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COVID-19: EMERGING THEMES FROM THE SYSTEMATIC REVIEW RECORDS PERFORMED IN THE PROSPERO

[1]Souza, Maria de Lourdes de, [2]Conceição Júnior, Alceu Ramos; [3]Bentes, Cheila Maria Lins; [4]Teixeira, Eneida Patrícia; [5]Bentes, Marcos do Nascimento; [6]Jesus, Stefhanie Conceição de; [7]Suazo, Sandra Valenzuela; [8]Campo, Varinia Alejandra Rodríguez and [9]Lynn, Fiona

[1]PhD in Public Health. Full Professor of Postgraduate Program in Nursing at the Federal University of Santa Catarina (UFSC), Brazil; [2]University student in Computer Science at Federal University of Santa Catarina (UFSC), Brazil; [3]Doctor in Nursing. Professor at State University of Amazonas (UEA), Brazil; [4]PhD student in Nursing at Federal University of Santa Catarina (UFSC), Brazil; [5]Master. Physician in Hematology and Hemotherapy Hospital Foundation of Amazonas (HEMOAM), Brazil; [6]Master in Nursing Science at Federal University of Santa Catarina (UFSC), Brazil; [7]PhD in Nursing. Full professor of Nursing Faculty at Concepcion University, Chile; [8]PhD in Nursing at Nursing Faculty at Concepcion University, Chile; [9]PhD. Lecture at School of Nursing and Midwifery – Centre for Evidence and Social Innovation – Queen's University os Belfast, UK

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Corresponding author:
Souza, Maria de Lourdes de

ABSTRACT

The pandemic caused by SARS-CoV-2, the etiological agent of COVID-19, is highly infectious and until April 29, 2021, in 223 Countries, areas, or territories with cases, 148,999,876 people contracted the disease. Due to the importance of the pandemic, the objective for this study was defined: to determine the proportion of records of systematic review in the PROSPERO about COVID-19 and to identify their themes in the global context. As a method, the "mapping review" was chosen about the protocols registered in the period from December 1, 2019, to January 14, 2021. We adopted as an eligibility criterion that, in the registered review protocol, COVID should be inserted in the title, in the question, and/or in the objective. Therefore, protocols that did not contemplate this requirement were not included in the present study. We found 2,397 protocols, with the following themes identified most frequently: pharmacological technologies (n = 521/21.7%); comorbidity x severity (n = 376/15.7%); signs and symptoms of COVID-19 (n = 261/10.9%) and laboratory diagnosis (n = 256/10.7%). Standing out less frequently: Signs and symptoms after COVID-19 (n = 37/1.5%); study relating MERS/SARS/EBOLA/HIV (n = 35/1.5%); Vaccine (n = 28/1.2%) and virus genome (n = 19/0.8%). The emerging themes associated with COVID-19 registered in PROSPERO in the systematic review protocols were diverse, demonstrating the various outlines of a pandemic and reaffirming the importance of this platform for scientific development.

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INTRODUCTION

Epidemiological studies have linked the emergence of COVID-19 in December 2019 to a seafood market in Wuhan, China. In less than three months the disease was declared by the World Health Organization (WHO) to be a Public Health Emergency of International Interest (PHEIC), as it was detected in more than 120 countries (WHO, 2021). The International Committee on Virus Taxonomy officially classified it as severe acute respiratory syndrome coronavirus 2 (SARS - CoV-2) (Su et al., 2020). The avian infectious bronchitis virus (IBV), which was described in 1937, is the first CoV to be isolated. It has a genome consisting of single-stranded RNA, positive polarity, and enveloped. It is a spherical morphology with spicules of glycoproteins similar to a solar corona, being called coronavirus (Latin: corona = corona). There are four subfamilies: alpha, beta. The pandemic caused by SARS-CoV-2, the etiological agent of COVID-19, is highly infectious, and, until April 29, 2021, in 223 Countries, areas, or territories with cases, more than 148,999,876 people contracted the disease and 3,140,115 deaths were reported to WHO. Its dissemination capacity has a geometric growth, causing a great socioeconomic impact in the world context (WHO, 2021). Children are susceptible to COVID-19 infection with a lower

incidence than adults. Studies refer to the entry of the SARS-CoV-2 virus "in the host cell through the binding of its spike (S) protein to the ACE2 receptor." This receptor is more expressed in adults than children (Whittaker et al., 2020). The spread of COVID-19 occurs from person to person by direct transmission, transmission by contact, and aerial transmissions. The common ways of spreading the disease arecoughing, sneezing, droplet inhalation, contact with oral, nasal, and ocular mucous membranes. It also occurs from the respiratory tract, saliva, feces, and urine. "The viral load is higher and longer in patients with severe COVID-19 (Umakanthan et al., 2020)". The period of infection of the disease varies from 01 to 14 days, and the average onset is around five to eight days. Transmissibility to another person is currently 48 hours before symptom onset, 14 days after symptom resolution, or test date for asymptomatic patients (WHO, 2020; Su et al., 2020; Mulabbi et al., 2021; Velavan & Meyer, 2020; Whittaker et al., 2020; Umakanthan et al., 2020). Some individuals infected with SARS-CoV-2 are asymptomatic. For those who develop the disease, the clinical manifestations are a cold, fever, runny nose, earache, sore throat, headache, loss of smell and taste, which may progress to severe cases and hospitalization. In critical cases: respiratory failure, septic shock, and/or multiple organ failure. Gastrointestinal symptoms such as vomiting and diarrhea occur in up to 57% of cases (WHO, 2020; Whittaker et al., 2020; Umakanthan et al., 2020; CDC, 2020; Zheng et al., 2020). Measures such as epidemiological bulletins, resolutions, and protocols are disseminated to the population aiming at reducing the number of infected people, overburdening health services, and the collapse in the health system. The media fires information about COVID-19 every minute, generating dread, fear of death, and lack of assistance. The uncertainty of the cure and the rapid proliferation of the disease, also results in opportunities for the expansion of the technological park, based on studies of protective measures such as personal protective equipment (PPE), chemical agents, drugs for treatment, including in an associated way, and, vaccines.

Research related to COVID-19 is being carried out. Despite this, questions remain unanswered, for example, the specific coronavirus treatment. Every effort must be made to understand, prevent and control such a disease, which is why this study is carried out by consulting the PROSPERO database, a system for registering a systematic review protocol. PROSPERO: what sets it apart from other databases? It is a public database for the registration of systematic review protocols created in 2011, which has more than 35,000 registered protocols. The prospective registration of these protocols is already recommended by many health journals to minimize the risk of publication bias and duplication of reviews to answer the same clinical question (Pacheco et al., 2018; Page et al., 2018; Rombey et al., 2020; Schiavo, 2019). Considering the importance of this platform, the research question defined for this mapping review is - which themes emerge in the context of the COVID-19 pandemic in the records of the systematic review protocol in PROSPERO? The objective was to determine the proportion of systematic review protocol records in PROSPERO about COVID-19 and to identify their themes in the global context.

METHODS

This is a mapping review (Cooper, 2016; O'Cathain et al., 2013). The mapping took place from the protocol records of the systematic reviews (CRD/SR) inserted in the PROSPERO platform, with COVID-19 as the central theme. The inclusion criterion was the presence of the term "COVID" in the title, question, and/or objective of the protocol. Therefore, protocols that did not meet this requirement were not included in this study. Until recently, only systematic reviews were produced through organizations with collaborations with The Cochrane, Campbell Collaborations, and Joanna Briggs Institute, the preparation of a protocol was mandatory. However, researchers pointed out the need to prepare and register systematic review protocols in the academic community to increase the reliability and accessibility of these studies, reducing duplication of efforts and publication bias. Thus, a platform for international registration was created - PROSPERO (International prospective register of systematic reviews), open access through the electronic address: https://www.crd.york.ac.uk/prospero, adopted by the Center for Reviews and Dissemination, York University, UK. For registration, information is required on 22 mandatory and 18 optional items on the project proposal, a priori, on the procedures for conducting the review (Pacheco et al., 2018; Page et al., 2018; Moher et al., 2009; Moher et al., 2015; Shamseer et al., 2015).

In this study, we collected data between January 10 and 14, 2021. To search the platform, we used the term Mesh "covid-19". This study included all records found from December 1, 2019, to January 14, 2021, according to the defined search term. We exported the records from PROSPERO, through the file extension.ris, available by the platform. The file was inserted in the bibliographic manager Endnote, to organize the records with the main information. For data extraction, the records of the protocols were accessed individually, and the data were extracted, compiled, and organized in an Excel spreadsheet, according to the 40 items of the PROSPERO form.

Two researchers analyzed the data organized in the spreadsheet independently, and the records were classified into 14 categories: 1) comorbidity x severity; 2) laboratory diagnosis; 3) signs and symptoms; 4) pregnancy, childbirth, and the puerperium; 5) MERS/SARs/EBOLA/HIV; 6) risk of illness and transmissibility; 7) mortality/lethality; 8) non-pharmacological technologies; 9) pharmacological technologies; 10) mental health; 11) vaccine; 12) post-covid signs and symptoms; 13) virus genome; 14) others. In cases of disagreement regarding the classification in the categories, three researchers participated in a review as a conciliation meeting to finalize the classification. The records were grouped according to the categories and presented with the distribution of absolute frequency and relative frequency. The results are presented in the form of figures, to visualize the classified categories; the economic situation of the countries of origin of the authors of the registered protocol. To classify the countries' economic situation, we adopted the International Monetary Fund (IMF) classification list (IMF, 2019). This review ensures all ethical aspects to the authorship of the protocols registered on a consulting basis. Also, as this review uses secondary data, there was no need for an appraisal by the ethics committee.

RESULTS

Considering the importance of the pandemic and the need for knowledge production, the term defined and searched on the PROSPERO platform was "COVID-19" and, in this, 2,397 records (CRD) were identified. The distribution of these records presented the following categories with greater frequency: pharmacological technologies (n = 521/21.7%); comorbidity x severity (n = 376/15.7%); signs and symptoms of COVID-19 (n = 261/10.9%) and laboratory diagnosis (n = 256/10.7%). The categories that obtained the least number of records were signs and symptoms after covid-19 (n = 37/1.5%); study relating MERS/SARS/EBOLA/HIV (n = 35/1.5%); Vaccine (n = 28/1.2%) and virus genome (n = 19/0.8%). The protocols for systematic review registered in the PROSPERO Platform came from 103 countries, three of which were more frequent: China (24.0%), England (11.5%), and Brazil (10.2%), presented in Table 01.

All continents have registered a Systematic Review Protocol with PROSPERO, with the following frequencies: Africa 8.09%; Americas 32.17%, Asia 51.11%, Europe 28.29% and Oceania 3.92%. Asia has the largest number of records of systematic review protocols planned on the topic and only with professionals from Asian countries did it obtain a percentage frequency of 42.09%, that is, 1009 CRD. Results in data shown in figures 01 and 02 represents the distribution of the categories of publications of the systematic review protocols according to the economic situation of the countries of origin of the authors of the protocol registered in PROSPERO.

Table 1. Selected articles for review. SOURCE: Elaborated by authors

Categories	Brazil		China		England	
	n	%	n	%	n	%
Comorbidities	35	14.40%	91	15.83%	47	17.09%
Diagnosis	23	9.47%	70	12.17%	19	6.91%
Signals and symptoms	31	12.76%	46	8.00%	24	8.73%
Pregnancy / childbirth, puerperium and newborn	12	4.94%	8	1.39%	18	6.55%
Crossover study of MERS/SARS/COVID-19	3	1.23%	6	1.04%	5	1.82%
Risk of illness	19	7.82%	16	2.78%	27	9.82%
Mortality x Lethality	9	3.70%	22	3.83%	15	5.45%
Non-pharmacological technologies	35	14.40%	43	7.48%	22	8.00%
Pharmacological technologies	38	15.64%	224	38.96%	30	10.91%
Mental health / Suicide	17	7.00%	31	5.39%	31	11.27%
Vaccine	1	0.41%	3	0.52%	3	1.09%
Signs and symptoms after COVID-19	0	0.00%	7	1.22%	7	2.55%
Virus genome	5	2.06%	0	0.00%	5	1.82%
Others	15	6.17%	8	1.39%	22	8.00%
Total	243	100.00%	575	100.00%	275	100.00%

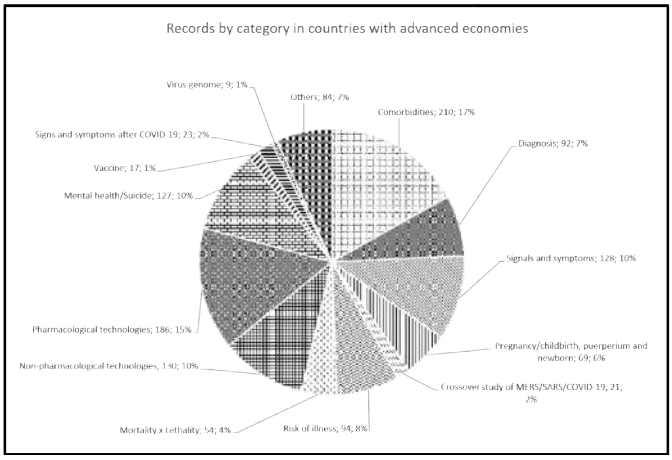

Figure 1. Records of systematic review protocols in PROSPERO by category in countries with advanced economies.SOURCE: Elaborated by authors

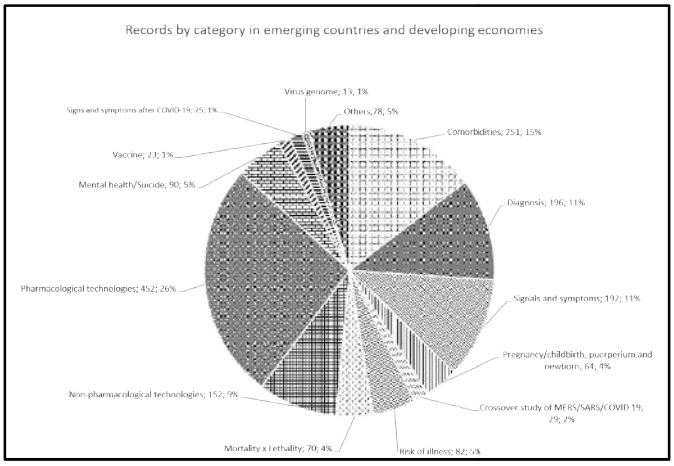

Figure 2. Records of systematic review protocols in PROSPERO by category in countries with developing economies.SOURCE: Elaborated by authors

DISCUSSION

In the same geometric way that COVID-19 spread, becoming in less than three months a Public Health Emergency of International Interest (PHEIC), institutions and research groups focused their studies on understanding the etiopathogenesis, diagnosis, treatment (pharmacological and non-pharmacological), and prophylactic measures to control the disease, which has a high infectivity power superior to the two epidemic outbreaks caused by viruses of the same family (Sarnaglia et al., 2021). In this study, we observed the records of systematic review protocols from 103 countries on the PROSPERO Platform, totaling 2,397 records, over one year. This high number of publications may be related to the exponential growth of the disease and related consequences. The pandemic caused by SARS-CoV-2, due to high infectivity, until April 29, 2021, in 223 Countries, areas, or territories with cases, more than 148,999,876 people contracted the disease and 3,140,115 deaths were reported to the World Health Organization.[1] This pandemic has been causing an overload on the health system, affecting economic activities, carrying social and psychological consequences. Every effort was made to develop solutions to remedy the effects that the pandemic has been causing in the countries of the different continents (Sachini et al., 2021). In this publication related to COVID-19 enabled co-authoring networks, they highlighted the international level of collaboration. This has been expanded with the accession of more countries, in a network aiming to research to contribute to the "global battle against the coronavirus", showing the mobilization of researchers around the theme COVID-19 (Sachini et al., 2021). In this study, in the PROSPERO Platform, the registration of systematic review protocols by researchers from all continents is in line with what the authors of another study describe. Although the registered protocols contain different research objectives and questions, in general, they have the same purpose, that is, to control or cure COVID-19, to manage its psycho-socio-economic consequences, and to prevent more devastating future outbreaks (Sachini et al., 2021). Four countries in Asia - China, India, Indonesia, and Iran - are among the ten with the highest number of registered systematic review protocols on the PROSPERO platform since the beginning of the current pandemic. The first outbreak mentioned by SARS-CoV, of the betacoronavirus family, originated in China, in Guangdong, reached 37 countries during 2002-03. In November 2019, Wuhan, another Chinese city, is affected by the Coronavirus. China has been acting with "implementation of political actions, social mobilization, regional coordination, resource allocation, incentive mechanism and international cooperation" aiming to develop scientific technologies to face COVID-19 (Yin & Zhang, 2021).

England, a country on the European continent, is the second in frequency of registration of systematic review protocols. The British health system NHS - National Health Service, a pioneer in the universalization of access to health with the principles of equity and integrality, has a hierarchy of a care system based on evidence and with wide performance in primary care, is considered a state system more efficient and accessible in the West with an emphasis on health promotion, disease prevention and the public good (Filippon et al., 2016). In developed countries, studies on comorbidity x severity obtained a frequency of 210 (17%) in SR records. The population of countries with an advanced economy has a life expectancy of over 79 years old. The advanced age of people infected with SARCS CoV2, in those countries that evolved to death, mostly had known comorbidities. One of the studies consulted when comparing this variable in developing countries (low and medium-income), deaths are more frequent in individuals without comorbidities, and/or comorbidities were not detected in places due to scarce resources (Ioannidis, 2021). When describing the demographic characteristics and comorbidities of patients hospitalized as a result of COVID-19 in Brazil, the authors highlight the higher prevalence in individuals who present comorbidities (diabetes mellitus, cardiovascular diseases, chronic kidney disease, and chronic lung diseases), classifying them into risk groups. Diabetes mellitus among patients in Brazil was (25%) higher than those hospitalized in Wuhan (19%) and Lombardy (17%), but lower than in New York (34%). Comorbidities can be potential markers of disease severity and greater vulnerability to contamination (Niquini et al., 2020). The complexity of SARS-Cov-2 at the beginning of the pandemic was exacerbated by the almost complete lack of knowledge about the disease's etiopathogenesis. The

existing knowledge referred to other coronaviruses, identified in the last century. The contribution of these researches helps as a basis for current studies, but they were ineffective in the management of COVID-19. Researchers related the pathophysiology of SARS-CoV-2 as a respiratory infection and studies have shown it to be a systemic disease (Guimarães, 2020). In this study, we observed that only 8% of the protocols came from countries with a developed economy and 5%, from developing countries, protocols that addressed the risk of illness and transmissibility. Studies on the risk of illness and transmissibility assist in making policy decisions and technological investments for interventions in the control and cure of the disease, directing prophylactic measures, equipping health institutions, and creating strategies to prevent future epidemic outbreaks (Yin& Zhang, 2021; Filippon et al., 2016; Ioannidis, 2021). In the context of the health system, the rapidity of the "illness and the severity of part of the patients" revealed the fragility of the health professionals and services and that the health institutions were not prepared to support, resulting in the collapse of the system (Guimarães, 2020). Social interaction, work activities, meetings between friends and family, leisure, and others were also disorganized, causing mental suffering. Suffering is also associated with the economic impact of countries, especially those in developing countries, weakened before the pandemic. Contributing to 70% of the global economic aggregate, urban areas are growing rapidly, with a high population density, narrow spaces, and large volumes of traffic. If these conditions are related to the transmissibility of the virus, these areas become an excellent chain of infection for transmission between human beings and high-risk outbreak sites (Yin & Zhang, 2020).

Conclusions and Limitations

The emerging themes associated with COVID-19 registered in PROSPERO in the systematic review protocols were diverse, showing several outlines of a pandemic and reaffirming the importance of this platform for scientific development. The similarity was observed in the percentages obtained by pharmacological and non-pharmacological interventions, and vaccines, between countries with advanced economies and with developing economies. The percentages reveal the similarity of the researchers'interest in contributing to the control of the pandemic, but they do not reflect the countries' investments. One of the limitations of this study is the lack of data on financing, infrastructure, and institutional and technical qualifications for the development of systematic reviews. However, we recognize that countries with advanced economies invest in research differently than those with developing economies.

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