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# SARS-$CoV_2$: A Brief Analysis of the History of an Asymptomatic Patient

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## Abstract

$COVID_{19}$ is the outcome of SARS-$CoV_2$ infection. The resulting disease prompted by this infection commonly includes symptoms associated with exacerbated inflammation, lung tissue damage, fever, dry cough, and the subsequent persistent pain or pressure in the chest, shortness of breath and consequently limited mobility. This study aimed to report a case of a positive, asymptomatic $COVID_{19}$ patient. Male patient, 38 years old, which described exercising regularly, with no previous co morbidities, maintaining a well-balanced diet. During the quarantine (decree Nº. 33519 of 03/19/2020 of March 23, 2020 at Fortaleza-CE), the patient completely interrupts his routine of physical activities, although kept a healthy diet. Nevertheless, it was described an increase of 5 kg between March and June (2020), as a result of the semi sedentary habits as a result of reduced physical activity. The absence of regular exercises was also related with alterations in the triglyceride index (< 150 mg/dL), total cholesterol (< 200 mg/dL), VLDL (< 40 mg/dL) and vitamin D (insufficient - 10 to 30 ng/mL). The patient did not report symptoms associated with SARS-$CoV_2$ infection, for this reason, no specific treatment strategy was prescribed. It is noteworthy that the patient possibly contracted the SARS-$CoV_2$ in his own residence, whereas the protective measures were applied. In conclusion, it has been described that $COVID_{19}$ is a potentially serious disease in individuals with previous comorbidities as diabetes, obesity and hearth diseases. Individuals who maintain a sedentary lifestyle are more likely to the worsening of these comorbidities, what could be a risk factor for $COVID_{19}$ severity.

**Keywords:** $COVID_{19}$; SARS-$CoV_2$; Asymptomatic patient; Physical exercise; Good nutrition

## Introduction

The first scientific study describing *Coronavirus* (H*CoV* - human *Coronavirus*) as a disease promoter human was released in the 1960s, although, the virus was initially founded in *Gallus gallusdomesticus*birds in 1930 [1]. Currently, coronaviruses are classified in the order *Nidovirales*, subfamily *Orthocoronavirinae* and subdivided in four genus: *Alphacoronavirus* (*α-CoV*), *Betacoronavirus* (*β-CoV*) and some members belonging to *Gammacoronavirus* (*γ-CoV*) are pathogens to mammalian, although some strains belonging to genus *γ-CoV* and *Deltacoronavirus* (*δ-CoV*) have adapted to cause disease in avian. Among the viral strains classified as H*CoV*, the following stand out: *α*-H$CoV_{229E}$, *α*-H$CoV_{NL63}$, *β*-H$CoV_{OC43}$, *β*-H$CoV_{HKU1}$, *β*-MERS-*CoV*, *β*-SARS-*CoV* and *β*-SARS-$CoV_2$.

The strains *α*-H$CoV_{229E}$ and *β*-H$CoV_{OC43}$ first identified in the mid-1960s [1-3], are closely related with the common cold syndrome and pneumonia [4-8], uncommonly causing severe diseases. It was also reported that both strains can cause LRTI (Lower Respiratory Tract Infections) and otitis media [3]. Often this virus is detected in co-infections with other strains of viruses and bacteria resulting respiratory infections [4 ,9-11]. In addition, this virus also is widely distribution worldwide with seasonal outbreaks [12]. H*CoV* infections have been described for decades, occurring in 2- to 3-year cycles [13], with seasons of high infections rates caused by strains *α*-H$CoV_{229E}$ or *β*-H$CoV_{OC43}$ and sporadic infections caused by strains belonging to the others H*CoV* groups [12].

The strain *α*-H$CoV_{NL63}$ was reported for the first time in 2004 in a baby from Netherlands suffering from bronchiolitis [11,14]. However, this strain seems to affect mostly immunocompromised children inducing symptoms as cough, fever, and rhinorrhea or severe LRTI, including as bronchiolitis and laryngotracheobronchitis (Kothai& Arul, 2020). Similarly, to *α*-H$CoV_{229E}$ and *β*-H$CoV_{OC43}$ strains, it is believed that the outbreaks of *α*-H$CoV_{NL63}$ occur every 2–3 years with seasonal peaks in winter [14] and it is estimated that 1-10% of the world's population is affected annually [3].

The strain *β*-H$CoV_{HKU1}$ was identified in 2005 in an elderly patient with pneumonia in Hong Kong. The infections by this strain commonly is associated with LRTI and mild URTI - Upper Respiratory Tract Infection [11,15], and in some cases it causes severe secondary respiratory infections, including bacterial pneumonia in immunocompromised pediatric and geriatric patients. It has been suggested that 0.9% of the population worldwide may be affected annually by the *β*-H$CoV_{HKU1}$[15]. Recently the strains *α*-H$CoV_{229E}$, *α*-H$CoV_{NL63}$, *β*-H$CoV_{OC43}$ and *β*-H$CoV_{HKU1}$are spread worldwide and associated with 4 to 15% of acute respiratory disorders in adults every year, raising to 35% at seasonal outbreaks [3].

In November of 2002, it was reported a new strain of *CoV* capable of causing severe acute respiratory syndrome, being further classified SARS-*CoV*[16]. Only in 2003, the genome of this strain was completely sequenced by Canada's National Microbiology Laboratory [17]. Chronic comorbidities may elevate the risk of severe SARS-*CoV* disease. This feature has been associated with increased of 3 to 6% [17,18]. Simmons and collaborators (2004), demonstrated that SARS-*CoV* was found in lung, trachea/bronchus, stomach, small intestine, distal convoluted renal tubule, sweat gland, parathyroid, pituitary, pancreas, adrenal gland, liver and cerebrum and that clinical changes

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may be due to the cytopathic effect mediated by local replication of the SARS-*CoV*; or indirectly as a result of systemic responses to respiratory failure or the harmful immune response induced by viral infection.

In 2012, the outbreak of a new *CoV* capable of causing Middle East respiratory syndrome (MERS-*CoV*) was reported, being the first case occurred in Kingdom of Saudi Arabia (KSA), recording at least 2468 cases and 851 deaths worldwide [19]. Another well-documented case of MERS-*CoV* occurred in May 2015, according to information from Korea Centers for Disease Control and Prevention (2015), an infected individual returning from the Middle East started the outbreak of MERS-*CoV* in South Korea, which spread over 16 hospitals and 186 patients. On the next year, were reported 1,728 confirmed new cases of MERS-*CoV*, and 624 deaths were notified in 27 countries [20]. In 2018 a new outbreak of MERS-*CoV* was recorded in the Saudi Arabia [21], with 96 new cases. After these outbreaks of MERS-*CoV*, very year's new cases are documented, usually associated with infected travels; often, these imported MERS cases resulted in nosocomial transmission [19]. Symptoms of MERS-*CoV* are fever, cough and upper respiratory tract (URT) signs and symptoms usually occur first, followed within a week by progressive LRT distress and lymphopenia[22].

The current pandemic of $COVID_{19}$ (*CO*rona*VI*rus*D*isease and 19 refers to year 2019, was first reported at Wuhan, China. The clinical manifestations are very similar to SARS-C*oV* infection (for that reason it was described as SARS-$CoV_2$). Elderly population stands out as the group with the highest risk, especially those that feature previous comorbidities [23]. In addition, Jordan and collaborators (2020), reported that the restrictions imposed as a control measure during SARS-$CoV_2$ pandemic, may lead elderly people to experience loneliness, isolation and loss of mental and physical stimulation, which could increase the severity of infection.

## Genetic characteristics of *CoV*

*CoV*s are featured by a positive single-stranded RNA. At the molecular level, *CoV*s usually feature high mutation rate due to the propensity of errors during their replication [23-25]. It has been shown that these viruses naturally present 20% homologous RNAs recombination mixed infections with different viral strains the same group [23].

Genetic recombination and point mutations in the genome of *CoV*s can be considered as mechanisms of adaptation between strains, since it is speculated that H$CoV_{NL63}$ has arisen from the evolution of H$CoV_{229E}$[26]. In 2018, Chinese scientists reported a new genotype of strain H$CoV_{OC43}$, named H by Zhu and collaborators (2018). It is possible that the H strain emerged as a result after genetic recombination involving seven other stains of H$CoV_{OC43}$[27], previously identified as H$CoV_{OC43}{}^{a}$ - H$CoV_{OC43}{}^{g}$. In 2006 was described the circulation of H$CoV_{HKU1}$ strain throughout the United States, however, with genetic differences from the stain originally identified in Hong Kong, revealing the easy adaptation of *CoV* strains to different environmental and climatic conditions [28].

Scientific approaches involving *in silico* simulation have been useful to address may hypotheses. In 2006, a prospective study developed by [29], using *in silico* predictions, analyzed 25 variants of H$CoV_{229E}$ disseminated in Australia, described during the years of 1979 to 2004. In the study, gene product S and N (spike protein and nucleoprotein) were selected, considering them primary role of facilitates the virus binding to the host cell. In this research the authors concluded that S protein has not mutated over the years, therefore, a type of positive selection mechanism exists, and probably are one of the mechanisms responsible for the emergence of new viral strains [29]. These results were corroborated by Li and collaborators (2019), considering the description of the same isoforms of protein S, featured by hydrophilic properties, which is a biochemical characteristic that facilitates conformational changes, allowing conversions of pre and post-fusion forms.A genetic analysis of MERS-*CoV* 2018 outbreak in South Korea showed that this strain isolated from throat swab (TS) sample and Caco-2 cells (TSVi) shared high degree of identity (99.85% – 99.90%) between its nucleotide compared to human MERS-*CoV* strain isolated at Saudi Arabia in 2017 [30]. However, the comparison between MERS-*CoV* isolated in 2018 on South Korea with the circulating strain previously identified in 2015 outbreak, demonstrated structural differences in the *N*-terminal of S protein and receptor-binding domain (RBD). In this case, three and nine nucleotides substitutions respectively, implying that the imported case in 2018 involved a different virus strain [31]. Regarding SARS-*CoV*, there are several data regarding the existence of genetic variability, due to the mutations that occurred over the years, whether due to environmental conditions or urban-social remodeling [15,32]. In 2019, a study conducted by Chinese researchers suggested that the 2002/2003 outbreak in southern China was probably caused by several genetic recombination events, which occurred among the ancestors of the SARS-related *CoV*(SARS-*CoV*s) in distinct bat species [15].It is clear that genetic diversity promotes a rapid evolution of the virus in host organism, which makes it difficult to use therapeutic strategies and the emergence of new vaccines candidates[33]. After sequencing of 558 SARS-$CoV_2$ isolates, it was demonstrated that the highest percentage of mutations occurred in the genes encoding protein S, RNA polymerase, RNA primase and nucleoprotein[32]. Thus, it is essential to observe and analyze what types of recombinant mechanisms occur most frequently in viral strains, so that new methods can be tested [32].

## Case report

The 38-year-old, dark-skinned, $COVID_{19}$-positive patient was diagnosed in May of 2020, after complain of headache episodes two to three times a week. The patient reported levels of glucose, triglycerides, HDL, LDL and total cholesterol altered for at least 10 years due to a sedentary lifestyle. Following medical guidelines, the patient gradually started physical activities (street running, at least three times a week) for the last 18 months. The routine of exercise was established in order to improve life quality and healthy status. Before starting the exercise routine, the patient exhibited a body weight of 98 kilograms, 1.64 m height and Body Mass Index (BMI) equal to 36.44, what is considered grade II obesity according to reference values (30.0 to 39.9).

After 18 months engaged on the exercise routine, the patient exhibited a weight loss of 18 kilograms. The social isolation required by the quarantine started at mid-February 2020 in Brazil due to the $COVID_{19}$ pandemic. Therefore, the patient reported a reduction in the routine of physical activities, reinforced by the decree Nº. 33519 of 03/19/2020 of the State of Ceará, where does he lives, which suggested the interruption of non-essential activities outside the home. Currently, the patient exhibits 83 kilograms, with a gain of 3 kilograms during quarantine, a body mass index equal to 30.86, which is classified as grade II obesity.

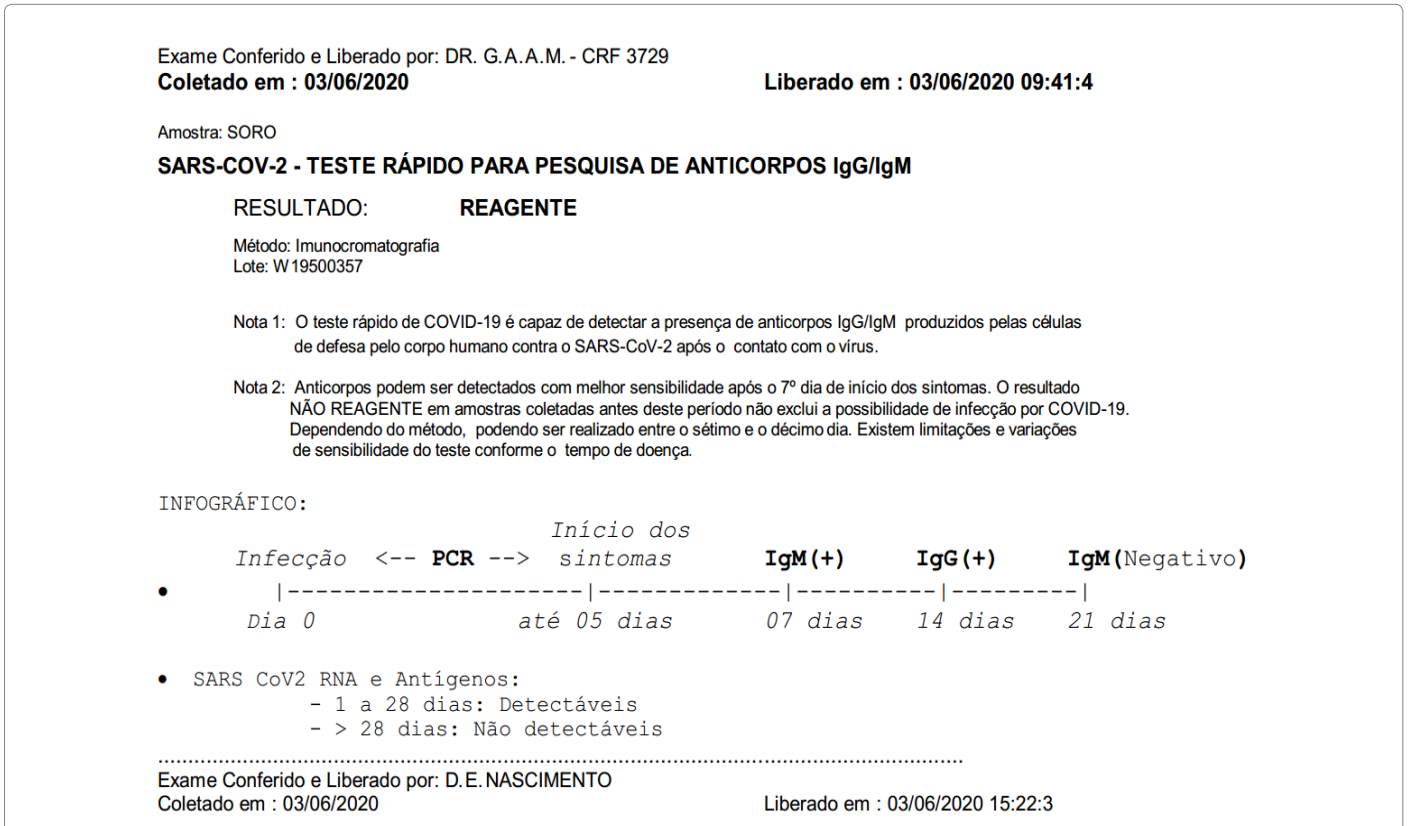
In mid-May 2020, the patient complained of severe headaches due to his health history, suspected the altered glycemic and/or cholesterol indexes, as he had not practiced physical exercises months ago. The patient went to a Hospital Geral Dr. César Cals in the city of Fortaleza-CE and requested a check-up of the indexes listed in (Figure 1).

## Results and discussion

After 10 years of clinical features resulting from changes in glucose, triglycerides, HDL, LDL and total cholesterol levels, the patient frequently follows up his healthy status whenever experienced symptoms as intense headache, and thereby improve or replace foods in your diet, and regulate time and frequency of physical activity. In this case, after experience these symptoms, the patient requested a biochemical evaluation revealing alterations in triglycerides, total cholesterol, very low-density lipoprotein (VLDL) and Vitamin D according to (Figure 1).

For Vallejo-Vaz and collaborators [34], patients with elevated indices of triglycerides may represent a subgroup exposed to higher risk of heart diseases, which requires more drastic interventions to minimize the harmful effects of proatherogenic lipoproteins like very low-density lipoproteins (VLDL). Among the lipoprotein's low-density lipoproteins belonging to the VLDL group, stands out the subgroup from low-density lipoprotein-cholesterol (LDL-C), which in turn is considered is both a causal and cumulative risk factor for atherosclerotic cardiovascular disease [35]. The evolution of coronary atherosclerosis is tightly induced by interactions between poor diet, sedentary life, absence of physical activity, abnormal lipid metabolism [36], and hypertriglyceridemia [37]. Hypertriglyceridemia usually negatively influence the function of $\beta$-cell and causing peripheral insulin resistance [38]. The ineffectiveness of $\beta$-cell function results in decreased glucose-induced insulin secretion, resulting in an increased glycemic level, which significantly increases the risk of cardiovascular disease. Some scientific reports demonstrated that LDL-particle size revealed a significantly negative correlation with the increased serum triglycerides levels [39,40], which means that the higher serum triglycerides rate, smaller is the LDL-particle size [37].

The patient reported the following symptoms at the same period that increased levels of triglycerides and VLDL were observed: feeling of imminent fainting, dizziness, confusion or blurred vision (occurring for a few seconds or even minutes after the person gets up, especially after a long period lying in bed or sitting), in addition to the previously reported intense headaches. In healthy individuals, these clinical manifestations may be associated with postural orthostatic tachycardia syndrome (POTS), meanwhile this phenomenon is uncommon. According to [41], it is necessary for individuals to be educated, and motivated to incorporate new healthy living practices into their lives to minimize POTS symptoms. Young adults are at heightened risk for academic decline, truancy, or delayed graduation from high school and college.In this case report, it was demonstrated that the patient had reduced levels of vitamin D. The decreased vitamin D rates are likely to be associated with the quarantine period considering that social isolation may reduce sun exposition. Vitamin D3 synthesis in the skin is induced by UVB radiation, which leads to thermal reaction of reaching 7-dehydrocholesterol. Vitamin D3 or oral vitamin D is converted to 25(OH)D in the liver and then to the hormonal metabolite, 1,25(OH)2D (calcitriol), in the kidneys or other organs as needed. In addition, it has been described that vitamin D minimizes the risk of contracting viral infections [41-43].



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**Coletado em : 03/06/2020** **Liberado em : 03/06/2020 09:41:4**

Amostra: SORO

**SARS-COV-2 - TESTE RÁPIDO PARA PESQUISA DE ANTICORPOS IgG/IgM**

RESULTADO: **REAGENTE**

Método: Imunocromatografia
Lote: W19500357

Nota 1: O teste rápido de COVID-19 é capaz de detectar a presença de anticorpos IgG/IgM produzidos pelas células de defesa pelo corpo humano contra o SARS-CoV-2 após o contato com o vírus.

Nota 2: Anticorpos podem ser detectados com melhor sensibilidade após o 7º dia de início dos sintomas. O resultado NÃO REAGENTE em amostras coletadas antes deste período não exclui a possibilidade de infecção por COVID-19. Dependendo do método, podendo ser realizado entre o sétimo e o décimo dia. Existem limitações e variações de sensibilidade do teste conforme o tempo de doença.

INFOGRÁFICO:

| *Infecção* | <-- **PCR** --> | *Início dos sintomas* | **IgM(+)** | **IgG(+)** | **IgM**(Negativo) |
|---|---|---|---|---|---|
| *Dia 0* | | *até 05 dias* | *07 dias* | *14 dias* | *21 dias* |

- SARS CoV2 RNA e Antígenos:
  - 1 a 28 dias: Detectáveis
  - > 28 dias: Não detectáveis

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**Figure 1:** Clinical confirmation of SARS-$CoV_2$: Quick test for IgG/IgM antibody research.

**Note 1:** The $COVID_{19}$ rapid test is able to detect the presence of IgG/IgM antibodies produced by the immune cells in the human body organism against SARS-$CoV_2$.

**Note 2:** Antibodies can be detected with better sensitivity after the 7th day of symptom onset. The NON-REAGENT result in samples collected before this period does not exclude the possibility of infection by SARS-$CoV_2$. Depending on the method, it can be performed between the seventh and the tenth day. There are limitations and variations in the sensitivity of the test according to the duration of the disease.

| Test | Results | Method | Reference value |
|---|---|---|---|
| Triglycerides | 263 mg/dL | Enzymatic | < 150 mg/dL |
| Total cholesterol | 218 mg/dL | Direct enzymatic | < 200 mg/dL |
| HDL | 48.5 mg/dl | Colorimetric without precipitation | 23-92 mg/dl |
| LDL | 106.0 mg/dL | Direct enzymatic | < 130 mg/dL |
| VLDL | 52.6 mg/dL | Calculation | < 40 mg/dL |
| Glucose | 88 mg/dL | Enzymatic | 70 – 99 mg/dL |
| Vitamin D | 27.7 ng/mL | Chemiluminescence – LIAISON DiaSorin | Insufficiency 10 – 30 ng/mL |
| Vitamin B12 | 566 pg/mL | immunoassay – Immulite 2000 XPI – Siemens | 193 – 982 pg/mL |
| Calcium | 7.8 mg/dL | Colorimetric | 8.6 – 10.3 mg/dL |
| Magnesium | 2.2 mg/dL | Colorimetric | 1.9 – 2.7 mg/dL |
| Urea | 31 mg/dL | Kinetics | 15 – 43 mg/dL |
| Creatinine | 0.9 mg/dL | Colorimetric | 0.6 – 1.3 mg/dL |
| Alkaline phosphatase | 59 U/L | Enzymatic | 34 – 104 U/L |
| GGT | 62 U/L | Colorimetric | 9 – 64 U/L |
| TGO | 22 U/L | Enzymatic | 13 – 39 U/L |
| TGP | 30 U/L | Enzymatic | 7 – 52 U/L |
| Serum phosphorus | 3.5 mg/dL | Colorimetric | 2.5 – 5 mg/dL |
| Chlorine | 106 mEq/L | Colorimetric | 98 – 107 mEq/L |
| Sodium | 139 mEq/L | Colorimetric | 136 – 145 mEq/L |
| Potassium | 4.4 mEq/L | Colorimetric | 3.5 – 5.1 mEq/L |
| TSH | 1.030 µIU/mL | Microparticle chemiluminescent immunoassay – Immulite – Siemens | 1.01 ng/dL |
| Free thyroxine (T4) | 1.01 ng/dL | Microparticle chemiluminescent immunoassay – Immulite – Siemens | 2000 XPI 0.89 – 1.79 ng/dL |

**Table 1**: Laboratory tests requested for Biochemical analysis, method used for diagnosis and reference values adopted at the Hospital Geral Dr. César Cals, Fortaleza-CE. All Indices listed in bold are considered changed.

It has been suggested that vitamin D helps to maintain tight junctions, gap junctions, and adherents junctions, however, viral infections can cause disturb at these junctions integrity, greatly increasing the likelihood of new viral infections and other microorganisms [44,45]. In this context, may be possible to suggest that the presence of SARS-$CoV_2$ in human hosts added to the low vitamin D index in the patient reported here, construct a synergism that weakened the immune defense barriers and, consequently, infection by the virus, although they did not show any classic symptoms of $COVID_{19}$. It is necessary to emphasize that the patient maintained a healthy diet, at least three times a week; he practiced physical exercises outdoors under the sun in the morning and, ingested daily citrus fruits or juices rich in vitamin C. Although the patient is 38 years old, does not present any cardiac or pulmonary abnormality, the main sites of manifestation of the symptoms of $COVID_{19}$, (Table 1) which is probably factors that mitigated the effects of the disease.

Diagnostic tests arise in the current SARS-$CoV_2$ pandemic as an essential tool for tracking the spread of $COVID_{19}$. Although there are different diagnostic tests for SARS-$CoV_2$ commercially available, few are easily obtained (1). Hsueh and collaborators [46], one of these diagnostic methods is based on the identification of serological responses, including the detection of presence of IgM (immunoglobulin M) and IgG (immunoglobulin G) virus-specific[47-51].

The antibody production occurs after a previous contact with a pathogen. In this context, during the acute phase of SARS-$CoV_2$ infection, its antigen stimulates the immune system to produce a protective response and specific antibodies are synthesized. Among the antibodies against the virus, the anti-SARS-$CoV_2$ IgM stands out, as the first to be produced and, being possible to detect 3 to 5 days after the onset of infection. Then, the synthesis of specific anti-SARS-$CoV_2$ IgM decreases and the synthesis of anti-SARS-$CoV_2$ IgG occur quickly. It has been described that the concentration of the anti-SARS-$CoV_2$ IgG antibody during recovery can be 4-fold higher compared to acute phase of $COVID_{19}$. Despite the levels of IgM and IgG of anti-SARS-$CoV_2$ were detected in the patient here reported, no symptoms usually associated with $COVID_{19}$ were diagnosed[52-56].

## Final considerations

The present study is a case report of a 38-year-old male individual diagnosed with $COVID_{19}$, however, with no clinical manifestations. Consistently with the current scientific production $COVID_{19}$, is commonly associated with poor outcome in elderly population, although this phenomenon has been registered in non-elderly individuals. It is possible that the severe manifestations of SARS-$CoV_2$ infection in the non-elderly population, are related with previous co morbidities, since the reports of deaths by $CODIV_{19}$, are mostly are mostly in individuals who suffer from chronic disease including obesity associated with a sedentary lifestyle. On the other hand, SARS-$CoV_2$ infected individuals who have a good diet and exercise regularly, seems to be asymptomatic, as occurred with the patient reported in this study. However, it is necessary further studies addressing cases of $COVID_{19}$, in order to demonstrate whether maintenance of healthier living habits is a factor capable of reducing the chances of mortality per SARS-$CoV_2$. It is possible to suggest that severe effects of $COVID_{19}$ may be related with exacerbated release of inflammatory factors and more aggressive immune responses which may be associated with sedentary lifestyle.

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