

Artigo

**Protective behaviors against SARS-CoV-2 infection:
a cohort study****Comportamentos de proteção contra a infecção por SARS-CoV-2:
um estudo de coorte**

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RESUMO: INTRODUÇÃO: Nós elaboramos um estudo prospectivo com o objetivo de avaliar fatores (adesão ao distanciamento social, uso de EPI's, etc.) que poderiam ser determinantes no desenvolvimento da COVID-19 que poderá subsidiar o desenvolvimento de estratégias de saúde eficazes no combate da infecção no município de Passos - Minas Gerais, Brasil, seja em ambientes hospitalar ou não-hospitalar. MÉTODOS: Trata-se de um estudo de coorte longitudinal onde foram incluídos 343 indivíduos da população que foram selecionados aleatoriamente por conglomerado. Os indivíduos selecionados responderam a um questionário relacionado às características clínicas, medidas preventivas, comorbidades e uso de medicamentos. Na ocasião foi realizado teste rápido nos indivíduos para detecção de anticorpos IgG e IgM. O tempo médio de acompanhamento foi de seis meses e, durante o acompanhamento, manteve-se contato telefônico a cada duas semanas. Ao final do seguimento, novo teste sorológico foi realizado e calculado o risco associado à presença de fatores de risco e à incidência da doença. RESULTADOS: Verificamos que 27,3% dos participantes que se infectaram no seguimento faziam uso de ivermectina e hidroxiquina como forma de prevenção, enquanto nós não infectados, 11,3% usavam esses medicamentos. Para os indivíduos que apresentaram a doença durante o seguimento 21,2% relataram respeitar o isolamento social, 27,3% relataram que saíram para trabalhar e 42,14% relataram que frequentaram ambientes hospitalares. Entre os participantes que tiveram a infecção, 12,1% relataram contato apenas com familiares, 9,1% com familiares e colegas de trabalho e 75,8% com profissionais de saúde. CONCLUSÕES: Este estudo forneceu dados epidemiológicos de indivíduos infectados pelo COVID-19, que podem contribuir com o sistema de saúde no estabelecimento de medidas preventivas.

PALAVRAS-CHAVE: COVID-19; SARS-CoV-2; Medidas preventivas; Medicação.

ABSTRACT: INTRODUCTION: We designed a prospective study aiming to assess factors (adherence to social distancing, use of PPE, etc.) that could be determinants in the development of COVID-19 that may subsidize the development of effective health strategies to combat the infection in the municipality of Passos - Minas Gerais, Brazil, whether in the hospital or non-hospital settings. METHODS: This is a longitudinal cohort study where 343 individuals from the population were included and randomly selected by clusters. The selected individuals answered a questionnaire related to clinical characteristics, preventive measures, comorbidities, and medication use. A rapid test was performed on the individuals to detect IgG and IgM antibodies. The average follow-up period was six months, and during the follow-up, telephone contact was maintained every two weeks. At the end of the follow-up, a new serological test was performed, and the risk associated with risk factors and disease incidence was calculated. RESULTS: We found that 27.3% of patients who became infected during follow-up were using ivermectin and hydroxychloroquine as a means of prevention, while in non-infected patients, 11.3% used these drugs. (p = 0.024). For patients who had the disease during follow-up, 21.2% reported respecting social isolation, 27.3% reported leaving for work, and 42.14% reported having attended hospital environments (p = 0.004). Among the participants who had the infection, 12.1% reported contact only with family members, 9.1% with family members and co-workers, and 75.8% with health professionals (p = 0.001). CONCLUSIONS: This study provided epidemiological data on patients infected with COVID-19, which can contribute to the health system's establishment of preventive measures.

KEYWORDS: COVID-19; SARS-CoV-2; Preventive measures; Medicines.

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INTRODUCTION

COVID-19 (Coronavirus Disease - 2019) was started in December 2019 in Wuhan, China, and on March 12, 2020 its was declared a pandemic by the World Health Organization¹. There are currently more than 150 million confirmed cases in the world and more than 3.15 million deaths (data from April 29, 2021), although the actual rates may be higher, considering the absence of confirmatory tests for suspected cases in some regions².

In Brazil, the first case of COVID-19 was confirmed in February 2020 and numerous procedures were carried out to contain the progress of the disease. On February 3, the country declared a Public Health Emergency of National Importance (ESPIN) (Brasil, 2019). Since then, the number of deaths caused by SARS-CoV-2 infection has reached 373 thousand deaths in Brazil, to date (data of April 19, 2021).

The relentless search for pharmacological alternatives against SARS-CoV-2- has been the subject of numerous researches around the world. Despite efforts, there is currently nothing concrete, and in this sense, reducing the rate of infection is a priority, which can be achieved through a set of preventive measures. Social distancing, the use of face masks and other personal protective equipment (PPE's) are tools in infection control^{3,4}.

In addition, the systematic analysis of 172 studies, which assessed the determining factors in the development of respiratory infections (COVID-19, SARS, or MERS) showed that the virus transmission was less with physical distance of 1 meter or more, compared to a distance less than 1 meter. Protection was considerably greater as the social distance increased. The use of a face mask resulted in a great reduction in the risk of infection with stronger associations with N95 or with similar respirators compared to disposable or similar surgical masks. Finally, eye protection was also associated with lower chances of infection⁴.

Knowledge about truly effective protective measures against SARS-CoV2 infection is extremely important for controlling the spread of the disease. Therefore, considering the need to reduce infection rates, we aimed to carry out a prospective cohort study to evaluate the relationship between risk factors (adherence to social distancing, use of PPE, etc.) and the development of COVID-19 in the population of the city of Passos, state of Minas Gerais in Brazil. that can subsidize the development of effective health strategies to combat the infection.

METHODS

A prospective longitudinal cohort study was carried out in which 343 individuals from the population were randomly selected by cluster. Individuals from the population registered at all the service stations in the city were used, and simple random sampling was performed

to select the patients at each of these stations. This study was carried out in the city of Passos, located in the interior of the state of Minas Gerais, whose total population is 115,000 inhabitants.

All individuals included in the study were invited to participate and those who agreed signed a free and informed consent form previously approved by the Research Ethics Committee (4.256.806).

We included adult patients (> 18 years), who had no current or previous diagnosis of COVID-19 and who agreed to participate in the study by signing an informed consent form. Patients who had been diagnosed with the disease and who did not agree to participate in the study were excluded from the study.

The scheduling of participants was carried out previously so as not to allow the accumulation of individuals in the care units on the same day. Participants were scheduled at individualized times in order to ensure minimal possibility of contagion. The selected individuals who agreed to participate in the study filled out a questionnaire related to the clinical characteristics of the participants, the adoption of preventive measures, the presence of comorbidities and the use of medications. At this same time, a rapid test was also performed on individuals for the detection of IgG and IgM antibodies. Positive results were repeated for confirmation and individuals with a previous or current SARS-CoV-2 infection were excluded.

In this first moment, 41 (11.9%) participants had a positive result for COVID-19 and 302 individuals were then followed prospectively. The average follow-up time was six months and during the follow-up, telephone calls were made every two weeks. During contact, participants were asked about any changes related to the preventive measures reported at the beginning of the study and whether they had flu-like symptoms or whether they had been infected with SARS-CoV-2. At the end of the follow-up, a new serological test was performed and the risk associated with the presence of risk factors and the incidence of the disease was calculated.

Statistical analysis

In the first stage, descriptive statistics (means, standard deviation and proportions) were calculated for each group. Comparisons between groups were assessed by Student's t-test or Mann-Whitney test when the variables had a uniform distribution or not, respectively. Categorical variables were compared using the chi-square or Fisher test and the strength of the association measured by the Odds Ratio analysis with a 95% confidence interval. The analyzes were performed using the IBM® SPSS Statistics 22.0 for Windows. For all variables, the respective relative risks will be calculated with their 95% confidence intervals. A significance level of 5% will be considered in all analyzes.

RESULTS

As previously mentioned, a total of 302 participants were followed, however at the end of the study 184 (61%) remained present. The losses were due to the withdrawals of

the research participants and not returning in the evaluation at the end of follow-up. The clinical characteristics of the patients included are shown in Table 1. The average age of the participants included was 45.72 years (SD 16.4 years) and 66.7% of the participants were women.

Table 1 - Distribution of the frequencies of the participants included in the study in terms of sociodemographic aspects.

	Category	Number of participants (%)
Gender	Men	228 (66.7%)
	Women	114 (33.3%)
Education	Illiterate	4 (1.2%)
	Incomplete high school	121 (35.4%)
	Complete high school	79 (23.1%)
	Incomplete higher	51 (14.9%)
	Graduated	87 (25.4%)
Profession	Minimal exposure	45 (13.2%)
	Low exposure	107 (31.3%)
	High exposure	148 (43.3%)
	Health professional	42 (12.3%)
Body mass index	<18 kg/m ²	5 (1.5%)
	18-25 kg/m ²	118 (36.5%)
	25-30 kg/m ²	131 (40.6%)
	>30 kg/m ²	69 (21.4%)
Comorbidities	No disease or not informed	160 (46.8%)
	Other diseases	49 (14.3%)
	Diabetes, hypertension, DPOC, CA	131 (38.3%)
	Immunodeficiencies	2 (0.6%)
Use of medicines	No	297 (86.8%)
	Yes	45 (13.2%)
Physical activity	No	219 (64.2%)
	Yes	122 (35.8%)
Smoker	No	281 (82.4%)
	Yes	60 (17.6%)
Blood type	O	117 (49.4%)
	A	87 (36.7%)
	B	23 (9.7%)
	AB	10 (4.2%)

The incidence of SARS-CoV-2 infection in our cohort was 17.9%. When comparing the epidemiological clinical characteristics with the incidence of infection, we found that the individuals who did not develop the disease during the follow-up had an average age of 46.30 (SD 16.31) whereas the individuals who did develop had an average age 40.42 (SD 17.07) ($p = 0.06$) (Figure 1).

Considering the use of drugs such as ivermectin and hydroxychloroquine as a form of prevention, we found that 27.3% of participants who became infected during follow-up were taking these drugs, while in individuals who were not infected, 11.3% used these drugs ($p = 0.024$). According to gender, body mass index (BMI), presence of comorbidities, smoking, blood type, physical activity, ethnicity and education, we did not find any significant differences (Table 2).

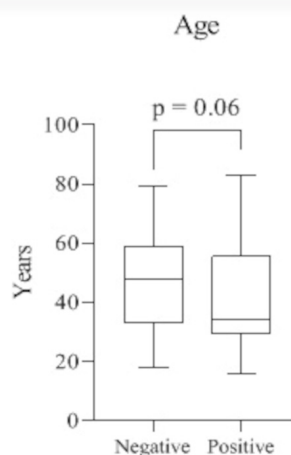


Figure 1 - Incidence of SARS-CoV-2 infection according to age.

Table 2 - Incidence of SARS-CoV-2 infection according to clinical and demographic characteristics.

Test Result	Variables analyzed					
	Use of medicines (related to Covid)					
	No % (n)	Yes % (n)			p	
Negative	88.1 (133)	11.9 (18)			0.024	
Positive	72.7 (24)	27.3 (9)				
	Gender					
	Women % (n)	Men % (n)			p	
Negative	62.3 (94)	37.7 (57)			0.141	
Positive	75.8 (25)	24.2 (8)				
	Body mass index					
	<18 % (n)	18-25 % (n)	25-30 % (n)	>30 % (n)		p
Negative	2.1 (3)	33.3 (47)	42.6 (60)	31 (22)		0.592
Positive	0	43.8 (14)	34.4 (11)	21.9 (7)		
	Comorbidities					
	No disease or not informed% (n)	Other diseases % (n)	Dia- betes, hyper- ten- sion, DPOC, CA% (n)	Immunodeficiencias % (n)		p
Negative	47 (71)	14.6 (22)	37.7 (57)	0.7 (1)		0.705
Positive	48.5 (16)	21.2 (7)	30.3 (10)	0		
	Smoker					
	No % (n)		Yes % (n)		p	
Negative	82 (123)		18 (27)		0.089	
Positive	93.9 (31)		6.1 (2)			
	Blood type					
	O % (n)	A % (n)	B % (n)	AB % (n)		p
Negative	52.9 (54)	31.4 (32)	11.8 (12)	3.9 (4)		0.164
Positive	40.7 (11)	44.4 (12)	3.7 (1)	11.1 (3)		
	Physical activity					
	No % (n)		Yes % (n)		p	
Negative	57.3 (86)		42.7 (64)		0.506	
Positive	63.6 (21)		36.4 (12)			
	Ethnicity					
	White % (n)	Black % (n)	Brown % (n)	Yellow % (n)		p
Negative	57.6 (87)	15.2 (23)	26.5 (40)	0.7 (1)		0.264
Positive	69.7 (23)	3 (1)	27.3 (9)	0		
	Education					
	Illiterate % (n)	Incom- plete high school % (n)	Com- plete high school % (n)	Incomplete higher % (n)	Graduated % (n)	p
Negative	1.3 (2)	29.1 (44)	23.2 (35)	17.9 (27)	28.5 (43)	0.278
Positive	0	21.2 (7)	39.4 (13)	9.1 (3)	30.3 (10)	

Considering configuration of exposure and preventive measures, we found that 42.2% of participants who did not have the disease during follow-up reported that they respected social isolation, 31.3% reported that they only went out to work and 14.3% reported that they attended hospital environment. For individuals who presented the disease during the follow-up 21.2% reported that they respected the social isolation, 27.3% reported that they went out to work and 42.14% reported that they attended hospital environments during the follow-up ($p = 0.004$).

According to the profession of the participants, it was found that for those who did not have the disease during the follow-up 31.8% had a profession associated with low exposure, 51.0% high exposure and only 5.3% were health professionals. Among the participants who had the disease, 15.2% had a profession considered to be of low exposure, 27.3% had a profession of high exposure and 45.5% were health professionals.

Participants also answered a question related to close contact with other people and in this analysis we found that individuals who did not have SARS-CoV-2 infection during follow-up, 41.1% reported that they maintained contact only with close family members, 18, 5% family members and co-workers and 37.1% reported that they had contact with health professionals. Among the participants who had the infection, 12.1% reported that they only had contact with family members, 9.1% with family members and co-workers and 75.8% reported that they had contact with health professionals ($p = 0.001$).

Considering the use of a mask 98% of our participants reported using it, so we did not consider this analysis. Hand hygiene with alcohol in gel or water and soap and the frequency of this hygiene was not statistically significant in our sample, however we emphasize that most of the research participants reported taking these preventive measures (Table 3).

Table 3 - Incidence of SARS-CoV-2 infection according to exposure settings and preventive measures.

Test Result	Exposure variables and preventive measures					
	Exposure setting					p
	Isolation % (n)	External work % (n)	Public transportation % (n)	Hospital environment % (n)	Not respect the isolation % (n)	
Negative	42.2 (62)	31.3 (46)	8.8 (13)	14.3 (21)	3.4 (5)	0.004
Positive	21.2 (7)	27.3 (9)	9.1 (3)	42.4 (14)	0	
	Profession					p
	Minimal exposure % (n)	Low exposure % (n)	High exposure % (n)	Health professional % (n)		
Negative	11.9 (18)	31.8 (48)	51 (77)	5.3 (8)		<0.0001
Positive	12.1 (4)	15.2 (5)	27.3 (9)	45.5 (15)		
	Close contact					p
	No information or close contacts% (n)	Fam-ily and social isolation % (n)	Co-workers or other environ-ments % (n)	Health professionals % (n)		
Negative	3.3 (5)	41.1 (62)	18.5 (28)	37.1 (56)		0.001
Positive	3 (1)	12.1 (4)	9.1 (3)	75.8 (25)		
	Face mask					p
	No % (n)	Yes % (n)				
Negative	1.3 (2)	98.7 (148)			0.505	
Positive	0	100 (33)				
	Alcohol gel					p
	No % (n)	Yes % (n)				
Negative	4 (6)	96 (143)			0.788	
Positive	3 (1)	97 (32)				
	Frequency of alcohol gel use					p
	Low % (n)	Average % (n)	High % (n)			
Negative	11.9 (17)	31.5 (45)	56.6 (81)		0,013	
Positive	6.2 (2)	9.4 (3)	84.4 (27)			
	Cleaning with soap and water					p
	No % (n)	Yes % (n)				
Negative	1.3 (2)	98.7 (147)			0.503	
Positive	0	33 (100)				
	Sanitation Frequency					p
	Low % (n)	Average % (n)	High % (n)			
Negative	6.1 (9)	23.8 (35)	70.1 (103)		0.205	
Positive	12.1 (4)	12.1 (4)	75.8 (25)			

DISCUSSION

We conducted a prospective cohort study in which 343 participants were included and followed for six months to assess incidence by SARS-CoV-2 and risk factors associated. Considering our significant results, we found that the incidence of COVID-19 was statistically associated with the use of medications (hydroxychloroquine and Ivermectin). In this sense, we found that participants who used these drugs preventively had a twice as high incidence compared to those who did not use these drugs. During the pandemic, we are experiencing an incessant search for effective treatments for the disease. However, to date, there is still no effective medication to prevent or treat the infection. Several studies have been carried out considering these two drugs, there is already sufficient evidence that indicates that Hydroxychloroquine does not prevent infection and has no effect on the treatment of the disease or on the reduction of mortality^{5,6,7}.

Ivermectin has been used as antiparasitic to treat onchocerciasis, strongyloidiasis, and lymphatic filaria, among other parasitoses. A study by Caly et al. reported that ivermectin inhibited the replication of SARS-CoV-2 *in vitro* and suggested to develop further investigation *in vivo*⁸. There is a study on ivermectin, a pilot clinical trial that found no significant differences in detection of the SARS-CoV-2 RNA from nasopharyngeal swabs at days four and seven after treating with a single oral dose of 400 mcg/Kg of ivermectin ($n = 12$) or placebo ($n = 12$)⁹. In 2006 was reported the case of a 20-year-old patient with microfilaria symptoms, treated with a single dose of ivermectin of 300 ug/kg, who developed severe hepatitis¹⁰. Moreover, more recently research related to ivermectin in COVID-19 has demonstrated serious methodological limitations resulting in very low certainty of the evidence, and continues to grow.

In our study, we did not find significant differences considering the ABO system, however, in our follow-up, the most prevalent blood type in individuals who did not have the infection was O, while in the participants who had the disease during the follow-up was A. COVID-19 with the ABO system has been discussed in the literature, some studies have indicated that the entry of the virus seems to occur more easily in cells of people with type A blood, indicating that these individuals are more prone to infection and some studies have also shown that these individuals are also more likely to develop more severe forms of the disease¹¹⁻¹³.

Risk factors associated with the severity of the disease include aging, diabetes, immunosuppression and organ failure¹⁴. The recognition of risk factors for morbidity and mortality is important to determine prevention strategies, as well as to direct high-risk populations to effective therapeutic measures. Interestingly, in our cohort, individuals who tested positive for COVID-19 had a lower average age than individuals who did not develop the

disease. Although the difference found was not significantly statistical, it is a relevant data that deserves attention. Some studies have also shown that although younger patients are considered to be at a lower risk of disease severity, in our study the participants who had the infection were all mild, so although the incidence of the disease was higher in younger individuals. None of our participants had a severe infection, which corroborates the data in the literature^{15,16}.

The exposure configuration, close contact and profession were some of the subtypes of risk factors that were observed in the study as having statistical significance considering the incidence of the infection. Of the individuals who tested positive for COVID-19, 42.4% attended the hospital environment for some reason. In addition, 75.8% of these individuals reported having had some type of contact with health professionals. Finally, when comparing the profession of participants who tested positive for COVID-19, 45.5% of participants worked in health sectors. The literature has already shown that health professionals, especially those who work in hospital environments, have a higher risk of infection. In Brazil and in other countries, thousands of health professionals have to leave their positions due to COVID-19 infection and many have died¹⁷.

Health professionals, who make up a group composed of different professionals, work directly in the care of patients infected with COVID-19 and, for this reason, are part of a specific risk group for infection. The current pandemic revealed the fragility of the health sectors in terms of guaranteeing the safety of the professionals involved in the treatment of infected individuals. During the performance of procedures in the patients' pathways, health professionals are exposed to a high risk of acquiring the disease, configuring what is recognized as a biological exposure^{18,19}. Confirming this increased risk, in our cohort, most participants who tested positive for COVID-19 are health professionals or are people who have had contact with these professionals. In a literature review that aimed to identify and analyze the national and international scientific production about occupational health and safety of health workers during the COVID-19 pandemic, it is concluded that there is a lack of up-to-date knowledge and failures in the protection of workers' health²⁰.

The use of masks is among the non-pharmaceutical intervention measures that can be implemented effectively at minimal cost and without drastically interrupting social practices. In our work, almost 100% of the participants reported the use of the mask. The standards for wearing a mask vary significantly between countries. However, due to the high consumption of hospital masks by the population, the National Health Surveillance Agency (ANVISA) and the WHO have recommended the use of non-professional masks, so that the use of fabric masks acquires importance in view of the possibility of their potential preventive, in addition to collaborating with the

reduction in the search for hospital masks, which should be primarily aimed at health professionals who provide assistance to critically ill patients^{21,22}. Li et al. (2020), conducted a study that combined mathematical models and existing scientific evidence to assess the potential impact of wearing masks in public to combat the COVID-19 pandemic. The authors concluded that the use of masks can be effectively combined with social distance to flatten the epidemic curve²³. Studies that evaluated effective protection measures during the pandemic were extremely important, in this sense an application to provide guidance on these safety measures was developed by Brazilian researchers and validated for use²⁴.

Limitations are small sample size that could impair in the cause-and-effect inferences, recall biases and the fact that the study was conducted in a very specific population impair the extrapolations of the results to larger populations.

The mechanisms underlying the associations that we find are not yet fully elucidated. However, we believe that

identifying and quantifying the strength of the association between pre-existing conditions of exposure, profession and preventive measures is important in helping to contain the pandemic by COVID-19.

CONCLUSION

In conclusion, our study confirms that the use of drugs such as ivermectin and hydroxychloroquine do not have a preventive effect on the development of COVID-19. In addition, exposure to the hospital environment and contact with health professionals are factors that increased the chance of SARS-CoV-2 infection. The extreme complexity of the disease and the level of care required by patients with COVID-19 infection represent a major challenge that can quickly overload hospital systems. Recognizing the factors that favor contamination, as well as those that prevent it is extremely important at this time, since it contributes to the establishment of effective measures to contain the SARS-CoV-2 virus.

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