# The possibility of SARS-COV-2 to infect and be transmitted by mosquitoes

## Project Summary

*Approach*

This paper is a mini-review based on the peer-reviewed papers published on PubMed. The keywords I searched were “SARS-COV-2 transmission”, “mosquito biology,” “virology in arthropods,” and “SARS-COV-2 replication/transmission in mosquitoes.”

*Rationale*

The review is a traditional paper. It helps make the conclusion by collecting and gathering scientific evidence and summarizing the essential information from credible resources.

*Challenges and future directions*

The challenge of this paper is the limited resources on the topic. Currently, few people have conducted studies on the infection and transmission of SARS-COV-2 by mosquitoes. Many resources falsify other coronavirus transmissions, such as MERS and SARS-COV, but not SARS-COV-2 itself. Therefore, these cannot be the strongest and direct evidence to demonstrate the possibility. In the future, some preprints from bioRxiv can also be considered. The paper should also be reviewed and discussed in case of any insufficient analysis.

## Introduction (Statement of the problem)

Since January 2020, the COVID-19 pandemic has caused 75 million cases worldwide with 1.6 million deaths.[1] COVID-19 is an acute respiratory syndrome caused by SARS-CoV-2. SARS-CoV-2 is a single-stranded positive-sense RNA virus belonging to the family of coronavirus. The virus is mainly transmitted through aerosol and droplet transmission, with the additional possibility of transmission through surfaces.[2] In fact, SARS-Cov-2 can survive more than 48 hours on metal surfaces at a low temperature.[2] Transmission via surfaces like door handles and subway handrails is also commonly seen. There are no real-world evidence showing that SARS-Cov-2 can be transmitted by mosquitoes[3,4] However, the potentiality of insects carrying the virus through contact with contaminated surfaces still exists.[5] Three major criteria are to decide whether a disease can be transmitted by mosq

uitoes: 1. There must be enough level of viremia to infect the mosquitoes feeding on a patient; 2. There must be virus replication inside the mosquitoes; 3. There must be enough dosage of the virus entering the host while feeding.[6] More evidence is needed to eliminate the possibility of bloodborne vector transmission of SARS-CoV-2.

**Arthropods are not hosts of SARS-CoV-2**

SARS-CoV-2 is very similar to related coronaviruses such as SARS-CoV and MERS. SARS-CoV enters the host cell by binding with the hACE2 receptor, using the Spike Protein (S-protein).[7] The S-protein is composed of the S1 domain in the N-terminal region and is followed by the S2 domain. Receptor Binding Domain (RBD) in S1 will be responsible for binding with the ACE2 and induce endocytosis. The S2 protein will facilitate viral entry through membrane fusion during the endocytosis.[8] SARS-CoV-2 was found to follow a similar process when entering host cells, which means the infection of SARS-CoV-2 rely heavily on the binding with ACE2.[9]

So far, there is no evidence that mosquito ACE2 can effectively bind with SARS-CoV-2 S1 protein. Natural reservoirs of SARS-CoV-2 were suspected to be bats and civet cats just like SARS-CoV.[10] However, the intermediate hosts are still not clearly defined. To identify the mammals that can host the virus, researchers made predictions based on the RBD sequencing.

Cats, dogs, pangolins, and Chinese hamsters might be infected by SARS-Cov-2 based on the simulation results of RBD-ACE2 interaction.[11]

ACE2 genes were also found in mosquitoes.[12] However, the ACE2 genes of mosquitoes and mammals are very different from each other. The homology of ACE2 genes decides how similar the ACE2 of an animal with the ACE2 of a human. For example, due to the lack of homology, mice cannot be infected by SARS-CoV-2.[13] Human ACE2 genes were transfected into mice to develop animal models to study SARS-CoV-2.[11] As an arthropod, mosquitoes are even less homologous with humans than mice. It indicates that the RBD of mosquito ACE2 has less potential to bind with SARS-CoV-2 Spike protein. Arthropods are not considered as hosts for SARS-CoV-2 as mammals, but other viruses like arboviruses. Mosquitoes can be virally infected, but they have evolved multiple mechanisms to tolerate constant infection and restrict viral replication via their antiviral immune system.[14] Such a phenomenon is not yet observed for the coronavirus family.

**The Lack of Viremia**

Similar to other closely related coronaviruses such as SARS-CoV and MERS, SARS-CoV-2 produce less virus in the blood than typical arthropod-borne viruses like dengue and yellow fever.[15] Clinical study of COVID-19 patients also found no significant level of virus in peripheral blood.[16] The lack of viremia suggests that it is implausible that an arthropod vector can be transmitted or mechanically transport enough virus to infect the next host.

The level of viremia contributes to deciding whether a virus can be transmitted through blood-feeding vectors. Dengue (DENV), Zika (ZIKV), Yellow Fever (YFV), and West Nile (WNV) virus belong to the genus *Flavivirus*. They are also the major mosquito-borne viruses that cause a huge public health burden. A high level of viremia is commonly seen during flavivirus infection.[17] Yellow Fever patients can develop a significant level of viremia two days prior to symptoms onsite.[18] However, even though with viremia, yellow fever cannot be transmitted from patients to mosquitoes, making humans a dean end host for yellow fever. For some flaviviruses, an infected human can transmit the virus to feeding mosquitoes. ZIKV is able to generate enough level of viremia to achieve the transmission.[19] Dengue patients are generally considered dead-end hosts because 75% of dengue patients are asymptomatic with insufficient levels of viremia. Recently, asymptomatic patients were also found to be able to infect mosquitoes given enough level of viremia.[20]

Viremia is not commonly observed in COVID-19 patients, especially mild symptom patients, which is nearly 80% of the case.

**No replication in mosquitoes**

To determine whether SARS-CoV-2 can replicate and infect mosquitoes, an intrathoracic inoculation experiment should be performed to test under extreme conditions, the biological possibility of viral replication. In an intrathoracic inoculation experiment, infectious virus was recovered in 13 out of 15 mosquitoes (*Ae. aegypti*, *Ae. albopictus* and *Cx. quinquefasciatus*) within 2 hours after the inoculation.[6] After 24 hours, no infectious virus was found in all 277 inoculated mosquitoes, suggesting that SARS-CoV-2 cannot replicate in mosquitoes and shows a rapid loss of infectivity once inoculated. For a virus to be transmitted by mosquitoes, a sufficient amount of virus must be ingested. The virus should be able to infect midgut epithelial cells and then disseminate to infect other organs in the hemocoel, especially the salivary glands.[21] By utilizing intrathoracic inoculation, the midgut wall and other barriers are bypassed, and the virus is sent directly into the hemocoel. Even if the virus can accomplish a short-term infection, it can never happen under natural circumstances. Evidence has shown that there is no viral replication of SARS-CoV-2 in arthropods. Therefore, if a mosquito feed on viremic patients and the virus is disseminated from the midgut, the lack of replication will eliminate the biological possibility of transmission.[6]

**Conclusion**

The transmission of SARS-CoV-2 through bloodborne arthropods is highly unlikely due to the following reasons:

- Arthropods are not hosts or reservoirs for coronaviruses.
- Mosquitoes are not likely to ingest enough viruses because of the lack of viremia of COVID-19 patients.
- SARS-CoV-2 cannot replicate in mosquitoes even if intrathoracic inoculated.

So far, there is no reported case of COVID-19 transmission through mosquitoes. Based on existing studies, virus transportation seems impossible both biologically and mechanically.

**Discussion**

Mosquitoes are effective disease vectors and can transmit several severe diseases include Zika virus, West Nile virus, Chikungunya virus, dengue, and malaria.[22] Mosquitoes are considered major public health concerns, especially in tropical areas where environmental factors facilitate mosquito activities.

Due to the COVID-19 pandemic, many initiatives controlling mosquito-borne diseases have been suspended. A surge of malaria has been reported in India because of the labor loss due to the pandemic.[23] Mosquito control programs require constant monitoring and resource allocation. The interruption caused by the pandemic could derail mosquito control programs and sabotage the current progress. More importantly, the research and surveillance of major mosquito-borne diseases like the Zika virus were impacted heavily by the pandemic. Laboratory resources and efforts were relocated to cope with the evolving situation of COVID-19.[24] we may observe a surge of mosquito-borne diseases during, and even after the COVID-19 pandemic. More than 80% of the global population is at risk of vector-borne diseases, with mosquito-borne diseases being the largest contributor to the human vector-borne disease burden.[25] Over 350 million malaria, dengue, and lymphatic filariasis cases were reported annually, while the endemic area is expanding due to climate change and globalization.[26] Studies have shown that if the global temperature increase by 2-3 ℃, the population at risk for malaria will increase by 3-5%.[27] At this point, we still cannot decide how the COVID-19 pandemic will influence global warming. However, it is almost certain that the pandemic will cause more poverty, a shortage of medical resources, and delay vaccine development for mosquito-borne diseases. Public health policymakers must focus on the prevention of mosquito-borne diseases even under the COVID-19 pandemic.

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