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Fatigue Symptom and Oximetry Sign in a Patient with a Positive Covid-19 Antigen Test for Sars-Cov-2

Síntoma Fatiga y Signo Oximetría en paciente con prueba de Antígeno Covid-19 positivo para Sars-Cov-2

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Abstract

The present study was carried out with a total of 1747 patients, out of which 418 tested positive with the Covid-19 antigen test. This test is the one used by the Ministry of Public Health of Guatemala. The study was carried out in Quetzaltenango, Guatemala, from the months of June of the year 2020 to August of the year 2021.

It is confirmed that mild to moderate fatigue is a frequent symptom. The oximetry sign, according to the frequency presented by the patients is less than or equal to 94 SpO₂, the range of patients between 90 to 94 and 95 to 98 SPO₂ is significant, in patients with a positive Covid-19 antigen test.

Symptoms and signs of temperature, malaise, muscle or joint pain, headache, cough, loss of taste, loss of smell, nasal congestion, vomiting or diarrhea, shortness of breath, wheezing, and pain when breathing obtained varied data. The male sex obtained a majority compared to female sex, the average age was 42 years.

The most common diseases were: diabetes, heart disease, and hypertension. The frequency obtained from co-workers and household relatives was five people. The most frequent occupations were: merchants, domestic employees, students, and housewives, among others.

It is suggested that the symptom of fatigue and the oximetry sign be included in the epidemiological form so that it serves as support for the treating physician to decide where the patient will carry out his convalescence.

Keywords: Epidemiological form, Oximetry Sign, Fatigue Symptom, Covid-19 Antigen Test, Convalescence.

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Introduction

Aguilar (2021) states that COVID-19 is a respiratory illness of recent emergence caused by coronavirus 2, of severe acute respiratory syndrome (SARS-coV-2), which recently became a pandemic (Jean et al., 2020).

The majority of patients with COVID-19 present mild or moderate symptoms, approximately 15% progress to severe pneumonia and 5% eventually develop the syndrome of Disseminated intravascular coagulation (Gao 2020).

In his study, Hafeez et al., (2020) explains that the most frequent signs and symptoms of COVID-19 are mild to moderate fatigue and breathing difficulty, which can be measured by oximetry according to a study (Manning et al., 2021).

The studies of Hafeez et al., (2020); Raveendran (2021); Halpin et al., (2021) state that out of 147 patients with Covid -19, 53% presented fatigue as a general symptom, 43% difficulty breathing, and 27% joint pain.

The objective of this study is to determine if Correlation exists between oximetry and fatigue level in the patient with a positive COVID-19 antigen test and to associate the main signs and symptoms that are present in the illness which are annotated in the epidemiological form of required use before carrying out the test.

The importance of this study is to evaluate if the symptomatology and most frequent signs that the patient presents in his epidemiological form at the moment of carrying out the antigen test for COVID-19 with positive swab results between June of the year 2020 to August of 2021 carried out at Aguilar Clinical Laboratory and Blood Bank located in the metropolitan area of Quetzaltenango are low oximetry and fatigue according to the described studies. (Arana et al., 2020; Tang & Kang 2020).

Coronavirus (CoV) is a large family of Positive-sense single-stranded RNA viruses belonging to the Nidovirales order. The order includes the families: Roniviridae, Arteriviridae and Coronaviridae. The Coronaviridae family is subdivided into the Torovirinae and Coronavirinae sub families. Coronavirinae is subclassified also

into COV alfa, beta, gamma, delta and currently omicron (Cobar & Cobar, 2022). The classification of these subtypes of viruses is explained by phylogenetic clustering. Its RNA genome varies from 26 to 32 kilobases in length. They are isolated from different animal species, these include: birds, livestock, and mammals like camels, bats, masked palm civets, mice, dogs and cats. The extensive distribution and infectivity of COV make it an important pathogen. (Hassan et al., 2020).

Human pathogenic subtypes of CoV present symptomatically or asymptotically. The coronavirus related to the acute respiratory syndrome (SARS-CoV), the 2020 outbreak, presented as pneumonia of unknown origin in Wuhan, China. Deep sequencing studies and laboratory investigations have identified the offender as a new strain of COV, this virus was named 2019-nCoV. However, the International Committee on Taxonomy of Viruses named the virus SARS-CoV-2 (Hassan et al., 2020; Salian et al., 2021).

In his article, Chauhan et al., (2021) details that the importance of miARNs is that they can regulate the pathogenesis of Covid-19 and can target the viral gene and inhibit its post-transcriptional expressions. The miARN cc (modified to 25-57 nucleotides) with strongest binding to the Sars-Cov-2 viral genome are: ID02510.3p-miARN, ID00448.3p-miARN, miARN 3154, miARN 7114-5p, miARN 5197-3p, ID02750.3p-miARN and ID01851.5p. These were identified using izMiR prediction software and PANTHER, classification systems based on bioinformatics. According to this study these are the possible viral miRNA and of mature host cell candidates that could play a significant role in the SARS-CoV-2 infection. Such miARN can be studied and administered successfully and safely so they can carry out their therapeutic effects though nanovaccines for prevention of Sars-Cov-2, and also for convalescence because in these moments a definitive treatment is lacking (Sevgin y Sevgin 2021).

The emergence of new Sar-CoV-2 variants is a big challenge due to the monitoring of the virus's

genetic mutations. Strains N501Y, S477N, 452R y E484K have emerged with greater affinity and therefore more infectivity. Different opinions exist regarding these mutations, not in terms of their infectivity, but rather that the neutralizing antibodies that are no longer produced are not significant enough to affect those acquired by currently established vaccines. Therefore it is important to monitor these mutations to maintain control of its infectivity (Islam; Liu; Mascola et al., 2021).

The pandemic caused by Sars-CoV-2 called COVID-19 is a significant problem for health and economy. Worldwide, a great amount of data has been generated since its appearance in December 2,019. It is important to keep it up to date to be capable of objectively preventing and managing the illness (Aguilar 2021; Cevik & Ho; Milovanovic et al., 2020).

Currently, there is no established treatment for the infection from Covid-19. The majority of drugs attempt to stop the infection through protein S, that binds to the angiotensin 2 (ACE2) enzyme (Cobar & Vargas; Galdamez; Gheblawi & Mishra et al., 2020; Bagshaw & Rewa, 2021).

Viral transmission is becoming more frequent every day, therefore it should be kept under control to understand which its possible infectious routes are and hence, the way in which it commonly presents in infected patients. It infects the lung's type I and type II alveolar epithelial cells, as well as alveolar macrophages. These are the primary producers of inflammatory cytokines characterized by a symptomatic or asymptomatic incubation stage that generally takes between 5 and 11 days. This stage is characterized with dry cough, headache, fever, difficulty breathing, fatigue, diarrhea and/or loss of taste or smell (Del Toro-Arreola et al., 2020; Ji et al., 2021).

Among degenerative diseases Baig (2020) mentions that the ones that create the most complications for patients are hypertension by 27% and diabetes mellitus by 26%, of a total of 82 observed patients. Therefore it is necessary to carry out more studies (AlJishi et., al 2021).

The entry of the coronaviruses is produced when its spike protein (S) binds with a specific cellular receptor called angiotensin converting enzyme 2

(ACE2), after which a transmembrane serine protease 2 (TMPRSS2) facilitates the entrance to the reached cell (Briones et al., 2020). The infected cell is multisystemic, therefore Covid-19 can be analyzed as an endothelial disease (Cugno et al., 2021; Morales 2021).

The signs and symptoms are varied; they range from a pulmonary process (Cruz 2020), mild asymptomatic or symptomatic to critical illness and death (Esakandari & Pascarella et al., 2020).

COVID-19 is an endothelial illness. As such, we can understand its pathophysiology and obtain its most frequent signs and symptoms involved in the infectious process (Libby & Lüscher y Aguilar & Cáceres 2020). The most frequent signs and symptoms are general fatigue, loss of taste, loss of smell, fever, dry cough, throat pain, difficulty breathing, and general malaise. In a study of 147 patients 53% presented with general fatigue as a symptom, 43% with difficult breathing and 27% with joint pain (Hafeez et al., 2020; Halpin et., Manning et al., y Raveendran 2021). Among the most frequent age ranges are patients between 18-40 who present with the previously described symptoms. Patients older than 60 years present with severe respiratory problems. Children are less frequently infected. (Logue; Stavem; Pérez et al., 2021; Rosales et al., 2020)

In his systematic review Tandon et al., (2021) mentions that his study involves 113 patients, details that 57 are men, 29 are women and 27 do not describe sex, characterizing in said study that the percentage of men is always greater than the one for women (Penna et., al 2020). This may be due to the amount of expression of angiotensin II which is higher in males than in females, therefore it is important to carry out more studies to confirm these percentages between both sexes to understand its pathogenesis (Rosales et al., 2020)

The diagnosis at the Guatemalan level according to Mazariegos et al., (2020) states that to confirm positive cases a test algorithm can be used in which a positive antigen patient is considered a confirmed case. However, in the case of negative patients, the result should be confirmed through molecular biology PCR.

Methodology.

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The patient with a medical or personal request to perform the Covid-19 antigen test was attended to. The epidemiological form authorized by the Ministry of Public Health and Social Assistance was filled out with their respective identification. The patient was placed in a private place and the declaration of conformity of the Covid-19 antigen test was read to him. A National Ethics committee evaluated all aspects involved in this investigation study before it was accepted (resolution PROZU-578-21). The use of informed consent was exempted and confidentiality of the information obtained from the patient's epidemiological forms was guaranteed. Before performing the test the oximetry measurement of the right finger was taken, each patient was asked verbally about their fatigue level which was classified as follows: Mild (1), Moderate (2) and Severe (3). Such classification was taken from a previous study for its analysis, tabulation and association with oximetry (Halpin et., al 2021). The swab was taken, for patients with positive Covid-19 antigen test, data from their epidemiological form was collected, and the fatigue sign and oximetry symptom were added. The negative patients' data

was tabulated to obtain the Odds Ratio of fatigue symptom. The obtained results were reported to the Ministry of Health's database for their respective follow-up in the Epiweb y Sicovid platform. Photocopies of the epidemiological forms were also taken and were delivered daily to the Metropolitan health area of Quetzaltenango for their respective follow-up as per instructions from the Ministry of Public Health and Social Assistance.

Results

A total of 1747 swabs were taken out of which 418 patients tested positive, there was a correlation of the quantitative variables of the epidemiological data obtained from each patient's forms through the chi-squared test (p: 0.00), for the variable of age, fever, work and household members and also for oximetry and fatigue.

The sign of mild to moderate fatigue is a frequent symptom in the patient with positive Covid-19 test (table 1) and the oximetry sign, according to the frequency presented by the patients, was less than or equal to 94 SpO2. (Figure 1)

Table 1 Chi-square test for the Variables: age, fever, work and household members as well as oximetry and fatigue.

Test Statistics						
	Age	Fever	Work Members	Household Members	Oximetry	Fatigue
Chi-squared gl	196.019 ^a	583.301 ^b	314.172 ^c	246.153 ^d	182.545 ^e	301.713 ^f
Sig.	81	36	11	7	8	3
Asymptotic	.000	.000	.000	.000	.000	.000

Source: experimental data, ^aAge: Cells (0.0%) have expected frequencies less than 5. The minimum frequency of the expected cell is 5.1, ^b Fever: Boxes (0.0%) had expected frequencies less than 5. The minimum frequency of the expected cell is 11.3, ^c Work Members: Cells (0.0%) have expected frequencies less than 5. The minimum frequency of the expected cell is 34.8, ^d

Household members: Cells (0.0%) have expected frequencies less than 5. The minimum frequency of the expected cell is 52.3, ^e Oximetry: Cells (0.0%) have expected frequencies less than 5. The minimum frequency of the expected cell is 46.4, ^f Fatigue: Cells (0.0%) have expected frequencies less than 5. The minimum frequency of the expected cell is 104.5.

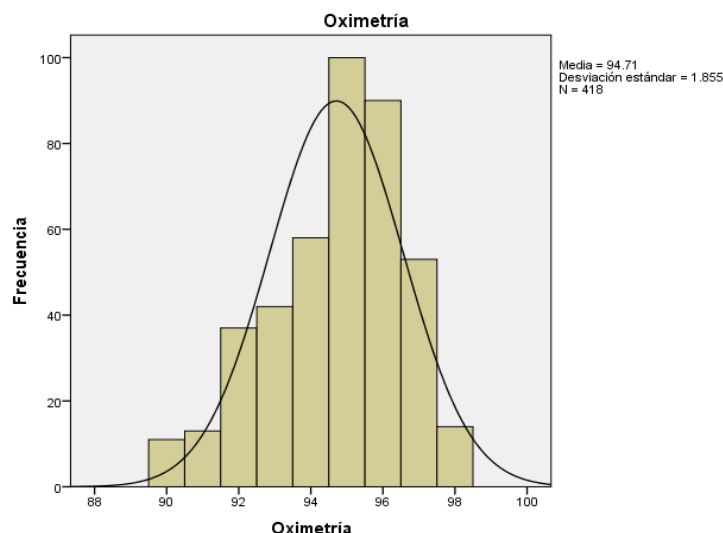


Figure 1. Measure of oximetry in positive patients. Source: experimental data

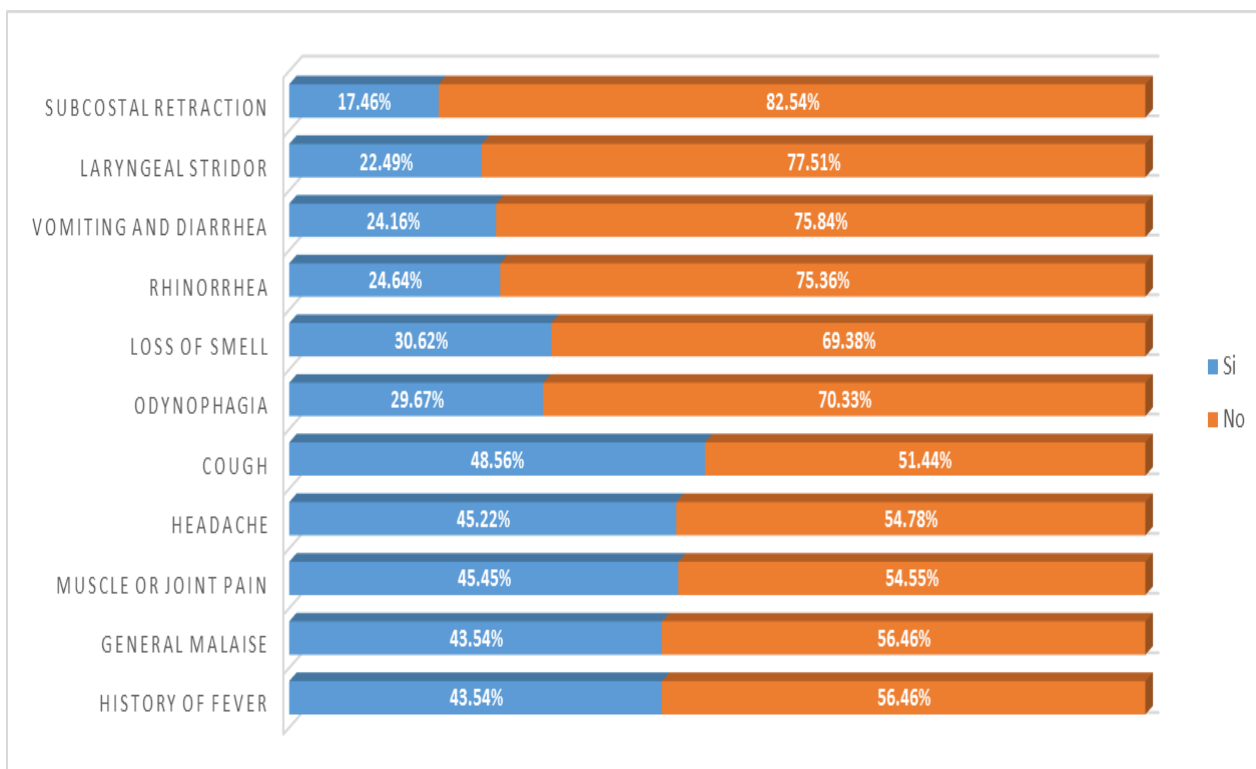


Figure 2. Signs and symptoms of the patient with positive Covid-19 antigen test. Source: experimental data

In the case of sex a majority was obtained for the male sex (53.8%) and the female sex obtained (46.2%). The age frequency in the majority of positive patients was 42 year. The most common diseases found were: diabetes (8.61%), Cardiopathy (3.59%), hypertension (2.15%) and the rest of the patients were without illness (85.65), The frequency of occupation that positive

patients presented was distributed mostly as follows: merchant (18.90%), Domestic employee (17.94%), Student (12.20%), Housewife (7.42%) among others. The frequency obtained for co workers and household members was 5 people. The demographic analysis confirms that the majority of tested patients were from the departments of Quetzaltenango (65.60 %),

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Guatemala (6.70%), San Marcos (1.0%), Retalhuleu, Quiche (0.2%), Totonicapan (0.5%) among others. The positive patients were

distributed between the years 2020 and 2021 (Figure 2).

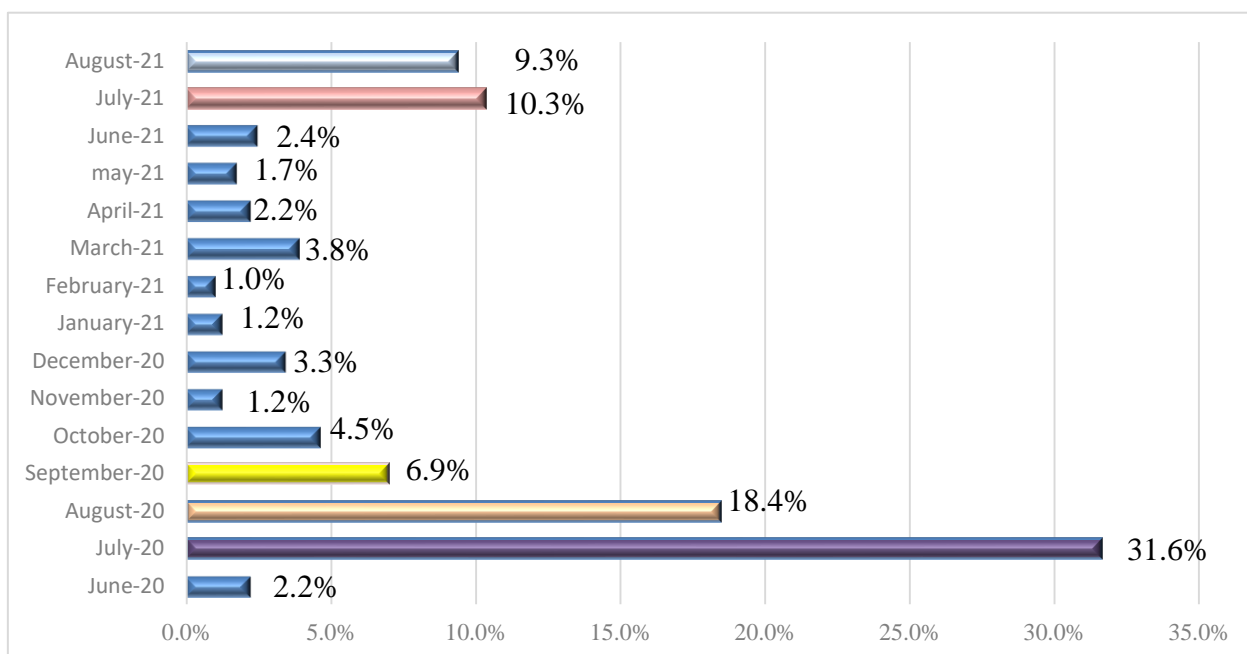


Figure 3. Frequency of months per year 2020 and 2021 of patients with positive tests. Source: experimental data.

The oximetry sign (p of 0.000) did not present in a normal manner in patients with positive antigen test. The value of Rho was 1.000 and with negative oximetry sign of -0.892 (two tailed p of 0.01). The Mann-Whitney test was used to confirm that a significant difference exists between the groups of 90 to 94 SPO₂ and of 95 to 98 SPO₂ among the groups obtaining a p value of 0.000. The chi-squared test (p : 0.000) indicated that there exists correlation between fatigue of the patients with positive Covid-19 test, for which the Odds Ratio of fatigue was obtained which was 26.39 times more probable to have a positive Covid-19 test with a confidence interval of 95% when a symptom of the epidemiologic form is present.

Discussion of Results

This study was carried out during the months of June of the year 2000 to August of the year 2021 obtaining a total of 1747 swabs out of which 418 patients tested positive. The test used was the antigen test with a sensibility of 52.54%, Specificity is 97.95%. The test was validated by the national laboratory of the Guatemalan

Ministry of Health. The methodology is the one which is currently being used by the health system for diagnosis; negative patients were referred to the nearest health center so that the Ministry of Health would confirm the test by PCR. (Arana et al., 2020).

All the epidemiological forms of patients with positive antigen test were tabulated, obtaining for the quantitative variables according to chi-squared (p : 0.000) for age, job and household members, as well as for the fatigue symptom and the signs of fever and oximetry (Table 1). Because the fatigue symptom and the oximetry sign do not appear as data of interest in the epidemiological form, the question regarding whether or not the symptom was present was asked before the test was performed. The answer was classified as mild, moderate and severe. It was confirmed through the identified frequency that the symptom of fatigue in its mild classification obtained a percentage of 21.5%, moderate 59.80%, severe 2.5% and 16% did not present such symptom. Currently investigations regarding Covid-19 detail that it is a common symptom of Covid-19 positive patients, and studies exist that ratify the frequency

of the symptom previously presented. (Manning; Hafeez et al., 2020; Halpin et al., 2021; Raveendran 2021).

The oximetry sign was measured with an oximeter placed on the index of the right hand and the result was annotated in the epidemiological form obtaining a mean value of 94.71 SPO₂ (Figure 1). Because the oximeter does not handle decimals the value of the mean obtained from oximetry is less than or equal to 94 SPO₂ (Manning et al., 2021). According to

the reproducibility index of Sars-Cov-2, which is 5.96 (Cugno et al., 2021), the mean obtained for the number of household members and co-workers which patients reported as suspected contact is 5. Reports of other studies have also stated that for each infected patient between 5 and 10 people can be infected, having said value is a contagion risk factor for obtaining a positive result in the antigen test (Aguilar, 2021; Cevik & Ho; Milovanovic et al., 2020). For the age variable the average obtained was 42 years. This is due to the variables of interest of Covid-19 that, according to genomic sequencing, were circulating. These affected each risk group in the months in which the study took place. Of the total of tabulated patients a male adult patient had gotten his single dose vaccine abroad 3 days prior. The other patients that tested positive were not vaccinated either because they did not qualify in Guatemala's Ministry of Health vaccination plan or because of lack of interest (National Vaccination Plan Against Covid-19 Republic of Guatemala).

The other signs and symptoms presented a descriptive variable statistic in positive patients (Figure 2), in the case of sex a majority was obtained for male sex (53.8%) and a minority for female sex (46.2 %). (Hafeez; Halpin; Manning; Raveendran 2021).

The most common degenerative illnesses that presented were: diabetes (8.61%), cardiopathy (3.59%) and hypertension (2.15%) among others (Baig, 2020; AlJishi et., al 2021).

The most affected occupations among the population served in the study were merchants (18.90%), domestic employees (17.94%), students (12.20%), and housewives (7.42%) among others. This can be a risk factor

for contagion because of the contact that exists when moving from one place to the other. In the case of housewives the risk occurs at the moment they share spaces with the home's inhabitants that were exposed in their own occupation. During the time the study was performed classes were virtual, therefore in students, the risk occurs due to a relaxation in preventative measures and distancing.

In the demographic analysis obtained it is confirmed that the majority of patients tested were from the Quetzaltenango department, among others. This is because Aguilar Clinical Laboratory and Blood Bank is located in the capital of the Quetzaltenango department. Frequency during the year 2020 was as follows: June (2.2%), July (31.6%), August (18.4%), September (6.9%), October (4.5%), November (1.2%), December (3.3%) and during the year 2021 January(1.2%), February (1.0%), March (3.8%), April (2.2%), May (1.7%), June (2.4%), July (10.3%), August (9.3%) (Figure 3). These results reflect the epidemiological traffic light employed by the Ministry of Health and Social Assistance of Guatemala. Quetzaltenango and its surrounding areas remained in red during the months the study was carried out. July and August of both years were the months of greatest infection as indicated by the sequencing Report of the Ministry of Public Health and Social Assistance published in the month of august of the year 2021.

The oximetry sign did not present normally (p: 0.000) in this study, for which ranges of 90 to 94 and 95 and 98 SP₀₂ were set (p: 0.000). These ranges were carried out according to their frequency, because according to recent studies low oximetries during a 24 hour continuous period can be an index of early severe pulmonary damage even when the patient is in home care. Such damage can result in pneumonia and pulmonary thromboembolism. Therefore it is important to consult a medic if oximetry is less than or equal to 94 SPO₂ accompanied by fatigue. Diagnostic laboratory tests and imaging tests can then be carried out to avoid complications. These tests will be useful to the doctor to better help improve the patients convalescence (Cruz 2020; Esakandari; Pascarella et al., 2020).

For the fatigue symptom and oximetry sign ($p: 0.000$) with an index of correlation of Rho Spearman of 1.00 for fatigue and of -0.892 for oximetry, both present a strong positive correlation for fatigue and a negative correlation for oximetry. The more fatigue present in the patient with a positive Covid-19 test, the lower his value of oximetry is. Because there existed a strong correlation between fatigue, positive and negative patients were tabulated, the result was that 82% of the positive patients presented such symptom while only 18% of the negative patients presented it (Hafeez et al., 2020; Halpin; Manning et al., 2021; Raveendran 2021).

The Odds ratio was calculated for the fatigue symptom and a risk probability was obtained. It is 26.39 times more likely to obtain a positive result in the antigen test if there is fatigue.

Conclusions

There exists correlation between the fatigue symptom and the oximetry sign in the patients with positive Covid-19 antigen test. Fatigue is a frequent symptom in unvaccinated patients with positive Covid antigen tests. If such a symptom is present there is a 26.39% probability of having a positive Covid-19 test along with the other symptoms that appear in the epidemiologic form of the Ministry of Health and Social Assistance of Guatemala. The value of oximetry presented by the patients with positive Covid-19 antigen test in their majority was less than or equal to a 94 SPO₂ and the range between 90 to 94 and 95 to 98 SPO₂ was significant. The background of the other signs and symptoms present in a variable manner in the patient with positive Covid-19 antigen test. The most frequent age according to the variables of genomic interest present at the time of the study was 42 years of age, being in their majority men over women.

Conflicts of Interest

It is stated that there is no conflict of interest on the test used and on the procedures carried out, with any company or with any institution for purchase or sale of supplies necessary in this investigation.

Ethical aspects of the study

A national ethics committee evaluated all aspects of said investigation study prior to being accepted with resolution OFZU0452-22.

Available resources

The resources to carry out this investigation will be covered by Aguilar Clinical Laboratory and Blood Bank as a scientific contribution to the Guatemalan people.

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