INPLASY PROTOCOL

To cite: Vilca-Alosilla et al. Comparing the accuracy of COVID-19 diagnostic tests: a systematic review and meta-analysis. Inplasy protocol 2022110090. doi: 10.37766/inplasy2022.11.0090

Received: 18 November 2022

Published: 18 November 2022

Corresponding author:
Miguel Angel Chávez-Fumagalli

mchavezf@ucsm.edu.pe

Author Affiliation:
Computational Biology and Chemistry Research Group, Vicerrectorado de Investigación, Universidad Católica de Santa María, Arequipa 04000, Peru.

Support: **grant 27574-R-2020grant 28048.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Comparing the accuracy of COVID-19 diagnostic tests: a systematic review and meta-analysis

Vilca-Alosilla, JJ[1]; Candia-Puma, MA[2]; Coronel-Monje, K[3]; Goyzueta-Mamani, LD[4]; Galdino, AS[5]; Machado-de-Ávila, RA[6]; Giunchetti, RC[7]; Coelho, EAF[8]; Chávez-Fumagalli, MA[9].

Review question / Objective: **The present study aims to systematically review and summarize the available literature on the diagnostic accuracy of COVID-19 diagnostic tests. To do this, a systematic review of the medical literature was carried out between 2020 and 2021. The results were analyzed through a meta-analysis based on the techniques developed and used in the diagnosis of COVID-19.**
Eligibility criteria: **The studies were selected in three stages. In the first, non-English language articles, duplicate articles, reviews, and meta-analyses were excluded, only articles published between 2020 and 2021 conducted on humans were included. In the second stage, the titles and ab-stracts of the articles selected through the search strategy were examined. Finally, the highly relevant full studies were retrieved and separated from the articles with a title or abstract that did not provide sufficient data to be included.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 November 2022 and was last updated on 18 November 2022 (registration number INPLASY2022110090).

INTRODUCTION

Review question / Objective: **The present study aims to systematically review and summarize the available literature on the diagnostic accuracy of COVID-19 diagnostic tests. To do this, a systematic review of the medical literature was carried out between 2020 and 2021. The results were analyzed through a meta-analysis**

based on the techniques developed and used in the diagnosis of COVID-19.

Condition being studied: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported at the end of 2019 in Wuhan, Hubei province, China. On 11 March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic, due to the high levels of spread worldwide. This disease is transmitted by direct contact with an infected person; by the expulsion of droplets and small particles when breathing, speaking, or coughing, or by drops of saliva with the virus that are deposited on surfaces or objects, which are transmitted through touch. According to the WHO, by September 2022, around 600 million confirmed cases of COVID-19 have been reported worldwide, including more than 6 million deaths. Likewise, the transmission of the virus by asymptomatic people is a major concern for community spread, where a study indicates that 35.1% of patients with COVID-19 did not present symptoms, so an early diagnosis of infection would allow the rapid spread of the virus to be controlled. It was estimated that a single symptomatic COVID-19 infection would have an average direct medical cost during infection of US$3 045, which would increase to $14 366 per hospitalization, making COVID-19 one of the greatest global health crises in human history.

METHODS

Search strategy:
The search was carried out until 10 June 2022 in the PubMed database (https://pubmed.ncbi.nlm.nih.gov/). The terms were associated with the terms "COVID-19" and "Sensitivity and Specificity"; generating the new search strings: (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (RT-PCR[MeSH Terms]) for RT-PCR; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (RT-LAMP assay[MeSH Terms]) for RT-LAMP; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (CRISPR[MeSH Terms]) for CRISPR; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (Microarray Analysis[MeSH Terms]) for MA; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (Next generation sequencing[MeSH Terms]) for NGS; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (ELISA[MeSH Terms]) for ELISA; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (Neutralization Tests[MeSH Terms]) for ANB; (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (Biosensing Technique[MeSH Terms]) for BS; and (Covid 19[MeSH Terms]) AND (sensitivity and specificity[MeSH Terms]) AND (Immunoassay[MeSH Terms]) for immunoassays.

Participant or population: Humans with COVID-19 and control groups without the disease.

Intervention: The information consigned for each study chosen included the diagnostic technique, the number, type, and clinical characteristics of patients with COVID-19 and healthy controls. All studies evaluating the sensitivity and specificity of COVID-19 diagnostic techniques have been included.

Comparator: Diagnostic techniques are compared by diagnostic accuracy (sensitivity and specificity).

Study designs to be included: Experimental studies.

Eligibility criteria: The studies were selected in three stages. In the first, non-English language articles, duplicate articles, reviews, and meta-analyses were excluded, only articles published between 2020 and 2021 conducted on humans were included. In the second stage, the titles and abstracts of the articles selected through the search strategy were examined. Finally, the highly relevant full studies were retrieved and separated from the articles with a title or abstract that did not provide sufficient data to be included.

Information sources: PubMed is one of the most widely used search engines for biomedical literature, developed and supported by the US NLM/National Center for Biotechnology Information (NCBI) [35]. The search for the terms associated in the literature with the diagnosis of COVID-19 was carried out using the MeSH term "COVID-19", the results were shown in a co-occurrence network map of MeSH terms in the VOSviewer software (version 1.6.18).

Main outcome(s): Ninety-nine scientific articles that met the criteria were examined and accepted in the meta-analysis, analyzing diagnostic accuracy through specificity and sensitivity. Molecular tests [Reverse transcription polymerase chain reaction (RT-PCR), reverse transcription loop-mediated isothermal amplification (RT-LAMP), and clustered regularly interspaced short palindromic repeats (CRISPR)] showed better performance in terms of sensitivity and specificity than serological tests [Enzyme-linked immunosorbent assay (ELISA), chemiluminescence immunoassay (CLIA), lateral flow immunoassay (LFIA), chemiluminescent microparticle immunoassays (CMIA), and Fluorescence immunoassay (FIA)]. The serological tests reported a higher specificity, especially with the detection of IgG, however, they showed a sensitivity below 90% in general. In addition, the antiviral neutralization bioassay (ANB) diagnostic technique demonstrated high potential in the diagnosis of COVID-19 since it obtained the highest area under the curve restricted to the false positive rates (AUCFPR) of 0.984.

Quality assessment / Risk of bias analysis: This systematic review was based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) technique.

Strategy of data synthesis: Results were entered into Microsoft Excel (version 10.0, Microsoft Corporation, Redmond, WA, USA) spreadsheets and analyzed in the R programming environment (version 4.2.1) using the package "mada" (version 0.5.11) https://cran.r-project.org/web/packages/mada/index.html (accessed on 24 October 2022); which employs a hierarchical model that accounts for within and between-study (heterogeneity) and the correlation between sensitivity and specificity. Initially, the number of true negatives (TP), false negatives (FN), true positives (TP), and false positives (FP) were analyzed separately for each diagnostic technique; while the evaluation of sensitivity (Se) and specificity (Sp) made it possible to determine the diagnostic performance.

Subgroup analysis: Additionally, the positive likelihood ratio (LR+) expresses the ratio between the probability of expecting a positive test in a patient and the probability of expecting a positive test in a patient without the disease; the negative likelihood ratio (LR–), which expresses the probability that a patient will test negative among people with the disease and the probability that a patient will test negative among people without disease; and the diagnostic likelihood ratio (DOR), which is the odds ratio of the positivity of a diagnostic test result in the diseased population relative to the non-diseased population; and the 95% confidence interval (CI) were determined. Summary receiver operating characteristic (sROC) curves were fitted, according to the parameters of the "Reitsma" model of the "mada" package, and were used to compare the diagnostic accuracy of CD diagnostic techniques.

Sensitivity analysis: The confidence level for all calculations was set to 95%, using a continuity correction of 0.5 if pertinent.

Language restriction: English.

Country(ies) involved: Peru and Brazil.

Keywords: SARS-CoV-2, COVID-19, Diagnostic Tests, Meta-analysis, Systematic review; Sensitivity and Specificity.

Contributions of each author:

Author 1 - Juan Jeferson Vilca-Alosilla.
Email: juan.vilca@ucsm.edu.pe

Author 2 - Mayron Antonio Candia-Puma.
Email: mcandia@ucsm.edu.pe
Author 3 - Katiusca Coronel-Monje.
Email: 74420396@ucsm.edu.pe
Author 4 - Luis Daniel Goyzueta-Maman.
Email: lgoyzueta@ucsm.edu.pe
Author 5 - Alexsandro Sobreira Galdino.
Email: asgaldino@ufsj.edu.br
Author 6 - Ricardo Andrez Machado-de-Ávila.
Email: r_andrez@yahoo.com.br
Author 7 - Rodolfo Cordeiro Giunchetti.
Email: giunchetti@gmail.com
Author 8 - Eduardo Antonio Ferraz Coelho.
Email: eduardoferrazcoelho@yahoo.com.br
Author 9 - Miguel Angel Chávez-Fumagalli.
Email: mchavezf@ucsm.edu.pe