International Journal of Family Medicine and Primary Care

Short Communication
Published: 25 Apr, 2020

Identified SARS-Cov-2 Infected Cases with Untraceable Epidemic Origin: Triple Values in Preventing Recurrence

Kai Li[1,3#], Jia Zhang[3], Pierre Sirois[5], Duan-Fang Liao[1,2] and Ai-Guo Dai[1,2,4]**

[1]Division of Stem Cell Application, Hunan University of Chinese Medicine, China

[2]Department of Respiratory Diseases, Hunan University of Chinese Medicine, China

[3]Translational Medicine Institute, University of South China, China

[4]Department of Respiratory, Hunan University of Chinese Medicine, China

[5]CHUL Research Center, Laval University, Canada

[#]Equal contribution to this manuscript

Short Communication

During the period of SARS-CoV-2 outbreak, the identification of a SARS-CoV-2 infected case with untraceable epidemic origin has three values

1. The region has community transmission of the virus.

2. A certain portion of population in the community is getting immunized and more individuals have already been immunized.

3. An unpredictable future risk exists for regions where there is no infected case with untraceable epidemic origin.

Minimizing or avoiding the aggregation infection through individuals with no clinical symptoms is crucial and possible as the occurrence of aggregation infection is mainly attributed to the local environment instead of being attributed to the misleading concept of super spreader with or without clinical symptom.

With SARS-CoV-2 world-wide spreading, more identified SARS-CoV-2 infected cases with untraceable epidemic origin will be reported in regions involved in the SARS-CoV-2 outbreak. To efficiently fight against the epidemic outbreak of SARS-CoV-2, the recognition of the triple values of newly identified cases with untraceable infection origin could help in guiding current strategies and preparing for future plans. First, it indicates that the region already has community transmission and needs preparation for the coming risk. The number of untraceable epidemic cases can be used as a parameter to assess the severity of community transmission of the virus to match medical facilities and material resources. The second and the third values are relevant and opposite: Whereas certain portions of population of region with such cases are getting immunized and more will have already been immunized, an unpredictable future risk exists in regions where there are no infected cases with untraceable epidemic origin. Based on this triple values approach, to minimizing sporadic infection and eliminating aggregation infection should be our major aims.

In the past several months, tens of thousands of COVID-19 patients have been reported and thousands have died. This demonstrates that SARS-CoV-2 has higher R0 and is more contagious than SARS. Although the R0 was initially reported to be between 2.24 to 3.58, the aggregation infections in diamond princess cruise and the South Korea Shincheonji Church suggests that the real R0 is much higher [1-6]. Several points can be learned from these two infections.

1. The initial virus spreaders who caused these two aggregation infections are reported patients but it is theoretically possible they could have been from individuals without clinical symptoms.

2. R0 cannot simply be calculated by the final number of infected cases as some of the infected cases are not directly transmitted from the initial virus spreaders.

3. The higher infection rate in these aggregation infections as compared to sporadic infections are possibly attributed to their local environments in which there was a relatively higher concentration of virus in the air.

OPEN ACCESS

Correspondence:
Duan-Fang Liao, Division of Stem Cell Application, Hunan University of Chinese Medicine, China, E-mail: dfliao@hnucm.edu.cn
Ai-Guo Dai, Division of Stem Cell Application, Hunan University of Chinese Medicine, China, E-mail: daiaiguo@126.com

Received Date: *02 Apr 2020*
Accepted Date: *21 Apr 2020*
Published Date: *25 Apr 2020*

Citation:
Li K, Zhang J, Sirois P, Liao D-F, Dai A-G. Identified SARS-Cov-2 Infected Cases with Untraceable Epidemic Origin: Triple Values in Preventing Recurrence. Int J Fam Med Prim Care. 2020; 1(2): 1009.

The third point has been indirectly supported by the higher rates of infection, the number of serious cases, and the number of deaths in Wuhan as compared to other areas in China and other countries in the world except Iran.

The eventual severity of the SARS-CoV-2 outbreak mainly depends on three factors:

1. The virulence

2. The season

3. The preventive strategies targeting isolation and identification of patients and infected individuals without clinical symptoms.

Actually, the third factor is the only one that can be controlled to some extent. The first wave of SARS-CoV-2 spreading in China is nearly ending. Significant differences in the severity have been found between Wuhan and other regions of Hubei province and among different provinces or major cities in China depending on the timing and the stringency of isolation strategy. When and how an isolation strategy should be initiated is a highly sensitive and political issue which could be highly variable among countries based on the population density, the weather, as well as the risk of aggregation infection from social activities and factors such as school sizes, transportation systems, sporting events, and religious events, etc.

However, some common diagnostic lessons learned from the experience in China in the past several months are helpful. The first lesson is gene testing should not be simply used as the gold standard to confirm or reject the diagnosis of COVID-19 [7]. Although Chinese diagnosis and treatment guide (from the first to the sixth editions) takes gene testing as the gold standard, it was fortunately not always practiced as the guide defined. Currently, RT-PCR and Next Generation Sequencing (NGS) are the two methods employed in gene testing of SARS-CoV-2. The assay with RT-PCR is faster and less expensive as compared to that with NGS and should be used as the first choice in clinical application. For suspected COVID-19 individuals who have no typical clinical symptoms, genetic testing using RT-PCR is urgently required. When the RT-PCR analysis is positive for the SARS-CoV-2 infection, an etiological diagnosis is then confirmed. However, for RT-PCR negative patients, the second gene testing should use the NGS. NGS is not more sensitive than RT-PCR but it can identify multiple pathogens including SARS-CoV-2. NGS will provide three possible results: i). Positive for SARS-CoV-2; ii). Negative for SARS-CoV-2 and seasonal flu viruses; and iii). Negative for SARS-CoV-2 but positive for seasonal flu viruses. The etiological diagnosis for the first and third results is evident in view of the positive results of the gene test. The second possibility is more questionable since it should be considered as a SARS-CoV-2 positive equivalent; in this situation the patients need to be treated as COVID-19 cases, particularly when supported by typical clinical features including CT scanning [8,9].

Positive gene testing as the gold standard in diagnosis has no clinical values in patient management. From a therapeutic point of view, no specific drug is available to inhibit SARS-CoV-2 and the clinical management of isolation the only treatment approach. Practically, throat swabs have very low copies of SARS-CoV-2, which is at least a part of the reason why some patients scored several consecutive negative tests before positive gene testing was reported. Treating these patients as seasonal flu patients will very likely result in an iatrogenic infection. In addition to its proper applications in diagnosis, RT-PCR is the assay of choice for the follow-up of cured cases. Most of the cured cases showed persistent negative results in gene testing. However quite a few returned positive in gene testing, which indicates that SARS-CoV-2 are not eliminated in the body in parallel to the clinical symptoms. In the worst situation, some fatal cases were reported for those who returned gene test positive after the initial standard COVID-19 cure.

Gene testing employing RT-PCR assay is routinely applied to screening individuals with epidemic history in close contact with identified SARS-CoV-2 infected cases no matter whether they are COVID-19 patients or virus carrier without clinical symptoms. Discharged patients whose gene testing returns to positive are monitored as virus carrier even if there are no clinical symptoms. As aforementioned, identification of SARS-CoV-2 infection with untraceable contact history indicates that the virus has spread in the community, and the number of these cases can guide the stringency of general strategies including personnel isolation and social gathering bans. Although China was late to initiate personnel isolation in Wuhan, high stringent nationwide strategies have shown their efficiency in decreasing R0 and prolonged the incubation period as well as the ratio of mild cases to severe cases. Presently, immunoassay targeting IgM against SARS-CoV-2 are tested in China for diagnostic purposes but gave a lot of false positive and false negative results. Better assay kits targeting IgM are needed as screening large population with RT-PCR and NGS is not financially possible and limited to laboratory output. However IgM assay can give information about the infection and immunization rate of the SARS-CoV-2 outbreak; this is very important data for predicting future risk and for preparing future strategies for the years to come.

The origin and the intermediate host of SARS-CoV-2 is not known yet [10,11]. At the molecular level, its gene sequence showed several crucial mutations that indicate that its matured virulence may not be formed via repeatedly cycling of viral mutations and mild infections of the host. It is highly contagious to almost the whole population as no subpopulation had the chance to be previously immunized to the early less virulent form of the virus. Thus, regions or local communities without identified epidemic untraceable case, as well as children born after this outbreak have a risk of a local outbreak of SARS-CoV-2, either this year or the coming years. Long incubation period and the efficient replication for weeks or months in some patients, together with much higher R0 than SARS, contribute to demonstrate that SARS-CoV-2 has a completely different performance than SARS and will repeatedly infect humans from now on. Recently the report of a positive gene testing in a Hong Kong dog further warned the world that SARS-CoV-2 may host many species such as dog and cat and is the result of a substitution at the 82 amino acid residue (Met to Tyr) which is one of the 6 binding residues at ACE2 [12]. Some species such as *macaque* and gorilla have no substitution at these 6 binding amino acid residues, and they can be ideal hosts for SARS-CoV-2 as well.

Epidemic outbreak of new airborne infectious diseases always develop starting from a sporadic infection to an aggregation infection in one region and its spreading by repeating similar cycles. So far, the worst aggregation infection event in the outbreak of SARS-CoV-2 was in the so called dinner party attended by tens of thousands of families in Wuhan and that pushed up the severity of the infected cases in the city. Similarly, the Diamond Princess Cruise event ignited and toned up the scale of the viral spreading internationally.

The most important warning from the second and third values of the identified source-untraceable cases is about the regions where no such cases were identified. If no specific vaccine or medicine becomes available in a short time, the lifestyle of the population may have to be adjusted in the coming months before the summer to avoid the outbreak of the virus similar to what happened in Wuhan and on the Diamond Princess Cruise. For example, NBA games and many other games with large crowds should either be cancelled or delayed several weeks. Hopefully, a SARS-CoV-2 vaccine and effective drugs to SARS-CoV-2 (such as remdesivir) are in development and should be available soon.

Finally, the concept of super spreader, no matter with or without clinical symptoms, linked to aggregation infection is somehow misleading. Most or all aggregation infection events are attributed to the particular local environment instead of to the viral spreader. When viral concentrations in the air are accumulated to the levels higher than the nonspecific immunity of people exposed, aggregation occurs. The triple values of the identified epidemically untraceable cases strongly recommend a more stringent regulation for social activities with large crowds involved, including public transportation, sporting events, and a variety of meetings. Only the region with a relatively large number of untraceable cases is considered to have been immunized by community spreading of SARS-CoV-2 and are less risk of occurrence. Possibly, we have to change our life style somehow to minimize aggregation infection and the occurrence of COVID-19 for the coming months before efficient vaccine is available.

References

1. Zhao S, Musa SS, Lin Q, Ran J, Yang G, Wang W, et al. Estimating the unreported number of novel Coronavirus (2019-ncov) cases in china in the first half of January 2020: A data-driven modeling analysis of the early outbreak. J Clin Med. 2020;9(2): pii: E388.
2. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. Euro Surveill. 2020;25(4).
3. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. Int J Infect Dis. 2020;92:214-7.
4. Wu JT, Leung K, Leung GM. Now casting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: A modeling study. Lancet. 2020;395(10255):689-97.
5. Rocklöv J, Sjödin H, Wilder-Smith A. COVID-19 outbreak on the diamond princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures. J Travel Med. 2020;28: pii: taaa030.
6. Why a South Korean church was the perfect petri-dish for coronavirus.
7. Liao DF, Tuo QH, Li K. (Article Type: Correspondence; Manuscript Number: THELANCET-D-20-01656). Lancet 2020, Current Status: With Editor.
8. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in china. N Engl J Med. 2020;28.
9. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis. 2020;20(4):425-34.
10. Benvenuto D, Giovanetti M, Ciccozzi A, Spoto S, Angeletti S, Ciccozzi M. The 2019-new coronavirus epidemic: Evidence for virus evolution. J Med Virol. 2020;92(4):455-59.
11. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. Lancet. 2020;395(10224):565-74.
12. Liu Z, Xiao X, Wei X, Li J, Yang J, Tan H, et al. Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2. J Med Virol. 2020.