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RESEARCH ARTICLE

META-ANALYSIS STUDY: NASOPHARYNGEAL SWABS ARE MORE SENSITIVE THAN OROPHARYNGEAL SWABS IN THE DETECTION OF THE VIRAL GENOME OF SARS-CoV-2

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ABSTRACT
One of the commendable steps to curb the spread of coronavirus disease is detecting the virus immediately. Hence, the most suitable sample and an accurate diagnostic test, such as a nasopharyngeal swab and oropharyngeal swab, can be critical for achieving this goal. However, there is not 100% reliant on the sampling method and used tests as there are possibilities of false negatives due to the inadequate viral genome in the sample. Therefore, this paper aims to conduct a meta-analysis study to collect shreds of evidence of the sensitivity from previously published articles and compare them to achieve the best sampling method for SARS-CoV-2 viral genome detection. A total of 10 studies were retrieved and evaluated accordingly. In addition, an independent t-test was used to compare the sensitivity percentage between nasopharyngeal and oropharyngeal swabs to identify the most suitable sampling method for coronavirus viral genome isolation. Results showed that the nasopharyngeal swab was statistically higher sensitive than the oropharyngeal swab, $t(18) = 2.111$, $p < 0.05$. Therefore, the nasopharyngeal swab is better than the oropharyngeal swab regarding sensitivity rate towards detecting the viral genome of SARS-CoV-2.

Keywords: 2019-nCoV, Covid-19, SARS-CoV-2, nasopharyngeal, oropharyngeal, swab, sensitivity, diagnosis.

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INTRODUCTION

With more than 623 million infected cases and a death count of 6.56 million worldwide up to October 2022, the COVID-19 pandemic has shaken up the whole world in more than Two years (Ritchie et al., 2020). What started as an unidentified outbreak of respiratory syndrome in Wuhan City, Hubei Province, China, was then announced as a global pandemic by the World Health Organization within three months of the outbreak's beginning in December 2019 as cases started being reported in different countries by then. The whole world is now exhausting the frontliners to diagnose and treat these patients while vaccines are being made and put into clinical trials though there has not been a successful vaccine to date.

This virus is a single-stranded RNA-enveloped virus that belongs to the β coronavirus family. The virus is transmitted from person to person via respiratory droplets and aerosols (Abdalqader et al., 2020; Parasher, 2021). According to the World Health Organization guidelines, patients have been said to present with minor flu-like symptoms like fever or chills, cough and sore throat, while some present with more severe symptoms like shortness of breath and loss of taste and smell. However, these symptoms are present even as late as two weeks after exposure to the virus, although the average days of the incubation period are around 5-6 days (Ghazi et al., 2020; Kamel et al., 2020; Malik, 2020; Organization, 2020). During this asymptomatic phase, the exposure to respiratory aerosol from another person binds to the nasal epithelial cells and undergoes local replication and propagation and spreads the infection to other ciliated cells in the airway. During this phase, though the viral load is low, the individual is exceptionally infectious. Keeping this in mind, the current gold standard of diagnosis for this SARS COV-2 is by a molecular test (RT-PCR) that detects the RNA of the virus in respiratory samples acquired through nasopharyngeal or oropharyngeal swabs and others of the same kind (Ads et al., 2020; Lai & Lam, 2021). When a swab is gently passed into the posterior nasopharynx through the nostril, rotated a couple of times and withdrawn slowly is called a nasopharyngeal swab (Ek et al., 2019). This procedure is said to cause more discomfort and droplet production in the nasal cavity. On the other hand, the oropharyngeal swab is taken by wiping the swab onto the pharyngeal tonsils and posterior pharynx, avoiding the tongue simultaneously. Patients often complain of nausea or vomiting during or after this procedure (H. Wang et al., 2020).

This article aims to perform a meta-analysis study to determine the higher sensitivity sampling method, nasopharyngeal or oropharyngeal swab, for detecting the SARS COV-2 viral genome in COVID-19 patients.

METHOD

Study Design

The study design applied in this review article is a meta-analysis study. It was developed based on the following question, "In Covid-19 patients, does a nasopharyngeal swab more sensitive than an oropharyngeal swab to detect the viral genome of coronavirus?". The meta-analysis study was developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines (Moher et al., 2015).

Search Strategy

All relevant studies were sourced using PubMed, Cochrane, Clinical Key, Scopus and Google Scholar. Search terms such as 2019-nCoV, Covid-19, SARS-CoV-2, nasopharyngeal, oropharyngeal, swab, sensitivity, diagnosis and other terms combined Boolean operators 'AND' and 'OR' were used. The search was also done through the websites of key healthcare organizations such as the CDC and WHO. A further search was performed through reference searching from the studies that were gathered.

Eligibility Criteria

Screening of the title and abstract, followed by full-text screening to determine eligibility, was done through the retrieved articles for final inclusion. Selection of the studies for the present meta-analysis was based on the eligibility criteria as follows: (i) sensitivity of the nasopharyngeal swabs and oropharyngeal swabs specimens for SARS-CoV-2 detection; (ii) diagnostic test for Covid-19; (iii) results that established quantitative analysis and (iv) observational studies, non-peer-reviewed studies and preprint were included. (v) Clinical trial studies and articles other than the English language were excluded. The articles were grouped into relevant categories, as indicated in the PRISMA flow diagram (Figure 1).

Data Extraction

Data from the articles that fulfilled the listed eligibility criteria underwent extraction. The following data were extracted author, year, number of patients, number of samples, sample type, the sensitivity of nasopharyngeal swabs and oropharyngeal swabs in percentage, evaluated method, and gene marker (Table 1).

Quality Assessment

Authors of this article evaluated the risk of bias in each study independently using the Jadad Score Calculation. An overall score out of 5 was determined based on the presence of a randomised study, the method of randomisation, the implementation of the double-blinded test, the method of double-blinding, statement on withdrawals and dropouts. At the same time, points were deducted if randomisation and double-blinded tests were not described properly (Jadad et al., 1996; Kung et al., 2010).

Data Synthesis

Statistical analysis of the Independent T-test was done using Graph Pad Prism version 5.01 (Graph Pad Software, USA) to establish a summary estimate based on sample type sensitivity. P values of < 0.05 were considered significant. Error bars were expressed in the graphs as ± SD.

RESULTS

A total of 47 articles were identified after the title and abstract screening. Full-text articles were assessed for eligibility, in which 37 articles were excluded (Figure 1). Ten studies were qualified for the final analysis in the present meta-analysis (Table 1). A total of 3282 specimens were tested for SARS-CoV-2, consisting of nasopharyngeal swabs specimens (52.7 %; 1731/3282) and oropharyngeal swabs specimens (47.2 %; 1551/3282). The number of nasopharyngeal swabs and oropharyngeal swabs specimens were not mentioned in four studies (Bwire et al., 2021; Carver & Jones, 2020; Liu et al., 2020; Manzoor, 2020). Three studies presented suspected cases of Covid-19 (Bwire et al., 2021; Manzoor, 2020; X. Wang et al., 2020), six studies included confirmed cases of Covid-19 (Carver & Jones, 2020; Hung et al., 2020; H. Wang et al., 2020; W. Wang et al., 2020; X. Wang et al., 2020; Yang et al., 2020), and there is one study consisting of confirmed or suspected cases of Covid-19 (Liu et al., 2020). One study presented oropharyngeal and nasopharyngeal swabs tested for SARS-CoV-2 RNA by the CDC through 3 March 2020 (Patel et al., 2021). Patients who were admitted to the hospital with any illnesses were included in one study (Manzoor, 2020). An independent sample t-test was used to compare the sensitivity (percentage) between nasopharyngeal swabs and oropharyngeal swabs for the detection of the viral genome of coronavirus. Shapiro-Wilk statistic was non-significant. This indicates that the assumption of normality was not violated. Levene's test was also non-significant. Thus, equal variances can be assumed. The t-test was statistically significant, with the nasopharyngeal swab (M = 58.38, SD = 26.36) had significantly higher sensitivity than oropharyngeal swab (M = 33.36, SD = 26.64), t (18) = 2.111, p < 0.049 (Figure 2).

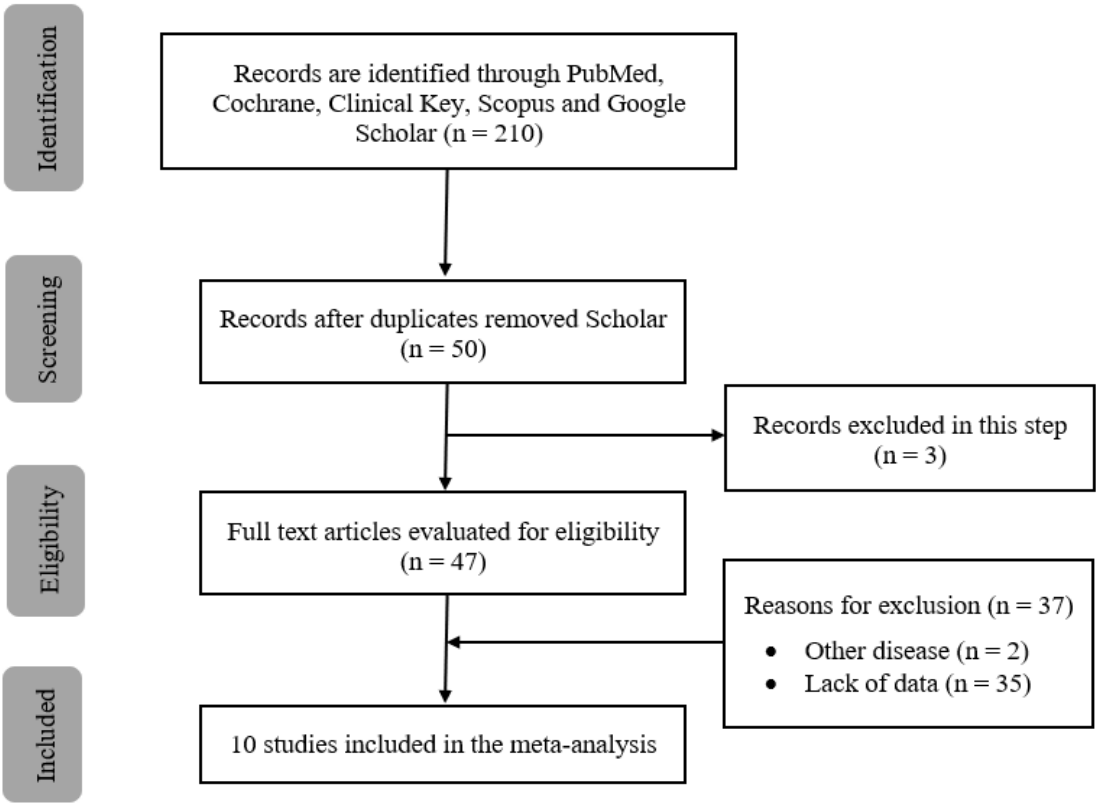

Figure 1: Prism flow chart showing study screening.

Table 1: Characteristics of the included studies

No	Study	No of Patients	No of Samples (N)	Sample Type	Sensitivity (%)	Evaluated Method
1	(H. Wang et al., 2020)	120	120 pairs	NS	98.3	RT-PCR
				OS	21.1	
2	(Patel et al., 2021)	205	270 pairs	NS	88.0	RT-PCR
				OS	84.0	
3	(Bwire et al., 2021)	-	-	NS	45.5	qRT-PCR
				NS	45.5	
4	(Liu et al., 2020)	48	-	NS	42.5	qRT-PCR
				OS	7.5	
5	(W. Wang et al., 2020)	205	8	NS	63	qRT-PCR
				398	OS	
6	(Carver & Jones, 2020)	-	-	NS	70	RT-PCR
				OS	60	
7	(Yang et al., 2020)	213	490	NS	73.2	qRT-PCR
				205	OS	
8	(X. Wang et al., 2020)	353	353	NS	19.0	RT-PCR
			353	OS	7.6	
9	(Manzoor, 2020)	626	-	NS	20.8	RT-PCR
				OS	17.6	
10	(Hung et al., 2020)	213	490	NS	63.45	RT-PCR
			205	OS	36.2	

No: Number, NS: Nasopharyngeal swabs, OS: Oropharyngeal swabs, RT-PCR: Reverse transcription polymerase chain reaction, qRT-PCR: Real-time quantitative reverse transcription-polymerase chain reaction.

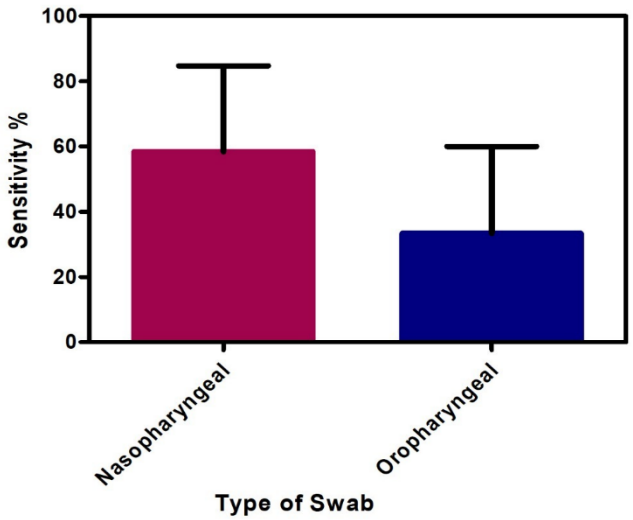

Figure 2: The mean of different types of swabs obtained. Nasopharyngeal swab shows significant sensitivity in the detection of the coronavirus genome (Unpaired t-test with two-tailed, $p < 0.049$). Error bars represent standard deviation.

DISCUSSION

Several studies have been conducted to find the best test for the rapid detection of Covid-19 antigens. Laboratories have been using nucleic acid amplification tests (NAATs), such as real-time reverse transcription polymerase chain reaction (rRT-PCR) assays, to detect the virus (Beeching et al., 2020; Organization, 2020). To perform the test, sample collection materials are needed, many of which are presently using nasopharyngeal (NP) and oropharyngeal (OP) specimens, but some studies have been conducted discussing the alternative samples that could also be used, such as saliva (Byrne et al., 2020; Hung et al., 2020; Jamal et al., 2021; To et al., 2020; Vaz et al., 2020; Williams et al., 2020; Wyllie et al., 2020). Several studies have investigated the sensitivity of NP and OP samples to detect SARS-CoV-2; the results are consistent with NP having higher sensitivity than OP. This study assesses the better sensitivity of NP samples and will further elaborate on them. A small sample study analyzed 48 patients with COVID-19 and found that the nasopharyngeal detection ratio was higher than the nasal swab, but there was no substantial difference between them; the oropharyngeal swab was the second (Liu et al., 2020). One study conducted by Wang et al., 2020 on 120 Covid-19 patients

documented that the SARS-CoV-2 detection rate in the NP sample was 46.7% (56/120), and the OP sample detection rate was 10.0% (12/120)(H. Wang et al., 2020). Furthermore, according to this study NP sample had a significantly higher detection rate when the sample was taken 21 days after the onset of symptoms. Though the NP sample's detection rate was also higher when taken less than 21 days after the onset of symptoms, the difference was not significant. This result gives us the information that a sample's sensitivity can depend on when the sample has been taken after the onset of symptoms. Patel et al., 2021 in their study of 146 Covid-19 patients, found that the NP sample had a lower cycle threshold value which suggests that NP swabs can detect SARS-CoV-2 more accurately (Patel et al., 2021). The absolute sensitivity for NP swabs was also higher (88%) compared to the OP sample (84%). At the same time, this study also mentions the increased sensitivity of viral load detection when the samples are paired to come to a diagnosis. Sensitivity is the percentage of true positives that each method accurately identifies. We used an independent sample t-test to analyze the sensitivity (percentage) between NP and OP swabs. The t-test was statistically significant, with a significantly higher sensitivity of the NP swabs than the OP swabs. This result was built using the positivity percentage in 10 articles stated in Table 1. The sensitivity of NPS in the study by Wang et al., 2020 was significantly higher than that of OPS ($P < 0.001$) (H. Wang et al., 2020).

In a prospective study by Wang et al., 2020 (H. Wang et al., 2020), the viral load was ten times higher in NP specimens as the mean NP Ct value was considerably lower than OPS, with lower Ct values equated to higher viral copy numbers. They suggest that the upper respiratory tract's viral load decreased in improved patients' cases, but NPS specimens can still be detected for a longer time. They believe that the amount of virus in the nasopharynx may also be higher than that in the oropharynx, and because of a larger nasopharynx surface region, this contributed to a more lavish virus collection. However, low viral loads of patients infected with SARS-CoV-2 during the late stage of infection can easily lead to false-negative nucleic acid results, thereby presenting significant challenges in the disease control of the current pandemic (Liu et al., 2020).

CONCLUSIONS

Laboratory diagnosis and SARS-COV-2 nucleic acid detection are crucial for identifying the patients and subsequently controlling the COVID-19 pandemic. The right and susceptible samples play a vital role in the accuracy and reliability of the test. The analysis of previously published articles through this meta-analysis study concluded that NP swabs usage is better in detecting the SARS-COV-2 viral genome than an OP swab. In comparison to OP samples, NP samples demonstrated a much greater SARS-CoV-2 detection rate, sensitivity, and viral load. NP swabs might lessen the number of droplets produced during swabs. Thus, use of NP swabs for COVID-19 diagnosis and viral load monitoring is advised.

ETHICAL CONSIDERATIONS COMPLIANCE WITH ETHICAL GUIDELINES

Not applicable. Ethical approval is not required for this study.

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AUTHOR'S CONTRIBUTIONS

All authors have made significant contributions to this manuscript and have approved the final version to be submitted.

Alhoot MA, PhD – Study conception and design, interpretation of data, drafting and revision of the article content.

Mai MYM, PhD – Data analysis and interpretation

Purwitasari N, PhD - Revision of the article and data organization.

Gunasekaran KK, Shamsul Rodzi NI, Kader Mohideen ZN, and Mohammad Mazli MA -Data acquisition, Data organization and drafting of the article

DISCLOSURE STATEMENT:

The authors report no conflict of interest.

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