

Viral Load, Detection Rate and Sensitivity of Nasopharyngeal and Oropharyngeal Swab Sampling for Diagnosis of COVID-19

Eyzawiah Hassan¹, Nuralia Akma Mohamad Mustafa², Nor Azirah Salahuddin¹, Siti Asmat Md Arepen¹

¹Surgical-based Department (Otorhinolaryngology Head and Neck Surgery), Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia (USIM)

²Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia (USIM)

Siti Asmat Md Arepen

Corresponding Author

Otorhinolaryngology Head and Neck Surgery, Surgical-based Department,
Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia (USIM)

E-mail: drsitiassmat@usim.edu.my

Abstract

The rapid spread of the COVID-19 pandemic has led to a major public health crisis. Accurate screening methods for COVID-19 infection is essential and crucial for case detection, isolation, prevention and control of the current pandemic. At present, nasopharyngeal and oropharyngeal swabs are typically used as the method of choice for the diagnosis of SARS-CoV-2 infection. We carried out a review on the accuracy of the two different sampling sites, the nasopharyngeal and oropharyngeal swab sampling, focusing on the viral load, detection of positive cases and sensitivity in real-time polymerase chain reaction (RT-PCR) assay in diagnosing COVID-19. A total of 25 articles related to the topic were selected out of 5221 articles searched online using Scopus, PubMed and Medline, Embase, Web of Science, and Google scholar with the keywords *COVID-19*, *SARS-CoV-2*, *nasopharyngeal swab*, *oropharyngeal swab*, *nasal swab* and *throat swab*. All full text original articles were obtained and reviewed. Nasopharyngeal swab had

Manuscript Received Date: 31/12/20

Manuscript Acceptance Date: 31/05/21

Manuscript Published Date: 19/06/21

©The Author(s) (2021). Published by USIM Press on behalf of the Universiti Sains Islam Malaysia. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact usimpress@usim.edu.my

doi: <https://doi.org/10.33102/uij.vol33no3.319>



Universiti Sains Islam Malaysia
<https://uijournal.usim.edu.my>

significantly higher SARS-CoV-2 load than oropharyngeal swab (mean Ct value ranging from 24.3-37.8, higher detection of positive rate (highest rate 62.5%) and sensitivity (highest sensitivity 98.3%, $P < 0.05$) in RT-PCR assay compared to oropharyngeal swab. Based on the scientific literature review, both nasopharyngeal and oropharyngeal swabs were reported to have 30% probability of yielding false negative results; thus clinically suspicious patients with negative results should be viewed with concern. In conclusion, although several methods of COVID-19 screening and type of specimen are available, nasopharyngeal swab is the best option for large scale screening as it yields significantly higher viral load, higher detection of positive rate among cases and higher sensitivity in RT-PCR assay compared to oropharyngeal swab in detecting SARS-CoV-2.

Keywords: COVID-19, nasopharyngeal swab, oropharyngeal swab, nasal swab, throat swab

1. Introduction

The first case of Coronavirus disease 2019 (COVID-19) was identified in Wuhan, China in December 2019. The patient presented with atypical pneumonia by an unrecognized pathogen. The agent causing the unusual pneumonia was from the Coronaviridae family and was formerly named 2019 novel coronavirus (2019-nCoV) (WHO, 2020). Early epidemiological reports of the viral transmission involved the population who lived in or had visited Wuhan and it was suggestive of human-to-human transmission. The World Health Organization (WHO) declared COVID-19 as a pandemic on 11 March 2020 (WHO, 2020). In Malaysia, the first cases of COVID-19 were reported on 25 January 2020, among visitors from China who entered the country via Singapore. Since then, the number of COVID-19 cases have rapidly increased in numbers with appearance of new clusters leading to the implementation of the Movement Control Order (MCO) on 18 March 2020 (Reuters, 2020).

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus is spread from human to human via respiratory droplets. According to the WHO, most of the patients infected by SARS-CoV-2 commonly presented with symptoms of fever, non-productive cough and fatigue. A research on common clinical manifestations of COVID-19 by Guan (2020) among thousands of COVID-19 patients in Wuhan showed that most (88.7%) developed fever during hospitalisation, more than half (67.8%) suffered from a cough, about 43.8% had fever on admission, and one-third (38.1%) had fatigue. The same study also found that 14.9% experienced myalgia, 13.9% sore throat, 0.8% conjunctivitis and 13.6% of patients experienced headache. Besides, less than 20% of the patients had shortness of breath, and only one-third (33.7%) of all patients were producing sputum. Other clinical manifestations included lymphopenia, radiographic findings suggestive of pneumonia, acute respiratory distress syndrome (ARDS) and acute respiratory failure in severe cases (Guan et al., 2020).

The screening of COVID-19 infection is essential and crucial to control the spread of the pandemic. Researchers in most screening centres across the world continue to study and understand COVID-19 disease. They use nasopharyngeal (NP) and oropharyngeal (OP) swabs as the methods of choice to detect SARS-CoV-2. Currently, real-time reverse transcriptase–polymerase chain reaction (rRT-PCR) of NP and OP swabs generally has been used to screen for SARS-CoV-2 infection. The specimens collected from different anatomical sites for rRT-PCR

might affect the test performance thus yielding different results. According to previous studies, there was significant difference in the viral loads of different specimens depending on where and when the samples were collected in the respiratory tract.

This review was performed based on available original articles to analyse NP and OP swabs sampling in terms of viral load, rate of detection of positive cases and the sensitivity of the rRT-PCR assay in diagnosing COVID-19.

2. Methodology

Search strategy

Relevant articles published in English from 2000 to 2021 were identified using the search engines Scopus, PubMed, Medline, Embase, Web of Science, and Google Scholar from 17 August 2020 to 25 February 2021. We identified 25 articles from a total of 5221 articles related to the topic using the keywords *COVID-19*, *SARS-CoV2*, *nasopharyngeal swab*, *oropharyngeal swab*, *nasal swab*, *throat swab and screening*.

Eligibility criteria

Eligible studies included cohort, case-control studies, retrospective, cross-sectional and descriptive studies reporting the diagnostic accuracy of the NP and OP swab sampling in terms of the viral load by both methods, detection of positive cases and sensitivity rate in rRT-PCR assay in diagnosing COVID-19. We excluded articles with sample sizes less than five. Studies that did not include both NP and OP swab sampling analysis, published in non-English language or conducted on non-human samples were omitted.

Data extraction and bias assessment

Publications identified were screened for their title and abstracts according to the eligibility criteria, and further shortlisted for full-text screening. Out of 5221, only 25 articles that met the eligibility criteria were shortlisted and included after the full text screening. The findings of only 12 articles which included comparison of both NP and OP swabs are summarised in Table 1.

3. Results

SARS-CoV-2 Load in Nasal and Throat Swab Specimens

Viral load plays a significant role in detecting SARS-CoV-2 infection. The trend of viral nucleic acid shedding in COVID-19 patients is different from SARS-CoV and MERS-CoV, which had minimal shedding in the early stages and peaked approximately 10 days after occurrence of symptoms (Peiris et al., 2003).

The recent study reported by Zou et al. among 18 patients infected by SARS-CoV-2 suggested that NP swab yielded a higher viral load than OP swab (Zou et al., 2020). This finding was supported the study by Wang W et al., where NP swab had a higher viral load than OP swab; the NP swab had mean cycle threshold (Ct) value of 24.3 (1.4×10^6 copies/mL) while mean Ct value of OP

swab was more than 30 ($<2.6 \times 10^4$ copies/mL). A cycle threshold value less than 40 was interpreted as positive for COVID-19 (Wang W et al., 2020). Cycle threshold was inversely proportionate to the amount of target nucleic acid in the sample. This study showed that the lower the Ct value, the higher the viral load but contrary to this finding, the result of a study by Yu et al., (2020) showed that the OP swab had significantly higher viral load than NP swab (2552 copies/test [SD=1965], $p < 0.001$) and (651 copies/test [SD= 501], $p < 0.001$) respectively.

Wang H. et al. (2020) conducted a study on the difference in SARS-CoV-2 viral load in 120-paired NP and OP specimens by rRT-PCR analysis. The Ct values were used to determine the SARS-CoV-2 RNA expression with lower Ct values corresponding to higher viral load (Wang H. et al., 2020). They found that NP swab had significant low Ct value compared to OP swab ($p < 0.001$) which suggested a higher viral load in NP swab samples. In among 57 positive COVID-19 patients, majority (91.2%) had lower Ct value of NP swab compared to OP swab which were 35.3% and 38.7%, respectively. Therefore, it indicates that the viral load in NP swab is significantly 10 times higher than OP swab. This finding was aligned with the result of studies conducted by Patel et al. (2021).

A study by Hernes et al. (2011) involving detection of other multiple respiratory viruses also found that NP swabs had lower Ct values than OP swabs (mean difference Ct 4.25, 95% CI [2.43, 6.07], $p < 0.001$) indicating higher viral load in NP swab specimens which was 19 times higher (95% CI [5.4, 67.2]) than OP swab specimens. Similar findings were reported by Peter et al. (2019).

Detection Rate and Sensitivity by Nasopharyngeal and Oropharyngeal Swabs Specimens in Diagnosing COVID-19

A descriptive study among 301 hospitalised COVID-19 patients showed different positive rates between NP and OP swabs specimens (Xiao et al., 2020). The researchers had performed 1113 tests using NP and OP swab specimens for SARS-CoV-2 detection by rRT-PCR analysis. Seventy-four (74) tests consisting of 37 pairs of both OP and NP swabs collected at the same time showed results of positive NP swab and negative OP swab in 12 pairs of tests (32.4%), but only two pairs of tests (5.4%) showed results of positive OP swab and negative NP swab. More than half (62.2%) pairs of tests had similar results of OP and NP swabs, of which four pairs had both positive results and 19 pairs had both negative results. They also did 46 swab samplings of both NP and OP at different points of time, where OP swabs were collected first, followed by NP swab. Unfortunately, the time frame between the OP and NP was not mentioned. The study found that 41.3% (19/46) of samples had negative OP swab followed by a positive NP swab which indicates high probability of false negative in a single collection of OP swab in the early stage of the illness. Therefore, it is estimated that about half (41.3%) of OP swab samples had false negative results of SARS-CoV-2 rRT-PCR assays compared to confirmed diagnosis of COVID-19 using NP swab. This study suggested that specimens for SARS-CoV-2 rRT-PCR assay should be obtained from NP swab as it was more sensitive and reliable for the assay compared to OP swab.

Wang H. et al. (2020) conducted a study among 120 COVID-19 patients to compare the detection rate for both NP and OP swabs. They defined the detection rate as the percentage of positive results from the total specimens. The sampling was done between the 3rd and 49th day from the onset of symptoms, at a median of 27.0 days (IQR 23.0–31.5). Among these 120 COVID-19

patients, the detection rate of NP swabs was nearly half (46.7%) of the total cases whereas the detection rate of OP swabs was only 10.0% from the total of positive cases. It showed that NP swab had a significantly higher detection rate of SARS-CoV-2 than OP swab ($p < 0.001$). The NP swab also had a significantly higher detection rate ($p < 0.001$) after 21 days following the onset of symptoms (Wang H et al., 2020).

Meanwhile, another study by Lin et al. (2020) which compared the detection rates of COVID-19 from sputum specimens and OP swab specimens showed that the positive detection rate was significantly higher in the sputum group compared to the throat swabs which were 76.9% and 44.2%, respectively (Lin et al., 2020). Similarly, Wang H et al. (2020) found that sputum had a higher positive rate, followed by NP swab and OP swab which were 72%, 63% and 32%, respectively.

In a study involving 213 COVID-19 patients, 866 samples from 61 respiratory tracts of the patients were obtained including NP swab and OP swab (Yang et al., 2020). The samples were obtained upon admission and at different points of time throughout the course of the disease. Sample collection dates were classified into three groups which were '0 to 7', '8 to 14' and ' ≥ 15 ' days after the onset of symptoms. The patients were also classified into 'severe' and 'mild' groups. A total of 205 OP swabs and 490 NP swabs were obtained. For the '0 to 7' days after symptom onset group, the positive rate of NP swabs (73.3% and 72.1% for severe and mild case, respectively) were higher than the OP swabs (60.0% and 61.3% for severe and mild case, respectively). In the group '8 to 14' days after symptom onset it was noted that the positive rate of 125 OP swabs was only 50% in severe and 29.6% in mild cases as compared to NP swab of 72.3% and 53.6% in the severe and mild groups, respectively. In the ' ≥ 15 ' after symptom onset group, it was revealed that NP swabs had a much higher positive rate than the OP swabs among the mild cases. This finding suggested that NP swabs are more reliable samples for virus detection. The OP swabs are not recommended for the SARS-CoV-2 virus screening, especially when the samples are obtained during 8 to 14 days and more than 14 days after onset of symptoms in mild cases as a significant proportion of false negative outcomes may result from this. However, in the same study by Yang et al. (2020), most of the specimens were obtained after antiviral therapy, which may have influenced viral shedding. Furthermore, care should be taken as a single negative result does not indicate that the patient is not infected. The sensitivity of the test depends on whether the sample collected by NP and OP swab is sufficient as well as the technological sensitivity of the test itself which has various sensitivity measures (Yang et al., 2020).

In another study by Patel et al. (2021), they reported only a slightly higher sensitivity for NP swabs in pairs of specimens collected less than seven days after symptoms onset compared to OP swabs.

However, OP swab sensitivity was comparatively low in swab pairs collected after seven days of illness onset (median, 12 days; IQR, 9–19); while 14 (23.7%) NP swabs tested positive, and 10 (17.0%) OP swabs tested positive ($p = .045$). Wang H et al. (2020) analysed the diagnostic sensitivity by using NP and OP swab specimens among 57 positive COVID-19 patients. They defined the sensitivity as the percentage of true positives correctly identified by both methods. The results showed that the sensitivity of NP swab (98.3%) specimen was significantly higher than OP swab (21.1%) specimen. In order to explain what medical conditions could influence the disparity in sensitivity, they categorized patients based on clinical features and laboratory values. In all

medical conditions, except for febrile patients, NP swab sensitivity was substantially higher than OP swab sensitivity ($p < 0.05$). Among the seven febrile patients, there was no significant difference in sensitivity between NP and OP swabs, which can be explained by the limited sample size. This discovery showed that the NP swab was more reliable diagnostically than the OP swab.

A similar observation was reported by Bwire et al. (2021) in which the positive detection rate for NP swab and OP swab were 45.5% and 7.6%, respectively. A study by Zhang et al. (2020) found that the positive rate in NP swabs (37.5%) was higher compared to OP swabs (20.8%). However, the result was not significant, likely due to the small sample size. In contrast, a study by Calame et al. (2021) showed there was significant correlation between OP swabs and NP swabs specimen with regards to the analytical sensitivity at the quantitative level.

Similarly, a previous study to investigate other respiratory viruses among 224 patients with lower respiratory tract infections, also showed a higher sensitivity rate for NP swabs (73.3%) as compared to OP swabs (52.4%) (Lieberman, et al., 2009). This finding was supported by the results of another study among patients with pharyngitis, which found that the sensitivity of NP swabs was 74% (95% CI [65,83]) which was significantly higher than OP swabs of 49% (95% CI [39, 60]) ($p < 0.01$) for detection of all viruses including coronavirus (Li, et al., 2013). Analysis of sensitivity for detecting influenza B virus, PIV 2 and PIV 3 by Kim et al. (2011) showed that NP swabs had significantly higher sensitivity compared to OP swabs for influenza B virus (83.3% vs. 61.5%, $p = 0.02$), PIV 2 (85.7%, vs. 39.3%, $p = 0.01$) and PIV 3 (83.9% vs. 67.4%, $p = 0.01$).

Table 1: The Viral Load, Detection Rate and Sensitivity of SARS-CoV-2 Viral Load in Nasopharyngeal and Oropharyngeal Swab Specimens

Author, year	Region/Country	Sample size and type of specimen	Timing	Laboratory technique and viral loads	Detection rate	Sensitivity	Conclusion & Recommendation
Zou et al., 2020	Guangdong Provincial Center for Disease Control and Prevention Guangzhou, China	N=18 mid-turbinate and NP: n=72 OP: n =72 * 1 to 9 sequential samples obtained from each patient	Consecutive paired sampling up to 9 times since day of admission	rRT-PCR Higher viral loads detected in the nasal than in the throat swab (lower Ct values)	Not specified	Not specified	Viral load in asymptomatic subject was similar to symptomatic patients, which suggests similar transmission potential
Wang W. et al., 2020	Hubei and Shandong , Beijing	Nasal: n=8 Pharyngeal: n=398	Nasal: 1 to 3 days after hospital admission Pharyngeal : through-out the illness	rRT-PCR Nasal mean Ct value = 24.3 Pharyngeal mean Ct value= 32.1	Nasal: 62.5% (5/8) Pharyngeal: 31.7% (126/398)	Not specified	Higher viral loads in nasal specimens
Wang H. et al., 2020	Wuhan, China	NP: n=120 OP: n=120 inpatients with confirmed COVID-19	Median: 27days (IQR 23.0–31.5), ranging between 3 and 49 days	rRT-PCR mean Ct value: NP= 37.8, 95% CI (37.0, 38.60) OP= 39.4, 95% CI: (38.9, 39.8) ($p < 0.001$)	NP:46.7% (56/120) OP:10.0% (12/120) ($p < 0.001$) ($p < 0.001$, Kappa = 0.19 with 95% CI (0.07, 0.31)	NP= 98.3% (56/57, 95% CI 94.8–100.0) OP= 21.1% (12/57, 95% CI $p < 0.001$)	SARS-CoV-2 load, detection rate and sensitivity was significantly higher in NP swab specimens than OP swab
Patel et al., 2020	Georgia, USA	NP: n=146 OP: n=146	≤7 days after illness onset	Real-time rRT-PCR Median Ct values : NP= 24.3 (IQR, 22.7–26.5) OP= 29.9 (IQR, 22.1–34.4)	18 (12.3%) pairs were concordantly positive 121 (82.9%) pairs were concordantly negative Detection rate: NP= 15.1% OP= 14.4%	NP= 88.0% (CI, 68.8%–97.5%) OP= 84.0% (CI, 63.9%–95.5%)	SARS-CoV-2 RNA diagnostic results were highly concordant between OP and NP swabs in early phase of the illness. NP swabs may comparatively be a more sensitive specimen type for testing persons who are later in the illness course.

Viral Load, Detection Rate and Sensitivity of Nasopharyngeal and Oropharyngeal Swab Sampling for Diagnosis of COVID-19

Yu et al., 2020	Beijing, China	N=76 confirmed COVID-19	Not specified and samples are not paired	Sputum: (17429, SD=6920 copies per test) Throat : (2552 SD=1965 copies per test, $p < 0.001$) Nasal: (651, SD=501 copies per test, $p < 0.001$)	Based on both RT-PCR and ddPCR: Sputum: (116, 35.9%) Nasal: (55, 17.0%) Throat: (134, 41.5%)	Not specified	The viral load in the early and progressive stages were significantly higher than that in the recovery stage. Sputum is a better indicator of viral replication in the body than throat and nasal swabs
Liu et al., 2020	Wuhan, China	N:4880 (among suspected cases)	Not specified	RT-PCR (viral load not specified)	Total +ve swabs: n=1875 (38.42%) NP & OP: n=4818 (38.25%) +ve swabs	Not specified	Repeat RT-PCR for suspected false negatives.
Yang et al., 2020	Guangdong Center for Disease Control and Prevention, China	N=213 Nasal swabs: n=490 OP: n=205	Days after illness onset: 0-7 days 8-14 days ≥ 15 after illness onset	RT-PCR	Type (severe/mild) Nasal (73.3%/72.1%) Throat (60.0%/61.3%) Nasal (72.3%/53.6%) Throat (50%/29.6%) Nasal (50%/54.5%) Throat (36.8%/11.1%)	Not specified	Nasal swabs may be the most widely applicable samples for virus detection. Throat swabs were not recommended for samples collected after day 8 of illness.

Bwire, et al. 2020	University of Health and Allied Sciences, Dar es Salaam, Tanzania.	N: 8136 NP: n=5662 Throat: n=3	Not specified	RT-PCR (systematic review)	NP: 45.5% (95% CI[31.2, 59.7]) OP: 7.6% (95% CI [5.7, 9.6])	Not specified	NP had a moderate positive rate and OP had a low positive rate as compared to high positive rate in broncoalveolar lavage and lower respiratory specimens.
Wang X et al. 2020	University of Science and Technology, Wuhan, China	N: 353	Not specified	RT-PCR	Combined positive: 21.5% (76/353) NP: 19.0% (67/353) OP: 7.6% (27/353)	Not specified	1. NP swabs showed higher positive rate than OP swabs for SARS-CoV-2 detection. 2. OP swabs may result in a high false negative rate
Zhang et al., 2020	Beijing Ditan Hospital, China	N:43 (total specimens=291)	≤14 days, 14–21 days >21 days	RT-PCR	Sputum: 79.2% NP: 37.5% ($p = 0.003$) OP: 20.8% ($p < 0.001$) Sputum: 63.6% NP: 18.2%; ($p < 0.001$) OP: 9.1%; ($p < 0.001$) Sputum (70.0%) NP: 15.0% ($p < 0.001$) OP: 10.0% ($p < 0.001$)		Sputum had the highest yield of SARS-CoV-2 detection. NP and OP swabs had a similar yield. If sputum is not feasible, a NP swab can be recommended for the detection of SARS-CoV-2, and early testing is needed.

4. Discussion

Most of the reviewed articles related to the detection of SARS-CoV-2 infection showed that nasal swab had a significantly higher viral load than throat swab (Zou et al., 2020; Wang W et al., 2020; Wang H. et al., 2020 and Patel et al., 2020). It was found that SARS-CoV-2 load was reported to be 10 times significantly higher for NP swab than OP swab with Ct value ranging from ‘24.3 to 37.8’ and ‘29.9 to 39.4’, respectively. The difference of Ct value by both methods was 3.3 (95% CI [2.2, 4.5], $p < 0.001$) which indicates that NP swab had higher viral load compared to OP swab. The Ct is inversely proportionate to the amount of target nucleic acid in the sample which means the lower the Ct, the higher the viral load. In contrast, we found only one study which reported

that OP swabs had significantly higher viral load than NP swabs (Yu et al., 2020). It can be theorised that higher viral load in NP specimens is due to higher amount of SARS-CoV-2 viral replication in the nasopharynx than in the oropharynx after infection sets in. Secondly, it might be due to larger contact surface when collecting the specimens in the nasopharynx that can allow more virus collection.

Although it has been demonstrated that sputum has higher viral load and detection rate as compared to NP and OP swabs, (Yu et al., 2020, and Zhang et al., 2020) the procedure to obtain samples from lower respiratory tract will induce aerosol production and expose the healthcare staff to a high risk of viral transmission. Therefore, upper respiratory tract specimen is preferable in practice. Since the viral load increases with time, early phase of infection may be missed by NP and OP swab tests; thus requiring a repeat test (Li et al., 2020). If we have to assess a population that is asymptomatic by swabbing, we should expect that the false negative rate will increase proportionally. The kinetics of viral RNA should be considered because in the early stages of SARS-CoV-2 infection, the viral load is very low thus yielding a negative result (Chen et al., 2020). As reported by Xiao et al. (2020), there is an estimate of 41.3% false negative rate of OP swabs. In fact, about 30% of clinically symptomatic patients' swabs give a false negative result (Loeffelholz et al., 2020).

Due to its ease of acquisition, NP swab has been preferred and used for diagnosis and dynamic observation of COVID-19 patients. Two successive negative SARS-CoV-2 RNA detections of NP swab specimens have been recognised as a prerequisite for hospital discharge or quarantine release. Nonetheless, the risk of false negative findings is a drawback of the NP swab, raising the question that the persistence of viral shedding could be present in the lower respiratory tract (Winichakoon et al., 2020). A study by Wang K. et al. (2020) of 68 COVID-19 patients who underwent both NP swab and sputum test reported that 20.6% (n=14) patients who initially experienced negative NP swab samples subsequently registered positive sputum specimen during follow-up. They found that the median duration of viral shedding from sputum specimens was significantly longer compared to NP swab specimen ($p<0.001$).

Meanwhile, a study on COVID-19 survivors by Zhou et al. (2020) reported that there was a median of 20 days and a mean of 37 days of viral shedding in the OP swab cases. However, in cases screened by the NP swab, viral shedding had a longer median period of 25 days and a longer mean duration of 41 days. These results suggested that after the onset of symptoms, the NP swab could detect SARS-CoV-2 for a longer duration.

NP and OP swabs are the recommended specimen types for COVID-19 diagnostic testing. Nevertheless, it may cause complications such as pain and can cause bleeding, especially in patients with low platelet counts (Chan et al., 2020). Other reported complications by the patients from NP and OP swabs were teary eyes, rhinorrhoea and emesis (Chan et al., 2020).

This review has some limitations. First, some studies did not define specifically the exact anatomical site for “nasal” and “pharyngeal” swab. The nasal swabs can be taken from anterior nares, mid turbinate or nasopharynx. Secondly, some studies did not provide details of clinical severity or grading, timing of sampling, very wide range of patient illness, therefore, the viral load detection rate and sensitivity may vary and unable to be correlated with disease course. Third, some studies did not pair the NP and OP swab specimens; hence the correlation may be less

accurate. Finally, the sample size and number of positive results were small in majority of the studies, hence it may affect the precision of the estimate of the test sensitivity. This review has provided good supporting evidence of the results of the comparisons between the two sampling techniques that are commonly used in large COVID-19 screening centres.

5. Conclusion

All currently available testing methods including NP and OP swab have their rates of sensitivity and specificity in diagnosing COVID-19. In our review, we can conclude that NP swab had a higher detection rate of positive SARS-CoV-2 viral load and higher sensitivity in RT-PCR assay compared to OP swab for diagnosis of COVID-19. Nevertheless, there is a possibility that both NP and OP swabs may yield false negative result thus investigators should be concerned of patients with clinical suspicion with negative NP and OP swab results. Clinicians should take note that NP swabs have longer duration of viral shredding while OP swabs contribute to higher percentage of false negative results.

Based on this review, NP swab is the best sampling technique to be practised as it is more reliable than OP swab in detecting SARS-CoV-2 infection. A single NP or OP swab sample during the early onset of the disease is not recommended as it has a probability of false negative result which can lead to misdiagnosis and increase the rate of SARS-CoV-2 transmission. For discharge criterion, although NP swab had a longer viral shredding than OP swab, it is recommended to take sputum sample specimen as it has the longest duration of viral shredding than both methods. Nevertheless, studies with larger sample sizes are required to effectively develop and establish a more specific diagnostic approach to improve detection of COVID-19 infection.

6. Acknowledgement

We would like to thank Universiti Sains Islam Malaysia (USIM) for funding this project under the USIM COVID Grant (PPPI/COVID-19_0120/FPSK/051000/10720).

References

- Bwire, G. M., Majigo, M. V., Njiro, B. J., & Mawazo, A. (2021). Detection profile of SARS-CoV-2 using RT-PCR in different types of clinical specimens: A systematic review and meta-analysis. *Journal of medical virology*, 93(2), 719-725.
- Calame, A., Mazza, L., Renzoni, A., Kaiser, L., & Schibler, M. (2021). Sensitivity of nasopharyngeal, oropharyngeal, and nasal wash specimens for SARS-CoV-2 detection in the setting of sampling device shortage. *European Journal of Clinical Microbiology & Infectious Diseases*, 40(2), 441-445.
- Chan, J. F. W., Yuan, S., Kok, K. H., To, K. K. W., Chu, H., Yang, J., ... & Yuen, K. Y. (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The lancet*, 395(10223), 514-523.
- Chen, Y., Chen, L., Deng, Q., Zhang, G., Wu, K., Ni, L., ... & Cheng, Z. (2020). The presence of SARS-CoV-2 RNA in the feces of COVID-19 patients. *Journal of medical virology*, 92(7), 833-840.

Viral Load, Detection Rate and Sensitivity of Nasopharyngeal and Oropharyngeal Swab Sampling for Diagnosis of COVID-19

- Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Zhong, N. S. (2020). Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine*, 382(18), 1708-1720.
- Hernes, S. S., Quarsten, H., Hagen, E., Lyngroth, A. L., Pripp, A. H., Bjorvatn, B., & Bakke, P. S. (2011). Swabbing for respiratory viral infections in older patients: a comparison of rayon and nylon flocked swabs. *European journal of clinical microbiology & infectious diseases*, 30(2), 159-165.
- Kim, C., Ahmed, J. A., Eidex, R. B., Nyoka, R., Waiboci, L. W., Erdman, D., ... & Katz, M. A. (2011). Comparison of nasopharyngeal and oropharyngeal swabs for the diagnosis of eight respiratory viruses by real-time reverse transcription-PCR assays. *PloS one*, 6(6), e21610.
- Lieberman, D., Lieberman, D., Shimoni, A., Keren-Naus, A., Steinberg, R., & Shemer-Avni, Y. (2009). Identification of respiratory viruses in adults: nasopharyngeal versus oropharyngeal sampling. *Journal of clinical microbiology*, 47(11), 3439-3443.
- Li, L., Chen, Q. Y., Li, Y. Y., Wang, Y. F., Yang, Z. F., & Zhong, N. S. (2013). Comparison among nasopharyngeal swab, nasal wash, and oropharyngeal swab for respiratory virus detection in adults with acute pharyngitis. *BMC infectious diseases*, 13(1), 1-5.
- Li, Z., Yi, Y., Luo, X., Xiong, N., Liu, Y., Li, S., ... & Ye, F. (2020). Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *Journal of medical virology*, 92(9), 1518-1524.
- Lin, C., Xiang, J., Yan, M., Li, H., Huang, S., & Shen, C. (2020). Comparison of throat swabs and sputum specimens for viral nucleic acid detection in 52 cases of novel coronavirus (SARS-Cov-2)-infected pneumonia (COVID-19). *Clinical Chemistry and Laboratory Medicine (CCLM)*, 58(7), 1089-1094.
- Liu, R., Han, H., Liu, F., Lv, Z., Wu, K., Liu, Y., ... & Zhu, C. (2020). Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. *Clinica Chimica Acta*, 505, 172-175.
- Loeffelholz, M. J., & Tang, Y. W. (2020). Laboratory diagnosis of emerging human coronavirus infections—the state of the art. *Emerging microbes & infections*, 9(1), 747-756.
- Patel, M. R., Carroll, D., Ussery, E., Whitham, H., Elkins, C. A., Noble-Wang, J., ... & Brooks, J. T. (2021). Performance of Oropharyngeal Swab Testing Compared With Nasopharyngeal Swab Testing for Diagnosis of Coronavirus Disease 2019—United States, January 2020–February 2020. *Clinical Infectious Diseases*, 72(3), 482-485.
- Peiris, J. S. M., Chu, C. M., Cheng, V. C. C., Chan, K. S., Hung, I. F. N., Poon, L. L., ... & HKU/UCH SARS Study Group. (2003). Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *The Lancet*, 361(9371), 1767-1772.

Peter, Ek., Böttiger, B., Dahlman, D., Hansen, K. B., Nyman, M., & Nilsson, A. C. (2019). A combination of naso-and oropharyngeal swabs improves the diagnostic yield of respiratory viruses in adult emergency department patients. *Infectious Diseases*, 51(4), 241-248

Reuters.com (25th January, 2020).Malaysia confirms first cases of coronavirus infection.. Available: <https://www.reuters.com/article/china-healthmalaysiaidUSL4N29U03A>.

Wang, H., Liu, Q., Hu, J., Zhou, M., Yu, M. Q., Li, K. Y., ... & Xu, S. Y. (2020). Nasopharyngeal swabs are more sensitive than oropharyngeal swabs for COVID-19 diagnosis and monitoring the SARS-CoV-2 load. *Frontiers in medicine*, 7, 334

Wang, K., Zhang, X., Sun, J., Ye, J., Wang, F., Hua, J., ... & Wu, X. (2020). Differences of severe acute respiratory syndrome coronavirus 2 shedding duration in sputum and nasopharyngeal swab specimens among adult inpatients with coronavirus disease 2019. *Chest*, 158(5), 1876-1884.

Wang, X., Tan, L., Wang, X., Liu, W., Lu, Y., Cheng, L., & Sun, Z. (2020). Comparison of nasopharyngeal and oropharyngeal swabs for SARS-CoV-2 detection in 353 patients received tests with both specimens simultaneously. *International Journal of Infectious Diseases*, 94, 107-109.

Wang, W., Xu, Y., Gao, R., Lu, R., Han, K., Wu, G., & Tan, W. (2020). Detection of SARS-CoV-2 in different types of clinical specimens. *Jama*, 323(18), 1843-1844

Winichakoon, P., Chaiwarith, R., Liwsrisakun, C., Salee, P., Goonna, A., Limsukon, A., & Kaewpoowat, Q. (2020). Negative nasopharyngeal and oropharyngeal swabs do not rule out COVID-19. *Journal of clinical microbiology*, 58(5).

World Health Organization (2020) Coronavirus disease (COVID-19). [Online].Available: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.

Wölfel, R., Corman, V. M., Guggemos, W., Seilmaier, M., Zange, S., Müller, M. A., ... & Wendtner, C. (2020). Virological assessment of hospitalized patients with COVID-2019. *Nature*, 581(7809), 465-469.

Yang, Y., Yang, M., Shen, C., Wang, F., Yuan, J., Li, J., ... & Liu, Y. (2020). Laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. *MedRxiv*

Yu, F., Yan, L., Wang, N., Yang, S., Wang, L., Tang, Y., ... & Zhang, F. (28). March 2020. Quantitative detection and viral load analysis of SARS-CoV-2 in infected patients. *Clin Infect Dis*, 71(15), 793-798

Xiao, A. T., Tong, Y. X., Gao, C., Zhu, L., Zhang, Y. J., & Zhang, S. (2020). Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: a descriptive study. *Journal of Clinical Virology*, 127, 104346.

Zhang, H., Chen, M., Zhang, Y., Wen, J., Wang, Y., Wang, L., ... & Zhang, F. (2020, October). The yield and consistency of the detection of SARS-CoV-2 in multiple respiratory specimens. In *Open forum infectious diseases* (Vol. 7, No. 10, p. ofaa379). US: Oxford University Press.

Viral Load, Detection Rate and Sensitivity of Nasopharyngeal and Oropharyngeal Swab Sampling for Diagnosis of COVID-19

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*, 395(10229), 1054-1062.

Zou, L., Ruan, F., Huang, M., Liang, L., Huang, H., Hong, Z., ... & Wu, J. (2020). SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *New England Journal of Medicine*, 382(12), 1177-1179.