Symptomatic manifestations of the disease caused by coronavirus (COVID-19) in adults: systematic review

Manifestações sintomáticas da doença causada por coronavírus (COVID-19) em adultos: revisão sistemática

Manifestaciones sintomáticas de la enfermedad causada por coronavirus (COVID-19) en adultos: revisión sistemática

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ABSTRACT

Objective: To identify symptoms of COVID-19 in adults in the scientific literature.
Method: Systematic review of studies published from December 1, 2019 to April 21, 2020 from the Scopus, Web of Science and PubMed databases, in order to answer the following research question: "What are the symptoms caused by COVID-19 in adults?" using the keywords "Symptoms", "Clinical Manifestations", "Coronavirus", "COVID-19".
Results: Of the total 105 references, 13 references that addressed the symptoms of COVID-19 were selected. Fever and normal or dry cough were symptoms present in all studies.
Conclusion: The symptoms identified in adult patients were fever, normal or dry cough, headache, pharyngalgia, dyspnea, diarrhea, myalgia, vomiting, sputum or expectoration, anxiety or chest pain, fatigue, nausea, anorexia, abdominal pain, rhinorrhea, runny nose or nasal congestion, dizziness, chills, systemic pain, mental confusion, hemoptysis, asthma, taste disorder, smell disorder, belching and tachycardia.
Keywords: COVID-19. General symptoms. Signs and symptoms. SARS-CoV-2.

RESUMO

Objetivo: Verificar na literatura científica as manifestações sintomáticas da COVID-19 em pessoas adultas.
Método: Revisão sistemática utilizando as bases Scopus, Web of Science e PubMed com estudos publicados de 1 de dezembro de 2019 a 21 de abril de 2020, a fim de responder à questão norteadora: "Quais as manifestações sintomáticas causada pela COVID-19 em pessoas adultas?" utilizando-se as palavra anxietys-chave: "Symptoms", "Clinical Manifestations", "Coronavirus", "COVID-19".
Resultados: Do total de 105 referências, foram selecionadas 13 que abordaram as manifestações sintomáticas da COVID-19, estando a febre e a tosse normal ou seca presente em todos os estudos.
Conclusão: As manifestações sintomáticas identificadas nos pacientes adultos foram: febre, tosse normal ou seca, cefaleia, faringalgia, dispneia, diarreia, mialgia, vômito, escarro ou expectoração, angústia ou dor no peito, fadiga, náusea, anorexia, dor abdominal, rinorreia, coriza ou congestão nasal, tontura, calafrios, dor sistêmica, confusão mental, hemoptise, asma, comprometimento do paladar, comprometimento do olfato, arroto e taquicardia.
Palavras-chave: COVID-19. Sintomas gerais. Sinais e sintomas. SARS-CoV-2.

RESUMEN

Objetivo: Verificar en la literatura científica las manifestaciones sintomáticas de COVID-19 en adultos.
Método: Una revisión sistemática realizada en las bases de datos Scopus, Web of Science y PubMed con estudios publicados del 1 de diciembre de 2019 al 21 de abril de 2020, con el fin de responder a la pregunta orientadora: "¿Cuáles son las manifestaciones sintomáticas causada por COVID-19 en adultos?" utilizando las palabras clave: "Síntomas", "Manifestaciones clínicas", "Coronavirus", "COVID-19".
Resultados: Del total de 105 referencias, se seleccionaron 13 que abordaron las manifestaciones sintomáticas de COVID-19, con fiebre y tos normal o seca presente en todos los estudios.
Conclusión: Las manifestaciones sintomáticas identificadas en pacientes adultos fueron: fiebre, tos normal o seca, dolor de cabeza, faringalgia, disnea, diarrea, mialgia, vómitos, esputo o expectoración, angustia o dolor en el pecho, fatiga, náuseas, anorexia, dolor abdominal, rinorrea, secreción nasal o congestión nasal, mareos, escalofríos, dolor sistémico, confusión mental, hemoptisis, asma, alteración del gusto, alteración del olfato, eructos y taquicardia.
Palabras clave: COVID-19. Síntomas generales. Signos y síntomas. SARS-CoV-2.

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■ INTRODUCTION

Coronaviruses (CoVs) are a large family of single-stranded RNA viruses that can infect from animals to humans and cause different clinical manifestations[1]. They are known as the largest RNA viruses and are divided into four different genera: alpha-coronavirus, beta-coronavirus, gamma-coronavirus and delta-coronavirus[2]. So far, six of these viruses that have the ability to target humans (HCoVs) have been identified, namely: HCoVs-NL63 and HCoVs-229E (alpha-CoVs); HCoVs-OC43, HCoVs-HKU1, as well as the cause of Severe Acute Respiratory Syndrome (SARS-CoV) and the cause of Middle East Respiratory Syndrome (MERS-CoV)[3–4].

In December 2019, a new disease caused by coronavirus (COVID-19) was identified in China, more precisely in Hubei province, which would have been caused by a new type of coronavirus that had not yet been reported in the scientific literature, SARS-CoV-2[5]. Studies have shown that this virus have different transmission channels, and that its speed and infection capacity are higher than those of SARS-CoV and MERS-CoV[6–7]. These factors, associated with the high mortality rates of the individuals affected, led the World Health Organization (WHO) to declare COVID-19 a pandemic on March 11, 2020[8]. As of May 31, 2020, the total number of confirmed cases worldwide was 6,057,853, with 371,166 deaths in 216 countries, areas or territories[9]. In this context, a wide range of symptoms has been described for this new coronavirus, which makes its clinical diagnosis difficult to make without the aid of laboratory diagnosis.

Due to the scientific relevance of the disease, and given its high mortality rates and the many aspects still unknown, a discussion based on scientific studies is necessary[10], especially with regard to patients' symptoms. Thus, this systematic review aims to identify symptoms of COVID-19 in adults in the scientific literature.

■ METHOD

This is a Systematic Literature Review that performed the following steps: development of the review protocol, formulation of the research question, search for studies, selection and assessment of studies (application of predetermined inclusion and exclusion criteria), critical examination of each of the articles and data collection with analysis by at least two researchers simultaneously)[11].

The study protocol was previously defined and registered (registration number: CRD42020188728)[12] in the International Prospective Register of Systematic Reviews (PROSPERO), online and open access database for registering systematic review protocols on health-related topics. This step aims to reduce the risk of publication bias and duplication of reviews to answer the same clinical question[13].

The research question was elaborated through the PICO statement[14] (P: Adult people; I: Symptoms; CO: COVID-19) in order to meet the desired objective: "What are the symptoms caused by COVID-19 in adults?" After the definition of the review's objective and formulation of the research question, searches were carried out (by two properly trained researchers), in the following databases Scopus (Elsevier), Web of Science e PubMed (developed by the *National Center for Biotechnology Information* – NCBI), using the combination of the following keywords: "Symptoms" [and] "Clinical Manifestations" [and] "Coronavirus" [and] "COVID- 19 ".

For the selection of studies related to this research, the following inclusion criteria were used: studies directly related to the topic, only with adults or mostly adults, original, without language restriction provided they have been carried out only with laboratory confirmed cases, published from December 1, 2019 to April 21, 2020. The exclusion criteria were articles outside the scope of the research, articles that addressed the infection only in children or mostly in children, duplicates, reviews, opinion articles, reflection papers, editorials and case studies articles.

Each step of the review was carried out independently (Selection, eligibility and inclusion). Researchers independently examined the titles and abstracts generated by the research based on the inclusion and exclusion criteria. Subsequently, both researchers made full reports of articles that appeared to meet the established criteria, or when there was some uncertainty. The authors discussed the reports for each article and decided whether or not they met the inclusion criteria.

A total of 78 articles were found in PubMed, 16 in Scopus and 11 in Web of Science. Then, duplicates were eliminated (only one study from each database was maintained, with data for identification, indexing and frequency of occurrence arranged in a table), so that all the remaining studies were submitted to a first screening, stage where the researchers screened only the titles and abstracts. Only 20 studies were picked. The remaining studies from the first screening were read in full, resulting in 13 articles for inclusion in this systematic review. The steps of identification, selection and eligibility for inclusion of the studies covered in this review are described in Figure 1 (based on the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis - PRISMA statement)[15].

The level of evidence for each study was assessed according to the Grading of Recommendations Assessment,

Identification

References found in the Databases (n=105). PubMed (n=78), Scopus (n=16) and Web of Science (n=11)

Duplicates: (n=21)

Selection

Studies maintained after elimination of duplicates (n=84)

Studies excluded after abstract reading (n=64)

Eligibility

Studies maintained after elimination of abstract reading (n=20)

Studies excluded after full-text reading (n=7)

Included

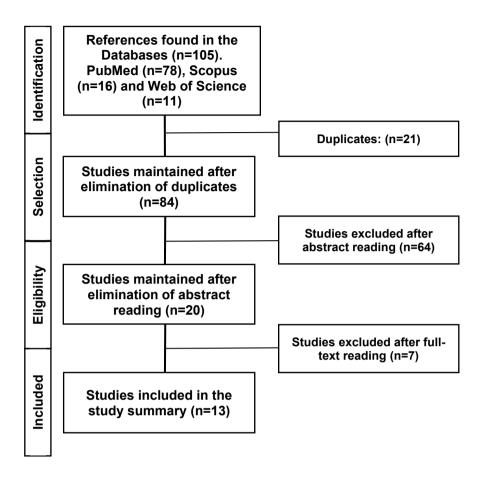Studies included in the study summary (n=13)

Figure 1 – Flowchart of the process of selection of articles in the scientific literature
Source: The authors, 2020.

Development and Evaluation (GRADE) system, where the quality of evidence can be classified into four levels (high, moderate, low and very low). Thus, randomized clinical trials start with a high score and observational studies with a low score. However, when methodological limitations, inconsistencies, indirect evidence, inaccuracies and publication biases occur, the level of evidence can be reduced. On the other hand, in the case of large effect size, residual confounding factors that reduce the magnitude of the effect and dose-response gradient, the evidence level may be high. It should be noted that this is a comprehensive instrument, which is not limited only to the study design, and is considered a complex evaluation system that requires qualitative judgments from the researchers[16]. The studies were also evaluated based on their projects, on the operationalization of their outcome measures and on whether or not they underwent a peer review process to ensure the reliability of the research.

The following data were extracted for the identification of the characteristics of the studies selected for this review: authors, year, country, journal, indexing database, title, publication language, type of study, number and average age of the participants. These data were displayed in a chart created with Microsoft® Word 2016 program. Results that included the clinical types of the disease of the patients and symptoms of COVID-19 in adults were also collected. Microsoft® Word 2016 was also used here to display the results in a chart. In order to synthesize the symptoms identified in the selected studies, these data were organized in spreadsheets with the aid of Microsoft® Excel 2016 to enable the calculation of the frequency of occurrence of the symptoms. The frequency of these symptoms was presented in a graph with the use of GraphPad Prism 8. Subsequently, a narrative synthesis of the data collected from the studies included in this review was performed to produce a summary of the evidence and meet the research objective.

RESULTS

A sample of 13 articles was obtained among those that met the inclusion criteria. The number of authors ranged from five to 18, and due to the high number of authors, only the first author's name was included. All studies were published in 2020 and conducted in China. Regarding the databases, all thirteen articles included were indexed in PubMed, three of which were also indexed in Scopus and only one was also indexed in Web of Science. Regarding the publication language, 11 were in English and two in Chinese. All studies were cross-sectional, with different levels of evidence. The number of study participants ranged from 11 to 1,012 and the average age was 35-57 years.

Chart 1 presents data on the articles analyzed in terms of order of organization, main author, year of publication, country of publication, date of publication, indexing database, title, language of publication, type of study, level of evidence, number and average age of the participants.

Regarding the main results of the studies, all addressed the symptoms of COVID-19. However, a few studies also included the clinical type of the disease. Data related to the answer to the research question of this study can be seen in Chart 2.

Several symptoms associated with COVID-19 have been described in adults. Fever and normal or dry cough were identified in all studies, followed by symptoms such as headache, pharyngalgia, dyspnea and diarrhea. The frequency of occurrence of the symptoms in the selected studies is shown in Figure 2.

Order	Author/ Year/Country	Periodical/ Database	Title/ Publication language	Type of study/ Level of Evidence	No. and average age of participants
A1[17]	Du W et al., 2020, China	Infection/ PubMed	Clinical characteristics of COVID-19 in children compared with adults in Shandong Province, China/ Inglês	Retrospective Cross-Sectional Study / Low	53 (41,47)
A2[18]	Li R et al., 2020, China	J Clin Virol/ PubMed	Clinical characteristics of 225 patients with COVID-19 in a tertiary Hospital near Wuhan, China/ Inglês	Retrospective Cross-Sectional Study / Moderate	225 (50 ± 14)
A3[19]	Sun C et al., 2020, China	Zhonghua Jie He He Hu Xi Za Zhi/ PubMed	Clinical analysis of 150 cases of 2019 novel coronavirus infection in Nanyang City, Henan Province/ Chinês	Retrospective Cross-Sectional Study / Moderate	150 (45 ± 16)
A4[20]	Mao L et al. 2020, China	JAMA Neurol/ PubMed	Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China/ Inglês	Retrospective Cross-Sectional Study / Moderate	214 (52,7 ± 15,5)
A5[21]	Peng L et al. 2020, China	Arch Iran Med/ PubMed e Web of Science	Improved Early Recognition of Coronavirus Disease-2019 (COVID-19): Single-Center Data from a Shanghai Screening Hospital/ Inglês	Retrospective Cross-Sectional Study / Very low	11 (40,73 ± 11,32)

Chart 1 – Characteristics of the selected studies

Order	Author/ Year/Country	Periodical/ Database	Title/ Publication language	Type of study/ Level of Evidence	No. and average age of participants
A6[22]	Wang X et al. 2020, China	Clin Microbiol Infect/ PubMed e Scopus	Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital/ Inglês	Retrospective Cross-sectional study/ Moderate	1012 (50)
A7[23]	Liu M et al. 2020, China	Zhonghua Jie He He Hu Xi Za Zhi/ PubMed	Clinical characteristics of 30 medical workers infected with new coronavirus pneumonia/ Chinês	Retrospective Cross-Sectional Study / Low	30 (35 ± 8)
A8[24]	Wu J et al. 2020, China	Clin Infect Dis/ PubMed	Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study/ Inglês	Retrospective Cross-Sectional Study / Moderate	80 (46,10 ± 15,42)
A9[25]	Xu X et al. 2020, China	Eur J Nucl Med Mol Imaging/ PubMed	Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2/ Inglês	Retrospective Cross-Sectional Study / Low	90 (50)
A10[26]	Wu J et al. 2020, China	Invest Radiol/ PubMed e Scopus	Chest CT Findings in Patients With Coronavirus Disease 2019 and Its Relationship With Clinical Features/ Inglês	Retrospective Cross-Sectional Study / Low	80 (44 ± 11)
A11[27]	Zhang JJ et al. 2020, China	Allergy/ PubMed e Scopus	Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China/ Inglês	Retrospective Cross-Sectional Study / Moderate	140 (57)
A12[28]	Liu K et al. 2020, China	Chin Med J (Engl)/ PubMed	Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province/ Inglês	Retrospective Cross-Sectional Study / Moderate	137 (55 ± 16)
A13[29]	Chen N et al. 2020, China	Lancet/ PubMed	Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study/ Inglês	Retrospective Cross-Sectional Study / Moderate	99 (55,5 ± 13,1)

Chart 1 – Cont.

Source: The authors, 2020.

Legend: No = Number.

Studies A1, A6, A9 and A11 did not include in their results the standard deviation of age

Order	Main Results
A1[17]	Regarding the clinical type: mild (15.1%), moderate (83%), severe (1.9%), critical (0%). Most common symptoms: fever (60.4%) and normal or dry cough (54.7%). Less common symptoms: sputum or expectoration (37.7%), pharyngalgia (35.8%), fatigue (32.1%), headache (20.8%), anorexia (15.1%), myalgia (13.2%), anxiety or chest pain (11.3%), nausea (5.7%), diarrhea (3.8%), dizziness (3.8%) and vomiting (1.9%).
A2[18]	Regarding the clinical type: severe (16.44%). Most common symptoms: fever (84.44%) and normal or dry cough (56.44%). Less common symptoms: dyspnea (4.00%), sputum or expectoration, fatigue, chills, headache, anxiety or chest pain and pharyngalgia (3.56% to 22.67%).
A3[19]	Regarding the clinical type: mild (4%), moderate (70%), severe (19%), critical (7%). Most common symptoms: fever (95%), normal/dry cough and sputum/expectoration (72%), fatigue (15%), anorexia (13%), asthma and dyspnea (10%). Less common symptoms: myalgia (4%), pharyngalgia (8%), headache (2%) and diarrhea (1%).
A4[20]	Regarding the clinical type: not severe (58.9%) and severe (41.1%). Most common symptoms: fever (61.7%) and normal or dry cough (50.0%). Less common symptoms: anorexia (31.8%), pharyngalgia (14.5%) and abdominal pain (4.7%). neurological manifestations were considered separately: Central Nervous System (CNS). The most common symptoms reported were dizziness (16.8%) and headache (13.1%). Regarding the Peripheral Nervous System (SNP) the most prevalent symptoms were taste disorder (5.6%) and smell disorder (5.1%).
A5[21]	No distinction was made as to the type of patient impairment. The most common symptoms were fever (91%), systemic pain (64%), normal or dry cough (55%). A less common symptom reported was pharyngalgia (9%).
A6[22]	No distinction was made as to the type of patient impairment. It was only reported that the 1,012 individuals were not critical patients. Most common symptoms: fever (75.2%) and normal or dry cough (52.4%). Less common symptoms: dyspnea (22.8%), sputum or expectoration (21.7%), chills (18.0%), myalgia (16.8%), headache (15.0%), diarrhea (15.0%), pharyngalgia (14.2%), nasal congestion (6.9%), rhinorrhea or runny nose (5.6%), vomiting (3.6%) and abdominal pain (3.7%).
A7[23]	Regarding the clinical type: moderate (86.67%) and severe (13.34%). Most common symptoms: normal or dry cough (83.33%), fever (76.67%), fatigue or systemic pain (70%) and headache (53.33%). Less common symptoms: dyspnea (46.67%) and gastrointestinal symptoms like nausea, vomiting or diarrhea (30%).
A8[24]	Regarding the clinical type: mild (35.00%), moderate (61.25%), severe (3.75%), critical (0%). Most common symptoms: fever (78.75%) and normal or dry cough (63.75%). Less common symptoms: dyspnea (37.50%), myalgia (22.50%), headache or mental confusion (16.25%), pharyngalgia (13.75%), rhinorrhea, nasal congestion or runny nose (6.10%), anxiety or chest pain (3.75%), diarrhea (1.25), nausea or vomiting (1.25%). The occurrence of more than one symptom (82.50%) was also assessed.
A9[25]	No distinction was made as to the type of patient impairment. Most common symptoms: fever (78%) and normal or dry cough (63%). Less common symptoms: sputum or expectoration (12%), fatigue (21%), myalgia (28%), pharyngalgia (26%), chills (7%), headache (4%), diarrhea (6%), nausea (6%) and vomiting (2%). The absence of obvious symptoms (7%) was also assessed.
A10[26]	No distinction was made as to the type of patient impairment. Most common symptoms: fever (76%) and normal or dry cough (73%). Less common symptoms: myalgia (16%), sputum or expectoration (14%), pharyngalgia (11%), dizziness or headache (10%), abdominal pain or diarrhea (9%), dyspnea (9%), anxiety or chest pain (6%) and hemoptysis (4%).
A11[27]	Regarding the clinical type: mild or conventional (58.57%) and severe (41.42). Most common symptoms: fever (91.7%), normal or dry cough (75%) and fatigue (75%). Less common symptoms: anxiety or chest pain, or dyspnea (36.7%), gastrointestinal symptoms (39.6%), including nausea (17.3%), diarrhea (12.9%), anorexia (12%), abdominal pain (5.8%), belching (5.0%) and vomiting (5.0%).
A12[28]	No distinction was made as to the type of patient impairment. Most common symptoms: fever (81.8%), normal or dry cough (48.2%). Less common symptoms: myalgia or fatigue (32.1%), dyspnea (19.0%), headache (9.5%), diarrhea (8.0%), tachycardia (7.3%), hemoptysis (5.1%) and sputum or expectoration (4.4%).

Chart 2 – Details of the articles analyzed according to the authors and the main results reported in the studies

Order	Main Results
A13[(29)]	No distinction was made as to the type of patient impairment. Most common symptoms: fever (83%) and normal or dry cough (82%). Less common symptoms: dyspnea (31%), myalgia (11%), mental confusion (9%), headache (8%), pharyngalgia (5%), rhinorrhea, nasal congestion or runny nose (4%), anxiety or chest pain (2%), diarrhea (2%) and vomiting (1%). The occurrence of more than one symptom (90%) was also assessed.

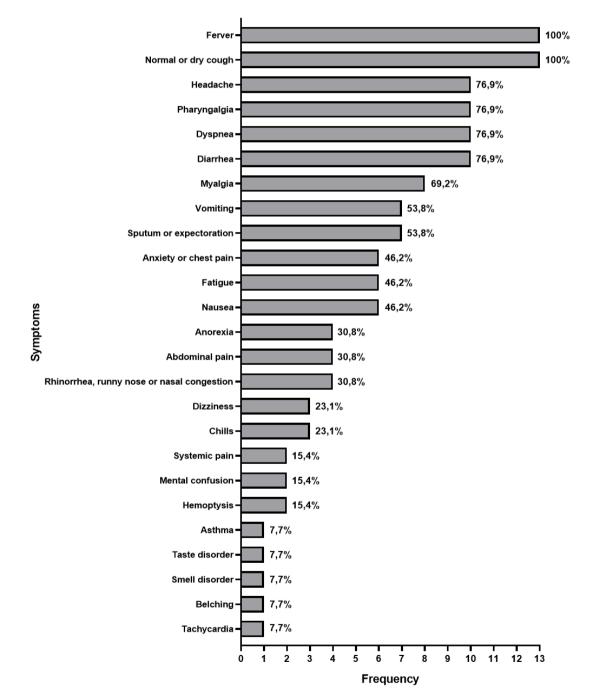**Chart 2** – Cont.
Source: The authors, 2020.

Figure 2 – Graph of the frequency of onset of symptoms of COVID-19 in the selected articles
Source: The authors, 2020.

■ DISCUSSION

All studies were published by Chinese researchers in 2020. This can be explained by the fact that COVID-19 appeared in China in late 2019[5]. However, due to the extensive dissemination of the disease[10], studies focused on clinical manifestations in different countries are essential, as in this proliferation process the pathogen can undergo mutations that may trigger new configurations without prior scientific description, due to the lack of diversity in the sample examined. Therefore, analyzes should be carried out in different countries and populations, in order to map the different presentations of the virus. In this context, a study described eight new virus mutations, suggesting that it evolved in different strains, which can lead to a coexistence of strains in different locations around the world, each, characterized by a different mutation pattern[30].

Regarding the clinical type, the forms can be mild cases, characterized by mild clinical symptoms, without chest x-ray findings of pneumonia; common cases, where fever associated with respiratory symptoms and chest x-ray manifestations of pneumonia occurs: severe cases that can lead to breathing difficulties (respiratory rate ≥ 30 breaths per minute - rpm), hypoxia (oxygen saturation at rest ≦ 93%), partial arterial oxygen pressure (PaO_2) divided by the inspired fraction of oxygen (FiO_2 ≦ 300 millimeters of mercury (mmHg). and finally, critical cases, where respiratory failure and the need for mechanical ventilation occur, and shock and more complications such as the failure of other organs may also occur. In this case, treatment should be performed in the Intensive Care Units (ICUs)[31].

Of the selected studies, five did not assess the clinical type of the manifestations[21,25-26,28-29]. Three of them considered the four divisions, but there was only agreement in the studies by Du et al. (2020) and Wu et al. (2020), where, in descending order, there were common, mild, serious and critical cases; as for Sun et al., (2020) the order was moderate, serious, mild and critical cases[17,19,24]. Another three studies subdivided the cases into two classifications[20,23,27]. Only two studies considered or only exposed one classification[18,22]. These findings revealed data collection, analysis or exposure gaps, since most authors did not include the clinical type of the patients evaluated.

Regarding the symptoms observed in adult patients with COVID-19, a total of 25 symptoms were identified, regarding the frequency of occurrence, which are not very specific and demonstrate the potential that SARS-CoV-2 has to affect different systems, more precisely respiratory, neurological and gastrointestinal[17-29]. The disease can also manifest itself in an asymptomatic form. However, data related to the estimate of the asymptomatic population is still scarce in the scientific literature; furthermore, these data will only be accurate if global large-scale testing of the population is conducted[32].

According to the Centers for Disease Control and Prevention – CDC of the United States, symptoms may appear 2 to 14 days after exposure to the virus[33]. In this review, fever was the most frequent symptom, being detected in more than half of the participants included in the thirteen studies assessed. Another important factor about fever is that it ranged from moderate to low[17-29]. Thus, health professionals must pay special attention to the measurement of patients' body temperature, either during daily screening or during the entire care process, as it is a symptom that can go unnoticed or be underestimated.

Symptoms that affected the respiratory system were identified in all studies, with cough, normal or dry, emerging as the second most prevalent symptom among patients infected with coronavirus[17-29]. It should be noted that patients are the main source of spread of the infection, since they produce a large amount of viruses in the upper respiratory tract; and transmission occurs mainly through respiratory droplets and contact, as well as through aerosols in relatively closed environments[34-36]. Nosocomial transmission can also occur, contaminating even health professionals themselves. Liu M et al.[23] described the contamination of 22 doctors and eight nurses, noting that many were contaminated due to non-use, or inappropriate use of Personal Protective Equipment (PPE)[23].

The second most affected system was the gastrointestinal system. Different symptoms were reported in 11 studies[17,19-20,22-29]. In their retrospective evaluation of 140 cases, Zhang JJ et al.[27] subdivided their results and found 39.6% of gastrointestinal symptoms (nausea 17.3%; diarrhea 12.9%; anorexia 12%; abdominal pain 5.8%, belching 5.0% and vomiting 5.0%). The subdivision of the gastrointestinal system and the identification of belching as a symptom (the only time this occurred) are the aspects that differentiated these results from those obtained in other articles[27].

Manifestations related to the neurological system have been described in 10 studies[17,19-20,22-26,28-29]. A study conducted in three special care centers in the city of Wuhan demonstrated high relevance of neurological symptoms, as it focused specifically on these symptoms and managed to identify, in addition to the involvement of the Central Nervous System (CNS), with symptoms such as dizziness (16.8%) and headache (13.1%), the symptoms that affect the Peripheral Nervous System (PNS), namely, taste disorder (5.6%) and smell disorder (5.1%)[20]. This was the only study among the others in this review that identified symptoms related to the PNS.

As previously discussed, due to the specificities of SARS-CoV-2, findings from the scientific literature from other parts of the world should be considered. In Brazil, a study carried out with 510 patients from a philanthropic hospital in the city of São Paulo (SP) found that the subjects, although most of them had a non-severe clinical type (95.9%), had several symptoms, such as fever (67.5%), nasal congestion (42.4%), cough (41.6%), myalgia or arthralgia (36.3%), sore throat (27.6%) , headache (23.7%), fatigue (13.5%), dyspnea (7.8%), diarrhea 22/510 (4.3%), chills (4.3%), nausea or vomiting (1, 8%), sputum production (1.0%), conjunctival congestion (0.4%), as well as other symptoms (2.4%), with only 18 patients being asymptomatic (3.5%)[37].

In this context, clinical and laboratory[38] evaluation of the symptoms of COVID-19 is recommended. Syndromic diagnosis of Covid 19 requires clinical-epidemiological investigation and physical examination, and health professionals must adopt a uniform conduct in all cases of Flu-like Syndrome (FS), because it is impossible to know at first the etiology of the disease. Laboratory diagnosis for the identification of the SARS-CoV-2 virus can be performed using RT-PCR techniques in real time (gold standard), or rapid serological tests validated by referral institutions (they detect IgG and IgM antibodies or antigens from the virus itself)[38].

As there is no vaccine available, prevention should be focused. Prevention measures include washing hands properly with soap and water or use a hand sanitizer containing 70% ethyl alcohol, practicing social or physical distancing, staying at least 6 feet from other people when going out to perform essential activities; respiratory cough etiquette, which consists of covering the mouth and nose with the forearm or handkerchiefs when coughing, or sneezing; seek care in case of fever, cough and difficulty breathing; avoid consumption of raw or undercooked animal products; wearing surgical masks, in the case of health professionals and suspected or confirmed patients, and cloth masks by the general population[39].

Therefore, we stress the need for further studies worldwide, with different methodological approaches and scientific rigor, in order to ensure higher levels of evidence and the consolidation of information about the symptoms caused by COVID-19. One limitation of the present study is the fact that all articles included were from only one country, in this case China, as well as the fact that all studies are cross-sectional, and during the evaluation their levels of evidence were reduced or stagnated due to lack of information. More precisely, regarding their levels of evidence, four studies of the total 13 studies were classified as low evidence; eight were classified as moderate evidence and only one as very low evidence.

■ CONCLUSION

The symptoms identified in adult patients with COVID-19 were fever, normal or dry cough, headache, pharyngalgia, dyspnea, diarrhea, myalgia, vomiting, sputum or expectoration, anxiety or chest pain, fatigue, nausea, anorexia, abdominal pain, rhinorrhea, runny nose or nasal congestion, dizziness, chills, systemic pain, mental confusion, hemoptysis, asthma, taste disorder, smell disorder, belching and tachycardia.

This study has important contributions to teaching, with valuable information about the main symptoms caused by COVID-19. It can assist in the creation of patient identification and care protocols, by health service managers and professionals, such as nurses, who are often responsible for screening assessments. Also, it is innovative, as it discusses and synthesizes scientific evidence facilitating understanding. However, it has one limitation, namely, the fact that China was the country of origin of all the articles included in the review, which also had the same methodological approach, due to the scarce number of original articles related to the topic in the databases and the impossibility of analyzing new published evidence on a daily basis.

Finally, it is recommended that studies related to Covid 19 are conducted in different locations, with different populations and with methodological rigor, in order to clarify and disseminate information on all its symptoms.

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