Revista de Ciencias Médicas de Pinar del Río

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2022; 26(3) Mayo-Junio e5511

ORIGINAL ARTICLE

Chronic diseases and smoking in SARS-CoV-2 infection in Pinar del Rio

Enfermedades crónicas y tabaquismo en la infección por SARS-CoV-2 en Pinar del Río

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Received: February 25, 2022
Accepted: April 19,2022
Published: June 15, 2022

Cite as: Valdés-Lanza L, Orraca-Castillo O, Lardoeyt-Ferrer R, Orraca-Castillo M, Martínez-Carmona Y, Miló-Valdés CA. Chronic diseases and smoking in SARS-CoV-2 infection in Pinar del Río. Rev Medical Sciences [Internet]. 2022 [cited: date of access]; 26(3): e5511. Available from: http://revcmpinar.sld.cu/index.php/publicaciones/article/view/5511

ABSTRACT

Introduction: the world deals with a new pandemic because of SARS-CoV-2 outbreak initiated in Wuhan, China in December 2019. Host genetic differences and risk factors such as: personal history, lifestyles and environmental factors may contribute to the marked inter-individual clinical variability in COVID-19.
Objective: to identify personal pathological history (chronic diseases and smoking) associated with SARS-CoV-2 infection.
Methods: analytical, observational study of cases and controls in Pinar del Rio in the period from March 2020 to March 2021. Personal history of chronic diseases and smoking as an environmental factor were explored.
Results: personal pathological history of allergies and asthma constituted risk factors to develop symptoms. History of active smoking is presented as a risk factor for infection.
Conclusions: the contribution of personal pathological history (allergy and asthma) and environmental (active smoking) to SARS-CoV-2 infection and to the development of symptoms in COVID-19 patients in Pinar del Rio is confirmed.

Keywords: Covid-19; SARS-COV-2; Coronavirus; Chronic Disease; Smoking.

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2022; 26(3) Mayo-Junio e5511

RESUMEN

Introducción: el mundo enfrenta una nueva pandemia ante el brote de SARS-CoV-2 iniciado en Wuhan, China en diciembre de 2019. Las diferencias genéticas del hospedero y factores de riesgo como: antecedentes personales, estilos de vida y factores ambientales pueden contribuir a la marcada variabilidad clínica interindividual en la COVID-19.
Objetivo: identificar los antecedentes patológicos personales (enfermedades crónicas y tabaquismo) asociados a la infección por SARS-CoV-2.
Métodos: estudio observacional analítico de casos y controles en Pinar del Río en el período comprendido entre marzo de 2020 a marzo de 2021. Se exploraron antecedentes personales de enfermedades crónicas y el antecedente de tabaquismo como factor ambiental.
Resultados: los antecedentes patológicos personales de alergia y asma constituyeron factores de riesgo para desarrollar síntomas. Se presenta el antecedente de fumador activo como un factor de riesgo para la infección.
Conclusiones: se demuestra la contribución de los antecedentes patológicos personales (alergia y asma), y ambientales (fumador activo) a la infección por SARS-CoV-2 y al desarrollo de síntomas en pacientes de COVID-19 en Pinar del Río.

Palabras clave: Covid-19; SARS-COV-2; Coronavirus; Enfermedades Crónicas; Tabaquismo.

INTRODUCTION

More than 100 years after the 1918 influenza pandemic that caused 50 million deaths, the world is facing a new pandemic with the outbreak of SARS-CoV-2 causing COVID-19 that has spread to all continents.[1] The new coronavirus appeared at the end of the 1918 influenza pandemic in Pinar del Rio.

The new coronavirus appeared at the end of December 2019, in Wuhan, a commercial city in central China.[1]

SARS-CoV-2 disease is clinically similar to other CoV infections in humans. Eighty percent of CoVID-19 sufferers have a mild respiratory clinical picture and are more common in children, adolescents and young adults. Fifteen percent present a severe picture, and 5 % require intensive care and are frequently seen in those over 65 years of age and in persons with non-communicable diseases such as diabetes mellitus, chronic obstructive pulmonary disease, cardiovascular or cerebrovascular disease, and arterial hypertension.[2]

Mortality from the disease affects 1 in 1,000 infected persons younger than 50 years with no underlying conditions, but more than 1 in 10 patients older than 80 years with multiple comorbidities.[2]

In SARS-CoV-2, host genetic variation may be a key factor influencing susceptibility, severity, and overall clinical outcomes of COVID-19 patients. In addition, gene expression also differs according to an individual's sex, lifestyles, and biological age.[3]

Aging is associated with the accumulation of molecular and cellular changes that reduce certain biological functions and decrease the immune response. It is also associated with an increased incidence of non-communicable diseases and low-grade inflammation.[4]

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2022; 26(3) Mayo-Junio e5511

On the other hand, the environment also has an impact on susceptibility to infection. It comprises all non-genetic factors that modulate the phenotype and may include both random environmental factors (climatic, geographic, demographic and socioeconomic) and lifestyle (diet, smoking, alcoholism and physical activity), which can be modified by the individual.[5]

Over the last decades, evidence has linked short- and long-term exposures to environmental pollution to the development of respiratory diseases and mortality from them.[6]

Permanent exposure to particulate matter compromises respiratory health status and weakens immunity, which promotes exposure to infectious particles and stimulates stress, which also favors epidemiological peaks of respiratory disease. In SARS-CoV-2 infection, there is evidence of association with environmental pollution.[6]

Smoking is a risk factor for many viral and bacterial respiratory infections that increase their severity. It has been shown that smokers, as well as those exposed to smoke (passive smokers), are more likely to contract influenza, pneumonia and tuberculosis. It is also observed that smokers had a higher morbidity and mortality during the MERS outbreak originating from MERS-CoV.[7]

In this sense, smoking could play a deleterious effect on SARS-CoV-2 infection. Active or passive smokers could have a greater vulnerability to infection or an unfavorable evolution of COVID-19.

In any disease, the combined effect of genetic and environmental factors is observed. SARS-CoV-2 infection and COVID-19 depend on SARS-CoV-2 interaction/host/environmental factors or history.[3] Hence, the present investigation aims to identify personal pathological history (comorbidities and smoking as an environmental factor) associated with SARS-CoV-2 infection and clinical course of COVID-19 patients.

METHODS

An epidemiological, observational analytical investigation of cases and controls was performed; according to four groups: cases/controls, asymptomatic/controls, symptomatic/controls, symptomatic/asymptomatic; for all analyses. The research was carried out in the municipalities affected by COVID-19 in Pinar del Río province during the period from March 2020 to March 2021 (Pinar del Río, Consolación, San Luis, Guane, Viñales, La Palma and Sandino).

A sample size of 450 individuals was taken, including 150 cases of autochthonous transmission with diagnosis of COVID-19 by polymerase chain reaction (PCR) and 300 controls selected from the same population that gave rise to the cases, paired in sex and age group.

To obtain the controls, a simple random sampling was also performed, matched by sex and age, from the same population that gave rise to the cases, complying with the 1:2 ratio.

A questionnaire was applied in primary health care that collected the general data of the cases, personal history of non-communicable diseases, and smoking as an environmental factor. (Table 1)

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Table 1. Variables used to explore personal history in the study of risk factors in SARS-CoV-2 infection and in the clinical presentation of COVID-19 in Pinar del Río.

Joint or general variables	Variables
Personal pathological history of NCD	Hypertension, diabetes, obesity, asthma, allergy, other cardiac diseases, vascular diseases, autoimmune diseases, chronic obstructive pulmonary disease (COPD).
Smoking (environmental factor)	Active smoker, passive smoker, former smoker.

In the analysis of the frequency of personal history of communicable diseases and smoking, an analysis of association was performed for each variable individually, using Pearson's Chi-square test of homogeneity and independence, with a significance level equal to 0.05. The Odds ratio and its confidence interval were determined as the magnitude of association.

The principles of medical ethics and the aspects established in the Helzinki Declaration were complied with.

RESULTS

Analysis of personal history of noncommunicable diseases in SARS-CoV-2 infection and the clinical presentation of COVID-19

Of the nine diseases explored in the frequency analysis of personal history of non-communicable diseases, it was observed that arterial hypertension (26,9 %), allergy (20,0 %), autoimmunity (14,9 %) and asthma (12,9 %) were the entities with the highest percentages for both cases and controls. In the cases, these morbidities were more frequent in the group of symptomatic patients compared to the asymptomatic ones.

The frequency of allergy, asthma and autoimmune diseases was higher in cases than in controls with values of 24,7 %, 15,3 %, 14,7 % respectively, although only the proportions of allergy and asthma showed significant results (Fig. 1).

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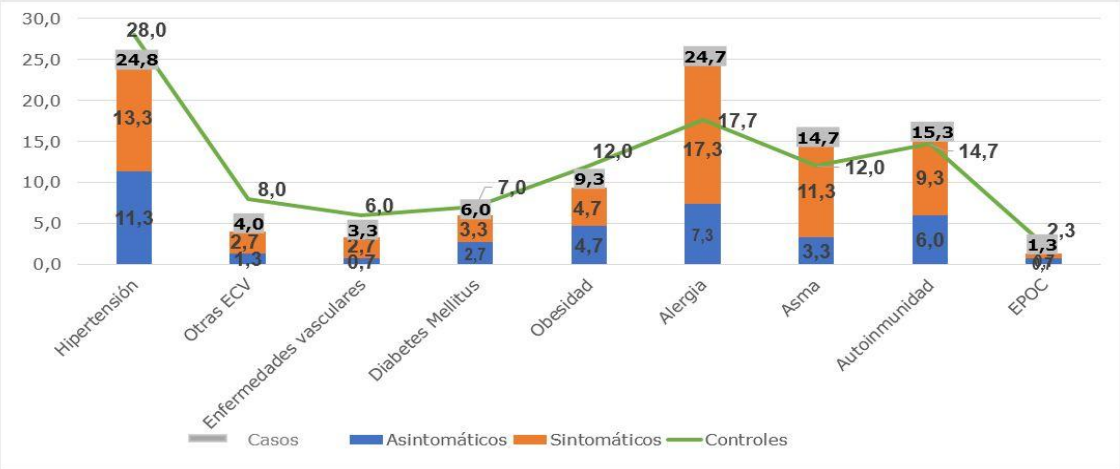

Fig. 1 Frequency distribution of non-communicable diseases in cases and controls in the study of risk factors in SARS-CoV-2 infection and in the clinical presentation of COVID-19.

In the analysis of the case/control and asymptomatic/control groups, no significant results were found for any of the comorbidities evaluated. However, for the symptomatic/control and symptomatic/asymptomatic groups, significant results were found for allergy and asthma. For allergy, in the symptomatic/control group a predominance was found in symptomatic cases with an OR of 2.054 and for asthma an OR of 1.833 was observed. In the symptomatic/asymptomatic group allergy and asthma also predominated in symptomatic for an OR of 2.241 and 3.096 respectively.

Table 2. Frequency analysis of history of allergy and asthma in the study of risk factors in SARS-CoV-2 infection and in the clinical presentation of COVID-19, Pinar del Río.

ENT	Cases		Controls		Total		X^2p/p	OR	OR IC 95 %	
	No.	%	No.	%	No	%			LI	LS
Allergy	37	24,7	53	17,7	90	20,0	3,063/0,080	1,526	0,949	2,454
Asthma	22	14,7	36	12,0	58	12,9	0,633/0,426	1,260	0,712	2,231
	Asymptomtics		**Controls**							
Allergy	11	16,7	53	17,7	64	17,5	0,037/0,846	0,932	0,457	1,900
Asthma	5	7,6	36	12,0	41	11,2	1,065/0,302	0,601	0,227	1,595
	Symptomatics		**Controls**							
Allergy	26	30,6	53	17,8	79	20,6	6,781/0,009	2,054	1,187	3,554
Asthma	17	20,0	36	12,1	53	13,8	4,587/0,049	1,833	0,971	3,461
	Symptomatic		**Asymptomatic**							
Allergy	26	31,0	11	16,7	37	24,7	4,059/0,44	2,241	1,012	4,967
Asthma	17	20,2	5	7,6	22	14,7	4,735/0,030	3,096	1,077	8,897

Symbology: NCD: non-communicable diseases, X2p: Pearson's Chi-Square, OR: Odds Ratio, OR 95 % CI: 95 % confidence interval, p: probability.

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Analysis of personal smoking history in SARS-CoV-2 infection and clinical presentation of COVID-19.

Of the three smoking variables analyzed: active smoker, passive smoker, ex-smoker; results of statistical significance were obtained only for the history of active smoking.

The most representative results are exposed, the rest shows the frequency of active smokers in cases and controls in the study of risk factors associated to SARS-CoV-2 infection and to the course of COVID-19 in Pinar del Río, four groups are analyzed (case/control, asymptomatic/control, symptomatic/control, symptomatic/asymptomatic). (Table 3).

A predominance was found in the cases with respect to the controls for the variable active smoker, which showed an OR 1.427.

Table 3. Frequency analysis of active smoking as an environmental factor in the study of risk factors in SARS-CoV-2 infection and in the clinical presentation of COVID-19.

Environental Factors	Cases		Controls		Total		X^2p/p	OR	OR IC 95%	
	No	%	No	%	No	%			LI	LS
Smoker active	9	6,0	39	13,0	48	10,7	5,142/0,023	1,427	0,201	1,907
	Asymptomatics		**Controls**							
Smoker active	3	4,5	39	13,0	42	11,5	3,807/0,051	0,319	0,095	1,065
	Symptomatics		**Controles**							
Smoker active	6	7,1	39	13,1	45	11,7	2,318/0,128	0,504	0,206	1,235
	Symptomatics		**Asymptomatics**							
Smoker active	6	7,1	3	4,5	9	6,0	0,442/0,506	1,615	0,388	6,717

Symbology: X2p: Pearson's Chi Square, OR: Odds Ratio, OR 95% CI: 95% Confidence Interval, p: probability.

An individual with a history of being an active smoker has a higher risk of presenting the infection when compared to non-smokers.

DISCUSSION

Since the emergence of SARS-CoV-2 and COVID-19, the highest mortality of cases is observed in patients with non-communicable diseases, and in those over 60 years of age are considered populations ten times more likely to die.[8]

A Medscape meta-analysis compiling studies from the year 2020 shows the prevalence of arterial hypertension and its exponential increase with age together with other cardiovascular diseases that contribute to the severe and critical evolution of cases with COVID-19.[9]

In China, with the first 44,672 confirmed cases, the case fatality rate reached 4,7 %. Studies in these cases show that patients without comorbidities have a lower case fatality rate (0,9 %). For those with cerebrovascular disease, diabetes mellitus and arterial hypertension have higher rates (10,5 %, 7,3 %, 6,5 % respectively).[10]

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Arterial hypertension is a health problem that affects 45 % of the world population, and in Cuba 30 % of the population. In Pinar del Río, the prevalence of arterial hypertension is 269,9 per 1,000 inhabitants, which is higher than in the rest of the provinces.[11]

In the study by Zhang et al, arterial hypertension is the most frequent comorbidity with 30% of the patients, it is also associated with lethality and states that hypertensive patients have a 3.48 times higher risk of suffering complications.[12]

Another investigation considers arterial hypertension as a risk factor for severe or fatal COVID-19, without clarifying the underlying mechanism. However, it hypothesizes that the virus enters the host cell through the angiotensin-converting enzyme receptor 2 (ACE2) and endocytosis of the virus-ACE2 complex reduces its function. All of this leads to overactivation of the renin/ angiotensin/ aldosterone complex; and complications such as acute respiratory distress syndrome and multiorgan failure.[13]

In this research, arterial hypertension constituted one of the most frequent diseases due to its high rate in the population of Pinar del Río, with no predominance of cases with respect to controls. It is necessary to emphasize that the study is carried out with the first cases of COVID-19 in Pinar del Río province, months after the beginning of the pandemic in most of the countries. Therefore, the sample is scarce with a reduced number of symptomatic patients.

The higher proportion of autoimmune diseases and rheumatologic manifestations in the cases could complicate the clinical course of the patients, given that robust immune reactions participate in the pathogenesis of both diseases.[14]

Results from a cross-sectional study in northeastern Italy indicate that patients with autoimmune diseases have infection rates similar to the general population in contrast to the research presented.[15]

However, an exaggerated immune response is known to mediate the more severe complications induced by SARS-CoV-2. Results from studies in China and Spain agree that patients with autoimmune diseases could be more prone to SARS-CoV-2 infection and have a more severe course when compared to controls.[15] In the current study, even with a high frequency of autoimmunity, no statistical association is observed. The lack of description of the type of autoimmune disease is a limitation.

Historically, the relationship between viral infections, immune response, allergy and asthma has been proposed. Several viruses, such as rhinoviruses and respiratory syncytial virus, have been the main focus of research.[16]

Asthma affects 4,4 % of the world population and allergic diseases increase with time and the industrial revolution. In Cuba, studies show that 45 % of the adolescent or young adult population suffers from allergies and that one out of every two people is asthmatic.[17] The prevalence of asthma in Pinar del Río is 8,9 per 100 inhabitants,[18] which could explain the frequency of this disease in the study population.

In respiratory allergies, genetic predisposition, deficient antiviral response with reduced levels of INF-β and INF-γ, deterioration of immune cells, together with epithelial damage and cytokine response may contribute to increased susceptibility to viral infection, incomplete viral clearance and persistence of airway inflammation, leading to adverse clinical outcomes.[19] A study in 182 children with COVID-19, shows that 43% were allergic, with lower elevation of acute phase reactants and no deaths reported. [20]

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In previous respiratory virus epidemics, there are contrasting results regarding the influence of asthma on clinical course and prognosis. Data from the 2003 SARS epidemic report that asthmatics have a reduced susceptibility to the coronavirus, with good prognosis while, in 2009, the H1N1 pandemic associates asthma with severe disease and need for ventilation.[19]

Furthermore, the study findings are consistent with the U.S. weekly mortality and morbidity report showing that 27 % of patients with moderate/severe COVID-19 symptomatology had asthma, which is higher than the U.S. asthma prevalence rate of 10 %.[21]

According to the World Health Organization (WHO), tobacco causes the death of 8 million people worldwide annually, and more than 7 million of these deaths are from direct tobacco use.[22]

Smoke exposure modulates innate and adaptive immune responses in humans. Systemic levels of inflammatory markers in smokers are reduced when compared to non-smokers.[23]

Graufi et al. in their review state that the vast majority of patients hospitalized for COVID-19 are non-smokers,[23] contrary to the findings obtained in the study. However, the study by Graufi et al. refers only to hospitalized patients. The prevalence of smoking in asymptomatic non-hospitalized patients is not known, which is a bias in the research.[23]

For its part, the WHO highlights the likelihood that smokers are more vulnerable to infection by the new CoV because of cigarette handling and contact of cigarettes with lips,[24] which is consistent with the results achieved in the study.

There are several reasons to assume that smokers are at higher risk for acquiring SARS-CoV-2 infection:

(a) There is evidence that infections by other viruses of the same family, such as MERS-CoV-2 affect smokers more frequently. [24]
b) There is evidence in the medical literature that respiratory infections caused by bacteria or viruses are more frequent in active smokers [24]
c) Toxic substances in tobacco smoke damage the immunologic, cellular and humoral mechanisms of the upper respiratory system. [24]
d) In smokers, the hand-mouth movement is repeated frequently, making them more likely to suffer from an orally transmitted infection. [24]It is also important to note that social isolation and social isolation are also important in smokers.

It is also important to note that social isolation and the quarantined state of the home, which encourages active smokers to expose non-smokers to secondhand smoke. Unfortunately, the latter can cause homologous harms to passive smokers.[7]

The research results demonstrate the contribution of personal (allergy and asthma) and environmental (active smoking) pathological history to SARS-CoV-2 infection and symptom development in COVID-19. Much remains to be clarified regarding this relationship, so more in-depth national and international cohort and experimental studies are required.

However, it is confirmed that host factors play a crucial role in SARS-CoV-2 infection: genes and comorbidities; those inherent to the virus; lifestyles and environmental factors (smoking) that regulate the clinical heterogeneity and evolution of patients affected by COVID-19.

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Conflict of Interest
The authors declare that there is no conflict of interest.

Authors' Contribution
LVL and OOC: were responsible for conceptualization, research, project management, supervision, visualization, writing - original draft, writing - revision and editing.
RLF and MOC: responsible for conceptualization, research, visualization, writing - original draft, writing - review and editing.
YMC and CAMV: participated in conceptualization, research, writing - original draft. All authors approved the final manuscript.

Funding
The authors did not receive funding for the development of this research.

Additional Material
Additional material to this article can be consulted in its electronic version available at: www.revcmpinar.sld.cu/index.php/publicaciones/rt/suppFiles/5511

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