

ORIGINAL ARTICLE

Chronology and symptoms of the new coronavirus disease 2019

A cronologia e os sintomas da doença do novo coronavírus 2019

La cronología y síntomas de la nueva enfermedad por coronavirus 2019

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ABSTRACT

The new coronavirus disease (COVID-19) is clinically characterized by the occurrence of flulike syndrome, with the presentation of symptoms such as fever, cough, odynophagia, dyspnea and respiratory distress. The disease can progress quickly to acute respiratory distress syndrome. The aim of the study is to show the signs and symptoms that constitute the clinical picture of COVID-19, in addition to describing the order of appearance and duration of the most prevalent symptoms. This is a retrospective quantitative study based on the medical records analysis of symptomatic patients with confirmed cases of COVID-19, which seeks to carry out an analysis of the occurrence and duration of symptoms. The most observed symptoms in the study population were: fever, asthenia, headache and cough, with the occurrence of these symptoms being more frequent in the early days of the disease. As for duration, the symptoms that lasted the longest were cough, ageusia and anosmia. The latter two usually occurred in association with each other. The occurrence and duration of symptoms in our study were similar to those of published studies, except for neurological symptoms, which had a higher occurrence in the population of our study.

Keywords: Coronavirus Infections; Signs and Symptoms; Chronology; 2019 novel coronavirus Outbreak.

RESUMO

A nova doença coronavírus (COVID-19) é clinicamente caracterizada pela ocorrência de síndrome semelhante à gripe, com apresentação de sintomas como febre, tosse, odinofagia, dispnéia e dificuldade respiratória. A doença pode progredir rapidamente para síndrome do desconforto respiratório agudo. O objetivo do estudo é mostrar os sinais e sintomas que constituem o quadro clínico da COVID-19, além de descrever a ordem de aparecimento e a duração dos sintomas mais prevalentes. Trata-se de um estudo quantitativo retrospectivo baseado na análise de prontuários de pacientes sintomáticos com casos confirmados de COVID-19, que visa realizar uma análise da ocorrência e duração dos sintomas. Os sintomas mais observados na população estudada foram: febre, astenia, cefaleia e tosse, sendo a ocorrência destes sintomas mais frequente nos primeiros dias da doença. Quanto à duração, os sintomas que mais duraram foram tosse, ageusia e anosmia. Os dois últimos geralmente ocorriam em associação. A ocorrência e a duração dos sintomas em nosso estudo foram semelhantes às dos estudos publicados, exceto pelos sintomas neurológicos, que tiveram maior ocorrência na população de nosso estudo.

Palavras-Chave: Infecções por Coronavírus; Sinais e Sintomas; Cronologia; Doença por Coronavírus 2019-nCoV.

RESUMEN

La enfermedad del nuevo coronavirus (COVID-19) se caracteriza clínicamente por la aparición de un síndrome gripal, con la presentación de síntomas como fiebre, tos, odinofagia, disnea y dificultad respiratoria. La enfermedad puede progresar rápidamente al síndrome de dificultad respiratoria aguda. El objetivo del estudio es mostrar los signos y síntomas que constituyen el cuadro clínico del COVID-19, además de describir el orden de aparición y duración de los síntomas más prevalentes. Se trata de un estudio cuantitativo retrospectivo basado en el análisis de historias clínicas de pacientes sintomáticos con casos confirmados de COVID-19, que busca realizar un análisis de la ocurrencia y duración de los síntomas. Los síntomas más observados en la población de estudio fueron: fiebre, astenia, dolor de cabeza y tos, siendo más frecuente la aparición de estos síntomas en los primeros días de la enfermedad. En cuanto a la duración, los síntomas más prolongados fueron tos, ageusia y anosmia. Los dos últimos generalmente ocurrieron en asociación entre sí. La ocurrencia y duración de los síntomas en nuestro estudio fueron similares a los de los estudios publicados, excepto por los síntomas neurológicos, que tuvieron una mayor ocurrencia en la población de nuestro estudio.

Palabras-Clave: Infecciones por Coronavirus; Signos y Síntomas; Cronología; Enfermedad por Coronavirus 2019-nCoV

INTRODUCTION

After the occurrence of hundreds of cases of pneumonia with unknown etiology on January 30, 2020, the World Health Organization (WHO) announced an international public health emergency. In February of the same year the causative agent was discovered, known as coronavirus of severe acute respiratory syndrome 2 (SARS-Cov-2). The disease became known as the new coronavirus disease (COVID-19), and the international health status was declared a pandemic on March 11, 2020.^{1,2}

The flu syndrome was identified by health authorities as the most common clinical presentation of COVID-19, characterized by an acute respiratory condition, recognized by feverish sensation or fever, accompanied by cough and / or odynophagia and / or runny nose and / or dyspnea and / or respiratory distress.³ In his research, Singhal (2020)⁴ mentions fever, odynophagia, myalgia, dry cough, asthenia and dyspnea as recurrent symptoms, emphasizing that they are nonspecific, common to several high frequency diseases, and are not mandatory as a symptom in all patients. In a study of 55,924 confirmed patients with SARS-Cov-2 infection, the following signs and symptoms were observed: fever (88.7%), cough (67.8%), asthenia (38.1%), sputum (33.4%), dyspnea (18.6%), myalgia or arthralgia (14.8%), odynophagia (13.9%), headache (13.6%), chills (11.4%), vomiting or nausea (5%), nasal congestion (4.8%) and diarrhea (3.8%).⁵ Regarding olfactory and gustatory dysfunctions, a frequency between 22.7% and 88.8% was found in the literature.⁶

The clinical spectrum of COVID-19 is broad and can be classified into 5 severity groups: asymptomatic, mild, moderate, severe and critical. Among symptomatic patients, 80% have a mild or moderate condition; 15% severe form and 5% tend to evolve to the critical form, with the possibility of rapid progression to Acute Respiratory Distress Syndrome (ARDS) (Bulut & Kato, 2020). Among patients who manifest the critical form, 50% die. In the elderly and / or immunosuppressed, the disease can present in an atypical way.⁸⁻¹⁰

The aims of this study are to point out the signs and symptoms that constitute the clinical spectrum of SARS-Cov-2

infection, as well as to describe the order of appearance and duration of each sign and symptom, using a population of 369 patients with laboratory confirmed cases of COVID-19.

METHODS

This is a retrospective quantitative study of medical records analysis, which observed 369 outpatients, symptomatic and with confirmed cases of COVID-19 from the city of Paranaíba - PI. It aims to raise frequency, duration and characterization of the signs and symptoms associated with the disease. There was no significant variation in gender in the population, 50.1% were women; and as for age, there was a variation from 1 to 93 years, with an average of 38.3 years, considering that 5% were up to 18 years old, 85% between 18 and 59 years old and 10% over 60 years old.

These patients were followed up by a remote monitoring team for a minimum of 14 days until they were asymptomatic, if necessary. For the identification of days throughout the text, the abbreviation "D" for day will be used, followed by the number referring to the day counted since the origin of the symptoms. The observational period was from April 1st to June 15th, 2020.

The data were collected and stored in the Excel program and then the calculations were performed with the statistical program SPSS, version 25. The data were tabulated and descriptive statistics were also performed with frequencies and chi-square distribution test.

RESULTS

The data referring to signs and symptoms were tabulated individually; the frequencies were calculated, organized and detailed regarding the days of follow-up. The parameterization of time took into account 15 days, a period in which the number of signs and symptoms was significant; after this period, the frequency of most signs and symptoms approached zero. Abdominal pain, chest pain, eye pain, arthralgia and anorexia do not appear on the table due to the low occurrence. It can be seen that some symptoms, in fact, have a higher prevalence than others, based on the outputs from chi-square statistical tests with $p < 0.05$, on each of the days observed.

In D1, the most identified signs and symptoms, in order of prevalence, are: fever, headache, cough, asthenia and myalgia, all present in more than 100 cases; followed by anosmia, ageusia, odynophagia, diarrhea and runny nose, present in more than 50 cases; in addition, cases of dyspnea, sneezing, chills, nausea and vomiting are identified. This pattern of appearances and prevalence continues until D5; when between D6 and D7 the cases are reduced to approximately half, with a tendency to be excluded on subsequent days. Running away from the pattern, the cases of anosmia and ageusia do not reduce until D7, and it is possible to verify the maintenance of these symptoms; in many cases, they appear between D7 and D8.

DISCUSSION

Fever was the most reported symptom, varying from 1 to 5 days, but in a non-continuous way, with irregular intervals of 3 to 9 days. The association of this complaint with other symptoms is common: 26.7% reported an association with myalgia, 26.2% with asthenia, and 4.3% with chills. Still

Tabela 1. Frequência dos sintomas da COVID-19 distribuídos nos dias.

Sinais/Sintomas	Total (n)	Total (%)	Dias														
			1º	2º	3º	4º	5º	6º	7º	8º	9º	10º	11º	12º	13º	14º	15º
Febre	232	62,8	213	203	197	182	174	154	133	110	96	83	74	60	42	26	0
Asthenia	191	51,7	117	115	120	112	113	99	98	84	79	77	65	58	42	28	1
Cefaleia	191	51,7	157	142	140	138	129	121	108	100	84	74	67	52	40	32	24
Tosse	173	46,8	126	132	123	116	113	108	99	87	87	78	74	59	51	38	34
Anosmia	153	41,4	80	86	85	86	82	92	100	102	91	79	68	56	51	38	28
Mialgia	134	36,3	115	114	104	93	72	71	56	54	40	38	35	29	21	14	9
Ageusia	125	33,8	78	79	77	77	80	82	85	84	77	52	49	49	46	28	19
Diarréia	97	26,2	55	57	56	56	54	54	41	40	32	28	28	22	19	13	6
Coriza	86	23,3	54	73	73	55	65	51	46	36	32	31	26	14	14	8	7
Odinofagia	79	21,4	74	75	72	72	70	62	60	47	42	40	34	24	19	11	8
Dispneia	55	14,9	32	31	29	31	30	30	26	29	25	23	19	19	16	12	0
Náusea	28	7,5	9	11	6	5	6	4	6	8	12	3	3	3	0	0	0
Espirro	19	5,1	14	11	11	8	7	6	6	4	3	3	1	1	2	1	0
Calafrio	18	4,8	12	12	11	7	4	10	10	9	6	5	8	4	2	1	0
Vômito	14	3,7	6	7	6	7	7	6	4	4	4	2	2	1	1	0	0
Valor <i>p</i> do qui-quadrado	-	-	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01	0,01

associated with fever, only three patients reported eye pain and one referred arthralgia. The uncommon association of these last two symptoms with fever in COVID-19 can be useful from a clinical point of view, especially in the differentiation of other infectious diseases, such as Dengue, which even with fever at the onset of the condition, it has the common association with arthralgia and oculalgia.¹⁰

Regarding the temperatures reached by the fever in COVID-19, they tend to be milder. Higher values in cases of exacerbation of the immune response or co-infections with bacterial agents.^{7,11} In our sample, most of the patients reported a temperature between 38° and 38.9°C, justified because they are outpatients, therefore, milder cases of the disease. Fever is a less frequent complaint in elderly patients, however, in our sample, 64% of the elderly have this symptom.¹¹

Asthenia was presented by 51.7% of the patients, with an average of 6.4 days, and the duration varied from 4 to 23 days. Myalgia was present in the clinical picture of 118 patients in D1, reaching 134 people up to D8, and only 5 patients after D10. Chills reached 18 patients, 4.8%, 12 of these also presented it in D1. Headache was reported by more than 50% of patients, diverging from the data found by Pimentel (2020).⁶

The cough reported by the 173 patients was of variable intensity, denying the existence of catarrhal and/or hemoptoic secretion. It was the symptom that remained the longest, with an average duration of 9.72 days, varying from 2 to 27 days, with the onset before D8 being more common. In cases of extended duration of the symptom, there was a strong association with chest pain referred to the sternal region, related to the muscular effort of the coughing act. Egypto Teixeira et al. (2020)¹³ compare the typical clinical manifestations of SARS-Cov-2 infection with H1N1, the first being described by non-productive cough, fatigue and gastrointestinal symptoms, and the second by productive cough and fever.

According to studies by Singhal (2020),⁴ the average time to onset of dyspnea is 5 days. In our study, the average for the beginning of the complaint was 9 days, with occurrence duration of 1 to 8 days. When dyspnea is associated with cardiovascular risk factors and / or disease, patients are more likely to develop complications such as viral pneumonitis, overlapping bacterial pneumonia and, in some cases, SARS.^{14,15}

Odynophagia was manifested by 79 patients (21.4%) over the course of the infection, usually appearing as an initial

symptom, 64 of them in D1. The duration of this symptom varied between 2 and 18 days, and 5 of the patients had odynophagia as the only symptom.

According to Oba et al (2020),¹⁶ in patients who did not manifest respiratory symptoms, diarrhea may be the first symptom of COVID-19. Coincidentally, in our study, out of the 55 patients who had diarrhea in D1, 80% had no respiratory symptoms. When diarrhea does not occur in D1, it follows respiratory symptoms 74% of the time. Rubin et al. (2020)¹⁷, already stated that the most common symptoms of COVID-19 are fever and respiratory symptoms; however, a significant portion presents alterations in the gastrointestinal tract, reflecting the inoculation of the virus in this system.

According to a study by Lin et al (2020),¹⁸ analyzing 95 confirmed patients for SARS-Cov-2 infection in China, 58 (61.1%) manifested gastrointestinal symptoms: diarrhea (23), anorexia (17), nausea (17), vomiting (4), gastroesophageal reflux (2) and epigastric discomfort (2). In our sample, the numbers were similar, with a predominance of diarrhea (97), nausea (28), abdominal pain (22), anorexia (15) and vomiting (14).

COVID-19-associated diarrhea is caused by the body's immune response, since it does not cause damage to the colon epithelium; on the other hand, inflammatory infiltrates are found throughout the gastrointestinal tract. In general, feces are described as yellow and watery, and may occur 2 to 9 times a day.¹⁶ In our research, diarrheal conditions usually occur for 1 to 4 days, not necessarily on consecutive days. The feces were characterized as pasty, non-fetid, of low volume, with 3 to 4 episodes per day, unrelated to food and with characteristic coloring.

Nausea was present in 28 (7.5%) patients during the progression of the disease, with an average duration of 1.9 days, ranging from 1 to 6 days. Regarding the appearance of the symptom, 8 patients presented in D1 and 10 presented after the D16 of evolution, the latest in D20. Vomiting reached 14 (3.7%) patients in the study, of which 7 patients had it in D1, usually as a single event, between D1 and D18. There was also an association of emesis with abdominal pain and diarrhea.

In our sample, neurological symptoms are more present than in studies by Carod-Artral (2020),¹⁹ which shows the frequency of onset: dizziness (16.8%), headache (13.1%), hypo-geusia (5.6%) and hyposmia (5.1%). In our sample, headache affected 51.7% of patients, 82.1% of whom were in D1, and it was described as diffuse and of moderate to high intensity,

with a variation in duration from 1 to 13 days. 31% of patients reported an association with one or more gastrointestinal symptoms, being: 26.7% with diarrhea, 7.3% with abdominal pain, 4.7% with nausea and 3.6% with episodes of emesis.

According to Santos Goularte et al. (2020),²⁰ the duration of anosmia and ageusia varied from 2 to 5 days. In our sample, the average anosmia duration was 9.18 days, with a range from 2 to 27 days; and ageusia of 7.62 days, ranging from 2 to 18 days. These olfactory dysfunctions are common in some infections, such as rhinovirus, Epstein-Barr virus, parainfluenza virus and some coronaviruses, due to the inflammatory reaction of the nasal mucosa and consequent developed rhinorrhea.

However, in the case of COVID-19, the proportion of patients with rhinorrhea is low, and not always present in patients with complaints of ageusia and anosmia; and observing the of information about the real pathophysiological mechanisms of this infection and its dysfunctions, it is difficult to establish a pattern.²¹ According to the analyzes made by Johanna et al (2020),²² it was observed that 31 patients, 35.5% had nasal congestion or associated rhinorrhea and 6.5% had as their exclusive symptom the complete loss of smell and taste. In our data, 23.3% of patients reported coryza, ranging from D1 to D10, being more common up to D5. Sneezing was an event related to runny nose, 89.5% of the time.

CONCLUSION

The rapid spread, the human and social impact of SARS-CoV-2 defined the notoriety of COVID-19. The characterization of clinical spectra, signs and symptoms becomes relevant when they are common to several high frequency diseases. In our study, fever was observed as the most frequent complaint, followed by asthenia, headache and cough. The occurrence and duration of symptoms was similar to that of other studies in the literature, except for neurological symptoms, which had a higher occurrence in our sample.

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