



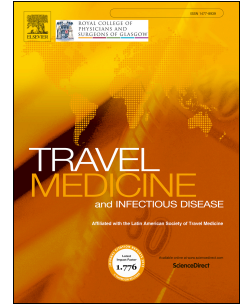
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal Pre-proof

False negative rate of COVID-19 is eliminated by using nasal swab test

Chaojun Xie, Jianyun Lu, Di Wu, Lin Zhang, Hongjun Zhao, Boqi Rao, Zhicong Yang



PII: S1477-8939(20)30136-8

DOI: <https://doi.org/10.1016/j.tmaid.2020.101668>

Reference: TMAID 101668

To appear in: *Travel Medicine and Infectious Disease*

Received Date: 10 March 2020

Revised Date: 6 April 2020

Accepted Date: 9 April 2020

Please cite this article as: Xie C, Lu J, Wu D, Zhang L, Zhao H, Rao B, Yang Z, False negative rate of COVID-19 is eliminated by using nasal swab test, *Travel Medicine and Infectious Disease* (2020), doi: <https://doi.org/10.1016/j.tmaid.2020.101668>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier Ltd.

False negative rate of COVID-19 is eliminated by using Nasal swab test

Chaojun Xie^{1, #}, Jianyun Lu^{1, #}, Di Wu^{1, #}, Lin Zhang^{1, #}, Hongjun Zhao^{2, #}, Boqi Rao²,
Zhicong Yang^{1, §}

¹ Guangzhou Center for Disease Control and Prevention, Guangzhou, 510440, P.R.
China.

² The Institute for Public Health, Guangzhou Medical University, Guangzhou, 510182,
P.R. China.

CX, JL, DW, LZ and HZ contributed equally.

§Corresponding author:

Dr. Zhicong Yang, Guangzhou Centre for Disease Control and Prevention, 1Qide
Road, Guangzhou, 510440, P.R. China.

E-mail addresses: yangzc@gzcdc.org.cn

Dear Editor,

Tons of studies of the new outbreak of COVID-19 patients on clinical, epidemiological, and radiological features have now published^{1,2}. a positive RT-PCR result of the discharged patients was reported by Lan et al³, we are now reporting the expanded population data of the re-positive patients in Guangzhou City, China.

Collect the discharged COVID-19 patients' information from former epidemiological investigation of Guangzhou Center for Disease Control and Prevention. Data was included the date of onset, date of conformed diagnose, date of discharge, date of first sampling, and the date of the nucleic acid test returned positive. All the discharged patients were followed the criteria of: (a) temperature returned to normal more than 3 days later, (b) Disappearance of respiratory symptoms, (c) substantially improved acute exudative lesions on chest computed tomography (CT) images, and (d) two consecutive negative nucleic acid tests separated by at least 1 day⁴.

A total of 161 discharged patients of COVID-19 in Guangzhou has retested for SARS-CoV-2, in which 22 patients whose nucleic acid tests were positive accounted for 13.66% (**Table S1** in the Supplementary Appendix). As shown in **Figure 1A**, the median time interval between onset of symptom to nucleic acid test return positive after discharge was 26 days (range, 14 to 37; mean, 26.05), in which the longest infection period is 37 days that suggested that the current 14-day medical observation period may be insufficient and needs to be re-evaluated, and the median time interval between the discharge to nucleic acid test return positive was 7.5 days (range, 1 to 14;

mean, 7.91) that indicated that the 14-day medical observation period after discharge is an essential measure for controlling epidemic spread.

The key point that differed the sampling after discharge from the sampling before discharge only including throat swabs and anal swabs is that we increased sampling of nasal swabs. The emergence of 22 discharged patients of return positive suggested that medical institutions should reassess discharge standards and improve sampling methods and types. As listed in **Figure 1B**, we selected 3 discharged patients to collect nasal swabs that all were detected to positive of SARS-CoV-2.

Notably, there are two familial clustering cases in the “re-positive” patients.

As previously reported by Zou LR et al⁵, higher viral loads were detected soon after symptom onset, with higher viral loads detected in the nose than in the throat, consequently we suggested that increase nasal swab sampling for SARS-Cov-2 test to reduce false negative rate of nucleic acid test. There were many kinds of specimens collected from one patient, but always only one specimen type was detected for positive of SARS-CoV-2, which indicated that specimen used for nucleic acid test should be collected from multiple body parts before discharge. There are 8 discharged patients tested positive only on the fourth test, including two tests before discharge and two tests after discharge, which shown that relatively high false negative rate was 36.4% (8/22) before the fourth test and suggested that increase the number of tests before discharge. The exact period of infection by far has not been determined, and the knowledge of epidemiological characteristics of COVID-19 were still insufficient so that we need to collect more information to explore.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of. Guangzhou Center for Disease Control and Prevention

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

None of the authors has any conflict of interest to declare.

Funding

General Guidance Project of Guangzhou Health and Family Planning Technology 20181A011050(C Xie), Health Industry Scientific Research Project of Gansu Province GSWSKY2018-18(H Zhao), and National Natural Science Foundation of China Grants 81803325(D Wu).

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

HJ Zhao and ZC Yang designed this study. CJ Xie, JY Lu, D Wu, L Zhang collated the data, and HJ Zhao and ZC Yang discovered and analyzed relevance. ZC Yang and CJ Xie contributed to interpreting the results. HJ Zhao, BQ Rao wrote the manuscript and analyzed the results. ZC Yang revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020:Epub ahead of print. doi:10.1001/jama.2020.1585
2. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020. doi:10.1056/NEJMoa2002032
3. Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. JAMA. 2020:Epub ahead of print. doi:10.1001/jama.2020.2783
4. China-National-Health-Commission. Diagnosis and treatment of 2019-nCoV pneumonia in China

(In Chinese). Published February 8, 2020. Accessed March 4, 2020. Web site.

<http://www.nhc.gov.cn/yzygj/s7653p/202002/d4b895337e19445f8d728fcdf1e3e13a.shtml>.

5. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. 2020:Epub ahead of print. doi:10.1056/NEJMc2001737

Journal Pre-proof

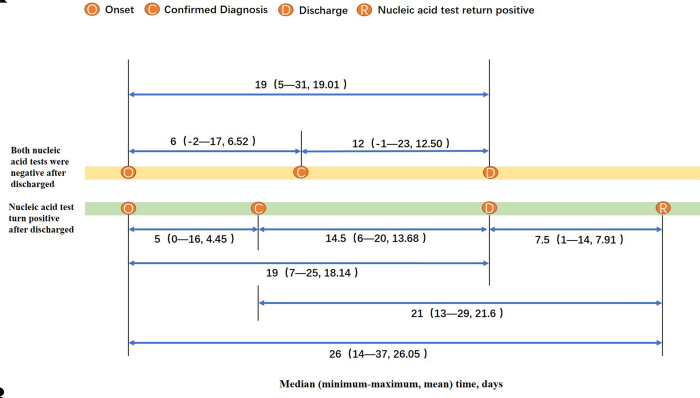
Figure 1.**A) Time interval of every two time points among the four time points**

Negative group: The median time interval between onset of symptom to diagnosis was 6 days (range, -2 to 17; mean, 6.52) and the median time interval between diagnosis to discharge was 12 days (range, -1 to 23; mean, 12.50). The median time interval between onset of symptom to discharge was 19 days (range, 5 to 31; mean, 19.01).

Positive group: The median time interval between onset of symptom to diagnosis was 5 days (range, 0 to 16; mean, 4.45). and the median time interval between diagnosis to discharge was 14.5 days (range, 6 to 20; mean, 13.68). The median time interval between onset of symptom to discharge was 19 days (range, 7 to 25; mean, 18.14) and the median time interval between onset of symptom to nucleic acid test turn positive after discharge (the last test was positive) was 26 days (range, 14 to 37; mean, 26.05). The median time interval between the discharge to nucleic acid test turn positive (the last test was positive) was 7.5 days (range, 1 to 14; mean, 7.91) and the median time interval between the diagnosis to nucleic acid test turn positive (the last test was positive) was 21 days (range, 13 to 29; mean, 21.61).

B) RT-PCR results of 22 cases.

A



B

No.	Date of onset	Date of discharge	Date of first sampling	Date of second sampling	First throat swab results	First anal swab results	First nasal swab results	Second throat swab results	Second anal swab results	Second nasal swab results	Time between Onset and Positive Test Results after Discharge (days)	Time between Discharge and Positive Test Results (days)
1	Jan26, 2020	Feb13, 2020	Feb19, 2020		-	+					24	6
2	Jan31, 2020	Feb16, 2020	Feb21, 2020		-	+					21	5
3	Feb10, 2020	Feb17, 2020	Feb21, 2020	Feb24, 2020	-	-		-	+		14	7
4	Jan26, 2020	Feb18, 2020	Feb21, 2020		+	-					26	3
5	Jan19, 2020	Feb5, 2020	Feb19, 2020		-	+					31	14
6	Jan27, 2020	Feb9, 2020	Feb18, 2020	Feb23, 2020	-	-				+	27	14
7	Jan23, 2020	Feb11, 2020	Feb18, 2020	Feb23, 2020	-	-		+			31	12
8	Jan19, 2020	Feb11, 2020	Feb18, 2020		+	-					30	7
9	Jan21, 2020	Feb12, 2020	Feb19, 2020	Feb22, 2020	-	-		+			32	10
10	Jan21, 2020	Feb12, 2020	Feb19, 2020	Feb23, 2020	-	-				+	33	11
11	Feb5, 2020	Feb13, 2020	Feb22, 2020		-	+					15	7
12	Jan21, 2020	Feb13, 2020	Feb20, 2020	Feb22, 2020	-	+		+			32	9
13	Jan29, 2020	Feb15, 2020	Feb21, 2020	Feb24, 2020	-	-		+	-		26	9
14	Jan27, 2020	Feb15, 2020	Feb21, 2020	Feb23, 2020	-	-		+			27	8
15	Jan30, 2020	Feb24, 2020	Feb25, 2020				+				26	1
16	Jan27, 2020	Feb11, 2020	Feb17, 2020		-	+					21	6
17	Jan22, 2020	Feb12, 2020	Feb17, 2020	Feb18, 2020	+	-		-	-		26	5
18	Jan16, 2020	Feb8, 2020	Feb18, 2020	Feb22, 2020	-	-		+	-		37	14
19	Jan26, 2020	Feb20, 2020	Feb22, 2020		+	-					27	2
20	Jan28, 2020	Feb6, 2020	Feb18, 2020		-	+					21	12
21	Jan28, 2020	Feb9, 2020	Feb18, 2020		-	+					21	9
22	Jan25, 2020	Feb16, 2020	Feb19, 2020		-	+					25	3
Median (days)											26.00	7.50

Title: False negative rate of COVID-19 is eliminated by using Nasal swab test

Authors: Chaojun Xie^{1, #}, Jianyun Lu^{1, #}, Di Wu^{1, #}, Lin Zhang^{1, #}, Hongjun Zhao^{2, #}, Boqi Rao², Zhicong Yang^{1, §}

Conflicts of interests

None of the authors has any conflict of interest to declare.

Signature: Chaojun Xie

Chaojun Xie, chaojunxie@foxmail.com

Signature: Jianyun Lu

Jianyun Lu, 258506273@qq.com

Signature: Di Wu

Di Wu, wudi0729@126.com

Signature: Lin Zhang

Lin Zhang, 13711396333@139.com

Signature: Hongjun Zhao

Hongjun zhao, hjzhao@stu.gzhmu.edu.cn

Signature: Boqi Rao

Boqi Rao, 2017216479@stu.gzhmu.edu.cn

Signature: Zhicong Yang

Zhicong Yang, yangzc@gzcdc.org.cn