disease to naïve patients

Covid-19 -an acute respiratory illness in humans caused by a coronavirus, capable of producing severe symptoms and in some cases death, especially in older people and those with underlying health conditions

Flu - a contagious respiratory illness caused by influenza viruses that infect the nose, throat, and sometimes the lungs.

Immunity - the ability of an organism to resist a particular infection or toxin by the action of specific antibodies or sensitized white blood cells

Immunochromatography assay - namely lateral flow test, is a simple device intended to detect the presence or absence of the target analyte.

Immunoglobulin G (IgG) - a type of antibody. Representing approximately 75% of serum antibodies in humans, IgG is the most common type of antibody found in blood circulation IgG molecules are created and released by plasma B cells

Immunoglobulin M (IgM) - one of several isotypes of antibodies (also known as immunoglobulin) that are produced by vertebrates. IgM is the largest antibody, and it is the first antibody to appear in the response to initial exposure to an antigen.

Pathogens - referred to as an infectious agent, or simply a germ

Pandemic - is a disease outbreak that spans several countries and affects a large number of people

P.O.C.T - Point-of-care testing is a form of testing in which the analysis is performed where healthcare is provided close to or near the patient

RT-PCR - Reverse Transcription Polymerase Chain Reaction nuclear-derived method for detecting the presence of specific genetic material in any pathogen, including a virus.

SARS-Cov-2 - severe acute respiratory syndrome coronavirus 2; a strain of coronavirus that causes COVID-19

Seroprevalence- the level of a pathogen in a population, as measured in blood serum

Symptomatic - serving as a symptom or sign, especially of something undesirable.

T-lymphocytes - also known as "T cells" a part of the immune system that focuses on specific foreign particles

2. Review of Related Literature

This chapter contains some related and relevant literature and articles which may seemingly be related to the present study. The following research, literature, and studies were reviewed and found to be related to the present study.

This chapter was also considered for the researchers to better understand the present study. Flu, Covid-19 disease, and antibody test theories and studies were included in this chapter. The literature and articles on the topic were presented as follows:

2.1. Covid-19 and Flu Diseases

Earlier in the year 2020, the world was shocked by diseases with similar symptoms like flu. The disease is believed to have started in Wuhan, China, and spread globally. It is found through research and studies that it is a disease-causing virus now known as severe acute respiratory syndrome coronavirus 2 and was named Covid-19 disease. (World Health Organization, n.d.) The coronavirus is a large family of viruses that causes mild to lethal upper-respiratory tract illnesses like a common cold. As of March 2022, the said disease was afflicted more than four hundred million people worldwide and has taken more than six million lives since it was first reported in late December of 2019. (Worldometers.info)

It was noted by World Health Organization that Covid-19 and flu have similar symptoms but from different causative agents. They were thought to spread mainly by respiratory droplets, airborne transmission, and some evidence also suggests spread via fomites. Fomites are anything that has been in contact with a person suffering from an infectious disease and may transmit the infection to others or objects or materials which are likely to carry infection, such as furniture, utensils, and clothes. According to the Centers for Disease and Prevention, Covid-19 and flu have common symptoms like fever or feeling feverish/having chills, cough, shortness of breath or difficulty breathing, fatigue (tiredness), sore throat, runny or stuffy nose, muscle pain, or body aches, headache, vomiting, diarrhea, change in or loss of taste or smell, although this is more frequent with Covid-19. Thus, both diseases can lead to complications and these are pneumonia, respiratory failure, acute respiratory distress syndrome (fluid in the lungs), sepsis (a life-threatening illness caused by the body's extreme response to an infection), for example heart attacks and stroke), multiple-organ failure (respiratory failure, kidney failure, shock), Worsening of chronic medical conditions (involving the lungs, heart, or nervous system or diabetes), inflammation of the heart, brain, or muscle tissues and other secondary infections (bacterial or fungal infections that can occur in people who have already been infected with flu or Covid-19).

However, these diseases have differences not only in their disease-causing agent but also in treatment and medications. Moreover, the viruses that cause Covid-19 are more contagious than flu viruses. It was also observed that Covid-19 spread rapidly and has more likely to occur in superspreading events. (Seasonal Flu, 2022) While flu is an infection caused by influenza virus, COVID-19 is caused by an infection with SARS-CoV-2. COVID-19 spreads more easily than flu and causes serious illnesses in some people. Because COVID-19 and flu have similar symptoms, it may be hard to distinguish between them based on symptoms alone and testing may be needed to help confirm a diagnosis.

2.2. Antibodies and Antibody Test on SARS-CoV-2

According to Dr. Lisa Maragakis, when your body is exposed to an antigen or germ or an infectious agent such as fungus, bacterium, parasite, or virus such as flu-like symptoms, your body can protect you from getting sick and that is how your immunity works.

Antibody tests can detect the presence of these antibodies in serum within days to weeks following acute infection. Antibody tests can identify persons with resolving or past SARS-CoV-2 infection and thereby help scientists and public health experts better understand the epidemiology of SARS-CoV-2. Although the immune correlates of protection are not fully understood, evidence indicates that antibody development following infection likely confers some degree of immunity from subsequent infection for at least 6 months. There different antibodies present in a human body specifically IgA, IgG, IgM, IgD, and IgE. The human body responds to various diseases through antibody development. Covid-19 as the new disease also developed antibody as the response of the body after being infected to the said disease. Infection with the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) initiates a cell-mediated and humoral response, that produces antibodies that interact with the specific antigen binding them, helping to eliminate the pathogen this according to West, R. Also, humans make SARS-CoV-2 specific antibodies, CD4+ T cells, and CD8+ T cells in response to SARS-Cov-2 infection. Studies of acute convalescent Covid-19 patients have observed that T cell responses may be important for control and resolution of primary SARS-Cov-2 infection. (Dan et al., 2021) Covid-19 reported having had experienced many symptoms, ranging from mild to severe illness. After exposure Covid-19, virus symptoms may appear for 2-14 days. The spike (S) and nucleocapsid (N) are the main immunogens amongst SARS-Cov-2 structural proteins. The antibodies against S and N proteins correlated well with neutralizing antibodies. SARS-Cov-2 antibodies have enabled researchers to examine naturally acquired immunity to Covid-19. There were reports published highlighting that a small proportion of Covid-19 cases may not develop antibodies. (Dogan al., 2021)

Antibody testing may be useful to support the diagnosis of COVID-19 illness or complications of COVID-19 in the following situations: 1.) A positive antibody test at least 7 days following acute illness onset in persons who had a previous negative antibody test (e., seroconversion) but did not receive a positive viral test might indicate SARS-CoV-2 infection between the dates of the negative and positive antibody tests. 2.) A positive antibody test can help support a diagnosis when patients present with complications of COVID-19, such as multisystem inflammatory syndrome or other post-acute sequelae of COVID-19. An antibody test detects the presence of antibodies, immunoglobulin G, and immunoglobulin M (IgG, IgM) in blood or serum, revealing if an individual has already been exposed to an infection or not.

Serology testing for coronavirus disease 2019 (COVID-19) is useful to determine whether people were previously infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This capability contrasts with diagnostic tests, which are used to determine if someone is currently infected and presumably capable of infecting others. Diagnostic tests either amplify viral genomic material or detect viral antigens present in a patient sample. Although patients can simultaneously have a positive test result for diagnostic and serologic tests, seropositivity is typically later in the course of the disease. Serology tests also require a blood sample, as opposed to the upper respiratory specimens typically needed for molecular diagnostics. Given rampant problems in diagnostic testing accessibility and the high incidence of asymptomatic infections, not everyone who is infected has the opportunity to be tested before clearing the virus. Antibody tests for SARS-CoV-2 can therefore provide important information about a person's medical history.

The study conducted by Hong Yan Hou, about "Detection of IgG and IgM antibodies in patients with Coronavirus disease 2019" The researcher stated that following a SARS infection, IgM is detectable after 3-6 days and IgG is detectable after 8 days, The researcher analyzed the detection results of specific antibody against SARS-CoV-2 in COVID-19 patients. The average levels of IgM and IgG in patients with the same disease courses from symptom onset until the first detection of antibodies and After SARS-CoV-2 infection, the level of IgM increased gradually during the first week, reached its peak after 2 weeks, and then reduced to near-

background levels in most patients. Meanwhile, IgG was generated after 1 week, reached its peak level in 3 weeks, and was maintained at a high level for an extended period, even over 48 days.

According to the study of Mr. Li, Z “Development of Clinical application of rapid IgM- IgG combined antibody test for SARS-CoV-19. Inspection Diagnosis. 27 February 2020, the researcher analyzed that the detection result was successfully developed a rapid IgG- IgM combined antibody test kit for COVID-19 diagnosis. The specificity and sensitivity of the kit were verified via the lab and clinical practice. This test kit provides a product to meet the urgent need for immunoassay tests in Chinese hospitals for the diagnosis of COVID-19. To make the kit suitable for different stages of the disease, the researcher developed an IgG-IgM combined antibody test for COVID-19 infection. It was also confirmed that the detection sensibility was higher in the IgG-IgM combined antibody test than in the individual IgG or IgM antibody test. Therefore, we more recommend the development of IgG-IgM combined antibody test kits than the separate IgG or IgM antibody test kits if there is a reliable technical system available. This is a better test for screening COVID-19 patients. It takes less than 15 minutes to generate results and determine whether there is a recent SARS-CoV-2 infection.

A suggestion to a study that SARS-CoV-2 viral specific antibody response profiles are distinct indifferent age groups.(Yang et al., 2021) Also, a study from Kopel et al., 2020 suggests that men tend to have a higher risk of severe infection and mortality related to COVID-19. It is believed that elevated estrogen levels in female COVID-19 patients may reduce the severity and mortality of COVID-19 deaths through an elevation in the innate and humoral response. In terms of occupation, a research states that there were no significant association on antibody testing among persons who had tested positive on SARS-CoV-2 antibodies. (Achiron et al., 2021)

According to CDC to an updated article last February 2022, if you think that you might have COVID-19 or if you are sick with COVID- 19, there are several steps that you can follow to help protect other people in your home and community and these steps can also help you in caring for yourself. Stay at home except when you need to get help or seek medical advice from a Physician. Separate yourself or keep your distance from other people. Get tested with COVID- 19, monitor yourself from any symptoms like shortness of breath or feeling of difficulty of breathing, call your Physician before visiting their clinic, wearing a well-fitting mask is a must, cover your mouth and nose when coughing or sneezing, wash your hands and keep your hands clean at all times. Improve your home ventilation. Avoid sharing your items. And countertops and surfaces must be clean at all times. And get vaccinated to boost your immune system against complications whenever you contacted this Covid 19 virus.

Covid-19 and flu were both misdiagnosed due to their similarities. They were both transmissible through droplets, airborne or other suggests spread via fomites. They both develop antibodies that may result to immunity. But somehow, there are antibodies that won't last longer. IgG and IgM are the commonly tests use to detect the presence antibody use for various diseases. It is noted that antibody on Covid-19 may start after 1 week of exposure and last until 8 months. To determine the presence of antibodies, serology test or antibody test is use. Antibody test plays a significant role to distinguish the past infection from Covid-19 and flu. It reveals if the person was infected by Covid-19 or not. Since, this not a mean to diagnose a current infection but it might be helpful to increase the health safety measures to an area. This will help public experts to understand the causes of health outcomes of SARS-Cov-2 to a population. Also, this will help the critical patients who had been infected by Covid-19 through convalescent plasma.

3. Research Methodology

This chapter presents the different methods and procedures that were employed in the determination of the accuracy of the findings in this study.

3.1. Research Design

The study was designed to determine the dependence of Covid-19 antibody development among persons who had experienced flu-like symptoms. Given the nature of the study, the descriptive method of research is the most suitable design to determine the dependence of antibody development such as demographic profile and vaccination status.

Descriptive research aims to obtain information to systematically describe a phenomenon, situation or population. This type of research methodology offers to produce hypotheses based on data collected.

For this study, the quantitative aspect was formed by a survey and antibody test participated by 50 different respondents. The purpose of this technique was to obtain to attain a reliable conclusion that was incorporated the verified data produced from the literature reviewed with results of the survey and antibody analysis.

3.2. Research Locale

The research was conducted in Pagsanjan, which is a 3rd class municipality in the landlocked province of Laguna with a population of more than forty-four thousand as of year 2020 census, which is subdivided into 16 Barangays.

This municipality land area of 27.40 square kilometers or 10.58 square miles, which constitutes 1.42% of Laguna's total area. Pagsanjan is also a well-known tourist spot in the Philippines because of its Pagsanjan Falls. It is also known for its historical infrastructures that attract the tourists to visit the municipality. However, the municipality of Pagsanjan also recorded Covid-19 cases of more than one thousand five hundred cases. The researchers chose this municipality because this is where they are currently living and working. There are also some undocumented Covid-19 cases in this area that have not been declared. This study could help the community, as well as healthcare workers, identify previous COVID-19 cases. Furthermore, assessed patients before receiving a jab on COVID-19.



Fig. 3. The map of Pagsanjan, Laguna

3.3. Subject of the Study

The subjects of the study were 50 persons from different age groups, genders, occupations, and Covid-19 vaccination status. The number of respondents was based on the number of respondents who voluntarily participated in the study.

Moreover, the purposive sampling technique was used in this research, which focused on the particular experiences of a population. This technique was employed since respondents beforehand identified to participate in the research.

3.4. Research Instrument

The researchers decided to conduct a quantitative study to approach subjects of the possibility of Covid-19 antibody development among persons who had experienced flu-like symptoms. The quantitative research performed survey and antibody test to 50 respondents who participated in the study. The respondents were composed of male and female from different age groups, occupation and vaccination who had experienced flu-like symptoms. The study used self-constructed survey questionnaires in a multiple-choice format. The self-constructed questionnaire was composed of four (4) parts. The first part was the demographic profile section which categorized the respondents based on their age, gender and occupation. The second part was composed of ten (10) different symptoms associated with flu and Covid-19 diseases. The experienced symptoms by the respondents were designed in order to understand the possibility of Covid-19 infection. The third part was the vaccination status of the respondents. The last part was the Covid-19 antibody test results that was filled up by the researchers.

The questionnaires were modified and some of it was adapted from different article and online sources.

The expert panels reviewed and validated the questionnaires to ensure its reliability and validity. Attached also is the letter of permission for respondents to answer the questionnaire.

3.5. Research Procedure

• Preliminaries

To gather data, first, seek the permission of the College Dean of Balian Community College to conduct the study. Upon approval, a similar letter will be given to the Head of the Local Government Unit and to the Municipal Health Officer to inform them of the researcher's intention to gather information, collect, and conduct a study on residents of Pagsanjan, Laguna. As soon as permission was approved, the researcher distributed the questionnaires to the respondents, then filled them up.

Filled-up questionnaires were collected then the respondents were started to collect some blood samples through finger-prick method.

The antibody testing was done in a DOH secondary clinical laboratory also thru point-of-care testing in Pagsanjan, Laguna. SARS-Cov-2 antibody test kit with FDA approval and RITM validation will be used in this research.

• Blood Sample Collection

The rapid antibody test for COVID-19 is a serologic test that detects the presence of specific antibodies – IgG which denotes past infection and IgM which denotes current infection. The rapid antibody test used for SARS-CoV-2 is a screening test for COVID-19 infection. The following were used: test cassette, buffer, alcohol pad, disposable dropper, package insert, timer and calibrated micropipette (optional). The test kits are stored between 4-30°C.

• Sample type

- The test can be used to test whole blood (venipuncture blood capillary finger prick blood), serum, or plasma (EDTA, heparin, citrate) specimens.
- Finger prick blood specimens should be collected and tested immediately.

• If the specimen is not tested immediately, it can be stored at 2-8°C for up to 3 days. The serum/plasma may be stored at -20°C for longer storage.

• **Procedure**

The patient is given a survey form to be filled up by the patient. The patient must wear a face mask and must observe health protocols at all times. The researcher will then verify all the information from the patient. After that, the patient may now proceed to the extraction area. The researcher will draw blood from the patient under the supervision of a medical technologist on-duty. The medical technologist on-duty or researcher performed the test.

• **Antibody testing procedure**

The test cassette was removed from the sealed pouch. Held the dropper vertically and transfer 1 drop (approximately 10ul) of specimen into the front of the specimen well (S) made sure that there are no air bubbles. For better precision, transfer specimen by a pipette capable of delivering 10ul of volume. Added 2 drops (approximately 70ul) of buffer immediately into the specimen well (S).

• **Display of results**

A total of three detection lines are on the strip. The control (C) line appears when the sample has flowed through the cartridge. The presence of anti-SARS-CoV-2 IgM and anti-SARS-CoV-2 IgG will be indicated by a red/pink test line in the M and G region. If only the control line (C) showed red, the sample is negative. Either M or G line or both lines turning into red indicates the presence of anti-SARS-CoV-2-IgM or anti-SARS-CoV-2-IgG or both antibodies in the specimen. If the control line does not appear red, the test is invalid, and the test should be repeated with another cartridge. Interpreted the test results in 15 minutes.

• **Documentation**

The results will be validated by the registered medical technologists. The result of the rapid antibody test for COVID-19 is documented in antibody testing research.

Upon completion of all filled out questionnaires and antibody test were done; the gathered data was tallied and statistical analysis was performed.

3.6. Statistical Treatment of Data

To know numbers of persons who developed antibody development after experiencing flu-like symptoms, the researchers grouped the data then used the frequency, percentage, and rank distribution. To test the dependence between the demographic profile and antibody development, and the dependence between the vaccination status and antibody development the researchers used the Chi-square as a statistical treatment.

1. Frequency

$$f = x_1 + x_2 + x_3 + \dots + x_n$$

2. Percentage distribution

$$\% = \frac{f}{N} \times 100$$

Where: % = Percent

f = frequency

N = number of samples

3. Chi-square

$$\chi^2 = \sum \frac{(O-E)^2}{E}$$

Where: o = the frequencies observed

E = the frequencies expected
 Σ = the sum of all entries

4. Presentation, Analysis and Interpretation of Data

This chapter deals with presentation, analysis, and interpretation of the data gathered by the researches through careful examination.

4.1. Demographic Profile of Respondents

Table 1. Frequency and percentage of the respondents' profile

Profile	Frequency	Percentage
Age		
10 and below	12	24%
11 to 20	5	10%
21 to 30	7	14%
31 to 40	9	18%
41 to 50	8	16%
51 and above	9	18%
Total	50	100%
Gender		
Male	14	28%
Female	36	72%
Total	50	100%
Occupation		
Student	13	26%
Unemployed	14	28%
Employed	23	46%
Total	50	100%

The table above shows the age distribution of the 50 respondents who have experienced flu-like symptoms. It can be seen that the age 10 years and below comprise 24 % of the sample respondents of this study (12 out of 50), the 11-20 years old is 10% of the sample respondents (5 out of 50), 21-30 years old is 14% (7 out of 50), 31-40 years old is 18% (9 out of 50), the 41-50 years old is 16% (8 out of 50), and 51 years old and above is 18% (9 out of 50). The highest percentage of the respondents came from the group of 10 years and below (24%), while the lowest percentage came from the group of 11-20 years old (10%). Most respondents who had experienced flu-like symptoms since the day the study was conducted were ages 10 years and below and got the lowest percentage in this study.

The table above also shows the gender distribution of the 50 respondents who have experienced flu-like symptoms. It can be seen that male group comprised 28% of the sample respondents of this study (14 out of 50), while the female group is 72% of the sample respondents (36 out of 50). Also, it can be implied from the frequency and percentage that the female group is higher than the size of the male group.

Lastly, the table shows the occupation distribution of the 50 respondents who have experienced flu-

like symptoms. It can be seen that the student group comprised 26% of the sample respondents of this study (13 out of 50), the unemployed is 28% of the sample respondents (14 out of 50), while employed is 46% (23 out of 50). The highest percentage the respondents came from the employed group (46%), while the lowest percentage came from the student group (26%). Respondents in the employed group reached the highest proportion of those who still go to work and experienced flu-like symptoms.

4.2. Flu-Like Symptoms Experienced by Respondents

Table 2. Frequency and percentage of the respondents based on flu-like symptoms that they have experienced

Symptoms	Frequency	Percentage
Fever	10	10%
Fatigue	7	7%
Cough	24	24%
Nausea/Vomiting	3	3%
Muscle/Body Aches	6	6%
Runny/Congested Nose	30	30%
Sore throat	2	2%
Diarrhea	6	6%
Headache	9	9%
Shortness of Breath	3	3%

The table above shows the frequency of respondents who are experiencing different variety of flu-like symptoms during the conduct of this study. It can be seen that 10 out of 50 respondents are experiencing fever of 10% from the overall symptoms rank as third, 7 are experiencing fatigue that gathered 7% and ranked in the 5th place, 24 are experiencing cough with percentage rate of 24% and ranked in 2nd place, 3 are experiencing nausea/vomiting that got 3% and ranked in 8th, 6 are experiencing muscles/body aches with the percentage rate of 6% and ranked in 6th place, 30 are experiencing runny/congested nose with percentage of 30% and ranked in 1st place, 2 are experiencing sore throat with percentage rate of 2% and ranked in the 10th place, 6 are experiencing diarrhea with percentage rate of 6% and also ranked in the 6th place, 9 are experiencing headache with percentage rate of 9% and ranked in 4th place, while 3 are experiencing shortness of breath with percentage of 3% and ranked in 8th place. Furthermore, it can be seen that the greatest number of cases from the 50 respondents were runny/congested nose (30 out of 50) and got highest in the rank, while the least case is sore throat (2 only) which is lowest in the rank. Runny nose/congested nose is the most dominant symptom during the study was conducted. Sore throat was the most least case since this symptom was not commonly seen to flu diseases.

4.3. Vaccination Status of Respondents

Table 3. Frequency and percentage of the respondents based on their Covid-19 vaccination status

Vaccination Status	Frequency	Percentage
Partially Vaccinated	1	2%
Fully Vaccinated	27	54%

Unvaccinated	22	44%
Total	50	100%

The table above shows the vaccination status distribution of the 50 respondents who have experienced flu-like symptoms. It can be seen that there is only 1 partially vaccinated (2% of the sample respondents), 27 are fully vaccinated (54 of the respondents), while 22 are unvaccinated (44% of the respondents). Majority of the respondents are fully vaccinated, while the partially vaccinated is only 1 (the least percentage, 2%). Most respondents who participated in the study was fully vaccinated the most concerned about the study while there is only 1 respondent who is partially vaccinated for the reason that he/she is the only partially vaccinated who agreed to participate in the study.

4.4. Antibodies Developed among the Respondents

Table 4. Frequency and percentage of the respondents based on the type of developed antibodies

Developed Antibodies	Frequency	Percentage
IgM Positive	3	6%
IgG Positive	32	64%
Both IgG and IgM Positive	9	18%
Both IgG and IgM Negative	6	12%
Total	50	100%

The table above shows the distribution of antibodies developed in the 50 respondents of this study. It can be seen that there are 3 respondents out of 50 (6%) who have developed IgM antibody, 32 (64% of the respondents) developed IgG antibody, 9 (18% of the respondents) developed both IgG and IgM antibodies, while 6 (12% of the respondents) neither developed IgG nor IgM antibodies. Majority of the respondents have developed IgG antibody (64% of the respondents). On the other hand, very few of the respondents have developed IgM antibody (only 6% of the respondents).

4.5. Dependence of Antibodies Developed in Demographic Profile

4.5.1. Dependence of Antibodies Development on Age

Table 5. Chi-Square test result of developed antibodies across age group

	IgM Positive	IgG Positive	Both IgG and IgM Positive	Both IgG and IgM Negative	Chi-square Value	Critical Value	P-value	Decision
10 yrs and below	0	7	1	4				
11 -20 yrs old	0	3	1	1				
21-30 yrs old	0	5	2	0				
31-40 yrs old	0	8	1	0	17.85	24.996	0.27058	
41-50 yrs old	2	4	2	0				

Not
Significant

51 yrs old and above
 alpha = .05

The table above shows the Chi-Square test result of developed antibodies across age group. It can be seen that majority of the respondents in all age groups are likely to develop IgG antibody. For age groups 11-20 years old and 10 years and below, they are unlikely to develop IgM antibody. For age groups 21-30, 31-40 and 51 years old and above, they are unlikely to develop IgM antibody, and at the same unlikely to be negative in IgM and IgG antibodies at the same time. On the other hand, 41-50 years old age group are unlikely to be negative in IgM and IgG antibodies at the same time. Though this is a known fact for the sample respondents for this study, the Chi-Square value (17.85122) being lower than the critical value (24.996) signifies that the development of antibodies does not depend on the age of the person. This is supported by the P-value 0.27058 which is greater than the alpha value (0.05). There is not enough evidence to claim that the development of antibodies significantly depends on the age of the person. This result was the same from other Covid-19 antibody development researches. Furthermore, children had higher antibody binding avidity compared with young adults.

4.5.2. Dependence of Antibodies Development on Gender

Table 6. Chi-Square test result of developed anti-bodies across gender group

	IgM Positive	IgG Positive	Both IgG and IgM Positive	Both IgG and IgM Negative	Chi-square Value	Critical Value	P-value	Decision
Male	0	9	3	2	1.37855	7.81	0.71055	Not Significant
Female	3	23	6	4				

alpha = 0.05

The table above shows the Chi-Square test result of developed antibodies across gender group. It can be seen that majority of the respondents in all gender groups are likely to develop IgG antibody. On the other hand, both the gender group shows unlikeliness of having developed IgM antibody. Though this is a known fact for the sample respondents in this study, the Chi-Square value (1.37855) being lower than the critical value (7.815) signifies that the development of antibodies does not depend on the gender of the person. This is supported by the P-value 0.710559 which is greater than the alpha value (0.05). With 95% level of confidence there is not enough evidence to claim that the development of antibody significantly depends on the gender of the person.

4.5.3. Dependence of Antibodies Development on Occupation

Table 7. Chi-Square test result of developed anti-bodies across occupation group

	IgM Positive	IgG Positive	Both IgG and IgM Positive	Both IgG and IgM Negative	Chi-square Value	Critical Value	P- value	Decision
Student	0	7	2	4	16.81896	12.592	0.01	Significant
Unemployed	3	8	1	2				
Employed	0	17	6	0				
alpha = 0.05								

The table above shows the Chi-Square test result of developed anti-bodies across occupation group. It can be seen that majority of the respondents in all occupation groups are likely to develop IgG antibody. The student group is unlikely to develop IgM antibody. The unemployed group is unlikely to develop IgG and

IgM antibodies at the same time. On the other hand, the employed group is unlikely to develop IgM antibody, and both IgG and IgM antibodies being negative at the same time. This known fact for the sample respondents in this study is established by the Chi-Square value (16.81896003) being higher than the critical value (12.592), signifying that the development of antibodies significantly depends on the occupation of the person. This is supported by the P-value 0.009972 which is lower than the alpha value (0.05). With 95% level of confidence there is enough evidence to claim that the development of antibodies significantly depends on the occupation of the person.

4.6. Dependence of Antibodies Development on Vaccination Status

Table 8. Chi-Square test result of developed anti-bodies across vaccination status group

	IgM Positive	IgG Positive	Both IgG and IgM Positive	Both IgG and IgM Negative	Chi- square Value	Critical Value	P-value	Decision
Partially Vaccinated	0	1	0	0	14.32029	12.592	0.026259	Significant
Fully Vaccinated	0	21	6	0				
Unvaccinated	3	10	3	6				
alpha = 0.05								

The table above shows the Chi-Square test result of developed antibodies across vaccination status group. It can be seen that majority of the respondents in all vaccination status groups are likely to develop IgG antibody. The partially vaccinated group is unlikely to develop IgM antibody, unlikely to be both positive IgG and IgM antibodies at the same time, and also unlikely to be both negative in IgG and IgM antibodies at the same time. The fully vaccinated group is unlikely to develop IgM antibody, and also unlikely to be both negative in IgG and IgM antibodies at the same time. On the other hand, the unvaccinated group is unlikely to develop IgM antibody, and also unlikely to be positive in IgG and IgM antibodies at the same time. This

known fact for the sample respondents in this study is established by the Chi-Square value (14.32029) being higher than the critical value (12.592), signifying that the development of antibodies significantly depends on the vaccination status of the person. This is supported by the P-value 0.026259 which is lower than the alpha value (0.05). With 95% level of confidence, there is enough evidence to claim that the development of antibodies significantly depends on the vaccination status of the person. Meanwhile, CDC cited antibody testing is not recommended to assess the immunity to SARS-Cov-2 following Covid-19 vaccination. This means those respondents who experienced flu-like symptoms regardless of vaccination status can be infected with Covid-19. This also shows that there were undocumented respondents who have been previously infected and recovered from Covid-19 disease.

4.7. Summary of Dependence of Antibodies to Various Demographic Profile

Table 9. Summary of Chi-Square test result of developed antibodies across different factors

	Chi-square Value	Critical Value	P-value	Decision
Age	17.85122	24.996	0.27058	Not Significant
Gender	1.378555	7.815	0.710559	Not Significant
Occupation	16.81896	12.592	0.009972	Significant
Vaccination Status	14.32029	12.592	0.026259	Significant

The table above shows the summary of Chi-Square test result of developed antibodies across various demographic profile. It can be seen that majority of the respondents in all age group are likely to develop IgG antibody. Among age, gender, occupation and vaccination status, development of antibody is significantly dependent only on occupation and vaccination status. With 95% level of confidence, there is enough evidence to claim that the development of antibodies significantly depends on the occupation and vaccination status of the person.

5. Summary of Findings, Conclusion and Recommendation

This chapter focuses on the summary, findings, conclusion and recommendation based on the results obtained from the research study on “Analysis of antibody development against Covid-19 among persons who had experienced flu-like symptoms in Pagsanjan, Laguna.”

5.1. Summary of Findings

The researchers attained the following results. The study on “Analysis of antibody development against Covid-19 among persons who had experienced flu-like symptoms in Pagsanjan, Laguna” aimed to provide data on Covid-19 antibody development in residents of Pagsanjan, Laguna. The researchers used descriptive quantitative research methodology and antibody tests to gather information from the respondents who voluntarily participated in the study.

The salient findings of the study are enumerated as follows:

- Based on the gathered data in regards with the demographic profile, 12 out of 50 respondents (24%) of the respondents and rank the highest on the age distribution were ages 10 years and below whom experienced mild flu-like symptoms. Most of them were toddlers and categorized as unemployed. On gender distribution, most respondents were female who rank the highest (72%) and had 36 respondents out of 50 who voluntarily participated in the study. Based also on the gathered data, the occupation distribution had 23 respondents from employed group out of 50 who participated in the study. The employed group got the highest and rank and 46% rate. These respondents had the highest possibility to be infected from their work.

- The most dominant symptom based on the gathered data was runny/congested nose that got the highest rank and percentage among symptoms experienced by the respondents. It can be seen on the data that this symptom was the most present during the study was conducted for the reason that it was flu season.
- The respondents who participated in the study were mostly fully vaccinated and had experienced flu-like symptoms. They are the most concerned about the study which got the 54% rate and highest rank with participants of 27 out of 50.
- Most of respondents who experienced flu-like symptoms based on gathered data had developed antibody against Covid-19. Both IgG and IgM antibody were present from all ages based on data from different gender and occupation. For some reasons, IgG got the highest rate of 64% which means that most of the respondents who experienced flu-like symptoms were previously infected to Covid-19.
- Among the demographic occupation is the only significant to antibody development which is the same with the other reviewed researches. Persons who were employed were like to developed antibody against Covid-19 due to different interactions outside their home. Employed group were the most vulnerable to get infected to Covid-19. Age and gender were not significant dependent on antibody development against Covid-19 that was also similar to other researches that was obtained.
- The same to other researches, vaccination status plays important role on antibody development against Covid-19. Vaccination status appeared to be significantly dependent on antibody development against Covid-19. This means that whatever vaccination status, persons who had experienced flu-like symptoms have the possibility to be previously infected to Covid-19.

5.2. Conclusions

Based on the salient findings of the study, the following conclusions were drawn:

The covid-19 disease had a tremendous impact on health care society not only in the Philippines and also globally. The spread of Covid-19 disease is still indistinct due to unreported and undocumented cases. The findings of this research are that majority of the respondents in all age groups are likely to develop IgG antibodies. Among age, gender, occupation, and vaccination status, the development of antibodies is significantly dependent only on occupation and vaccination status. With a 95% level of confidence, there is enough evidence to claim that the development of antibodies significantly depends on the occupation and vaccination status of the person.

5.3. Recommendations

In the light of the findings and conclusions, the following are offered as recommendations for possible actions:

To the medical institution and healthcare workers, we suggest to undergo antibody tests before getting Covid-19 jabs for the reason that there are several cases where those who experienced flu-like symptoms had developed antibodies against Covid-19. This means that the flu-like symptoms experienced by a person might be a Covid-19 disease. Also, quantitative and qualitative antibody tests could assist health workers in guiding rational vaccine choices. Furthermore, the Covid-19 antibody test may help to determine the length of immunity in a person's body after experiencing symptoms.

To future researchers, we suggest expanding the scope of the study and increasing the number of respondents to participate in the study. The period between the occurrence of the symptoms and the antibody test must take note during the study. We also suggest that future researchers who will use this study are encouraged to use a different method other than rapid test kits to determine the antibody development of the respondents. The neutralizing antibody test can also be used to further assess the antibody development quantitatively.

Lastly, local government unit, we suggest to enhance the safety measures to prevent wide spread of Covid-19 disease. Also, antibody test could also help identify Covid-19 cases were not documented due to

various reasons. This is also a path to further assessed if there is possible local transmission in a community so they may enhance safety measures in their respective areas.

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References

- Black, M. A., Shen, G., Feng, X., Garcia Beltran, W. F., Feng, Y., Vasudevaraja, V., Allison, D., Lin, L. H., Gindin, T., Astudillo, M., Yang, D., Murali, M., Iafate, A. J., Jour, G., Cotzia, P., & Snuderl, M. (2021). Analytical performance of lateral flow immunoassay for SARS-CoV-2 exposure screening on venous and capillary blood samples. *Journal of Immunological Methods*, 489. <https://doi.org/10.1016/j.jim.2020.112909>
- Burnet, F. M.: A modification of Jerne's theory of antibody production, using the concept of clonal selection. *Aust. J. Sci.*, 1957-1958, 20, 67-69. 61.
- Burnet, F. M.: Theories of immunity, *Perspect. Biol. Med.*, 1960, 3, 447-458.
- Burnet, F. M.: Immunity as an aspect of general biology. In: *Mechanisms of Antibody Formation*, New York, Academic Press, 1960, pp. 15-24.
- Burnet, F. M.: The mechanism of immunity. *Sci. Amer.* 1961, 204, 58-67.
- Dan, Jennifer M. et., al Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection PMID: 33408181 PMID: [PMC7919858](https://pubmed.ncbi.nlm.nih.gov/33408181/) DOI: [10.1126/science.abf4063](https://doi.org/10.1126/science.abf4063)
- Demey B., Daher N., François C., Lanoix J.P., Duverlie G., Castelain S., Brochet E. Dynamic profile for the detection of anti-SARS-CoV-2 antibodies using four immunochromatographic assays. *J Infect.* 2020 doi: 10.1016/j.jinf.2020.04.033. May 7. pii: S0163-4453(20)30244-9.
- Dogan, M., Kozhaya, L., Placek, L., Gunter, C., Yigit, M., Hardy, R., Plassmeyer, M., Coatney, P., Lillard, K., Bukhari, Z., Kleinberg, M., Hayes, C., Arditi, M., Klapper, E., Merin, N., Liang, B. T. T., Gupta, R., Alpan, O., & Unutmaz, D. (2021). SARS-CoV-2 specific antibody and neutralization assays reveal the wide range of the humoral immune response to virus. *Communications Biology*, 4(1). <https://doi.org/10.1038/s42003-021-01649-6>
- Döhla M., Boesecke C., Schulte B., Diegmann C., Sib E., Richter E., Eschbach-Bludau M., Aldabbagh S., Marx B., Eis-Hübinger A.M., Schmuthausen R.M., Streeck H. Rapid point-of-care testing for SARS-CoV-2 in a community screening setting shows low sensitivity. *Public Health.* 2020;182:170–172.
- Du Z., Zhu F., Guo F., Yang B., Wang T. Detection of antibodies against SARS-CoV-2 in patients with COVID-19. *J. Med. Virol.* 2020 doi: 10.1002/jmv.25820. Apr.
- Humphrey, John H.: Immune system London, 1976–81. | Description, Function, & Facts | Britannica - immune system Physiology - | Professor of Immunology, Royal Postgraduate Medical School, University of Coeditor of *Advances in Immunology*.
- La Marca Antonio, Martina Capuzzo, Tiziana Paglia, Laura Roli, Tommaso Trenti, Scott M. Nelson. [Testing for SARS-CoV-2 \(COVID-19\): a systematic review and clinical guide to molecular and serological in-vitro diagnostic assays](#) *Reprod Biomed Online.* 2020 Sep; 41(3): 483–499. Published online 2020 Jun 14. doi: 10.1016/j.rbmo.2020.06.001
- Lederberg, Joshua: Genes and antibodies. *Science*, 1959, 129, 1649-1653.
- Lee Y.L., Liao C.H., Liu P.Y., Cheng C.Y., Chung M.Y., Liu C.E., Chang S.Y., Hsueh P.R. Dynamics of anti-SARS-Cov-2 IgM and IgG antibodies among COVID-19 patients. *J. Infect.* 2020 Apr 23 pii: S0163-4453(20)30230-9. doi: 10.1016/j.jinf.2020.04.019.

- Mary Louise Turgeon EdD., Immunology and Serology in Laboratory Medicine Fifth Edition
- Paradiso A.V., De Summa S., Loconsole D., Procacci V., Sallustio A., Centrone F., Silvestris N., Cafagna V., De Palma G., Tufaro A., Garrisi V., Chironna M. Clinical meanings of rapid serological assay in patients tested for SARS-Co2 RT-PCR. medRxiv. 2020 doi: 10.1101/2020.04.03.20052183. 04.03.20052183;
- Q. Lei, et al. Antibody dynamics to SARS-CoV-2 in asymptomatic COVID-19 infections medRxiv (2020) Published online August 4, 2020.
- Q.-X. Long, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections Nat. Med., 26 (2020), pp. 1200-1204
- Ravi, A. B., Singh, V., Chandran, R., Venugopal, K., Haridas, K., & Kavitha, R. (2021). COVID-19 Antibody Tests: An Overview. Journal of pharmacy & bioallied sciences, 13(Suppl 1), S48–S51.
- Talmage, D. W.: Immunological specificity. Unique combinations of selected natural globulins provide an alternative to the classical concept. Science, 1959, 129, 1643-1648
- West, R. et al: COVID-19 Antibody Tests: A Valuable Public Health Tool with Limited Relevance to Individuals Trends in Microbiology, Volume 29, Issue 3, 2021, Pages 214-223, ISSN 0966-842X
- Yale J Biol Med. Theories of Antibody Formation: A Review 1964 Aug; 37(1): 1–30.PMCID: PMC2604596 PMID: 14197608.
- Y. Chen, et al. A comprehensive, longitudinal analysis of humoral responses specific to four recombinant antigens of SARS-CoV-2 in severe and non-severe COVID-19 patients PLoS Pathog., 16 (2020), Article e1008796
- Yadav, A. K., Ghosh, S., Kotwal, A., Kaushik, S. K., Bobdey, S., Sahu, R., Kapoor, S., Faujdar, D. S., Teli, P. T., & Anand, V. (2021). Seroconversion among COVID-19 patients admitted in a dedicated COVID hospital: A longitudinal prospective study of 1000 patients. Medical Journal Armed Forces India, 77, S379–S384. <https://doi.org/10.1016/j.mjafi.2021.06.007>
- Yang, H. S., Costa, V., Racine-Brzostek, S. E., Acker, K. P., Yee, J., Chen, Z., Karbaschi, M., Zuk, R., Rand, S., Sukhu, A., Klasse, P. J., Cushing, M. M., Chadburn, A., & Zhao, Z. (2021). Association of Age with SARS-CoV-2 Antibody Response. JAMA Network Open, 4(3). <https://doi.org/10.1001/jamanetworkopen.2021.4302>