

**Point of view**

## Genetic polymorphism and COVID-19: a short summary

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*Sri Lanka Journal of Child Health*, 2021; **51**(4): 613-614

DOI: <http://dx.doi.org/10.4038/sljch.v51i4.10381>

(Key words: Genetic, polymorphism, Covid-19)

### Introduction

In a disease, both environmental and genetic backgrounds can be significant determinants. Genetic background is an important factor affecting clinical nature of many diseases. The role of genetic factor might be suppressing, promoting or modifying the clinical nature. For COVID-19, the new emerging disease, the possible role of genetic factor is mentioned<sup>1,2</sup>. Here, the authors summarize and discuss the role of some important genetic polymorphisms on COVID-19.

### Important genetic polymorphisms and paediatric COVID-19

- *ACE2 polymorphism*  
Since the main cellular receptor allowing SARS CoV-2 virus to bind is the human angiotensin I converting enzyme 2 (ACE2), the effect of ACE2 polymorphism becomes a widely studied issue in infectious medicine and clinical genetics. There are many studies reporting the effect of ACE2 polymorphism on COVID-19 severity<sup>3,4</sup>. Devaux CA, *et al*<sup>5</sup> mentioned the impact of ACE2 expression and/or polymorphism on susceptibility to SARS-CoV-2 infection and the outcome of the disease. However, the significance of age and sex-dependent pattern of ACE2 receptor expression is well defined and the common question is on specific impact of ACE2 polymorphism in children. For children, impact of ACE2 polymorphism has also been assessed in many studies. Mohaghegh S, *et al*<sup>6</sup> mentioned the possible impact of age on effect of ACE2 polymorphism on COVID-19. For paediatric COVID-19, Mohaghegh S, *et al*<sup>6</sup> concluded that “the effect of ACE

polymorphism on the severity of COVID-19 depends on the patients age, same as of the pneumonia”. In another meta-analysis, a significant association of the ACE I/D polymorphism with the risk of acute lung injury and acute respiratory distress syndrome was observed in children, either Asians or Caucasians<sup>6</sup>.

- *Vitamin D binding protein polymorphism*  
Vitamin D binding protein polymorphism is mentioned for its clinical importance in COVID-19. Bayramoğlu E, *et al*<sup>7</sup> suggested that “Lower 25-hydroxy-vitamin D levels were associated with higher inflammation markers” and further implied the role of vitamin D in COVID-19 in children and adolescents. Hence, there might be effect of vitamin D binding protein and vitamin D binding protein polymorphism in paediatric COVID-19. In a recent report by Speeckaert MM, *et al*<sup>8</sup>, the influence of vitamin D binding protein polymorphism in children with COVID-19 was also shown.
- *ICAM-1 polymorphism*  
ICAM-1 polymorphism is mentioned for its importance in COVID-19<sup>9</sup>. Linkage between disease severity and polymorphism is mentioned but there is no specific report in the paediatric group.
- *Plasminogen activator inhibitor type 1 (PAI-1) polymorphism*  
There is an interesting case report on death of a preterm newborn born to a mother carrying 4G/5G polymorphism<sup>9</sup>. The transplacental transmission and placental pathology are proven in this case<sup>9</sup>.

### Discussion

The role of genetic polymorphism is mentioned in paediatric COVID-19. Regarding effect of age, some authors proposed a possible age effect on the observed impact of a genetic polymorphism. Of several genetic polymorphisms, ACE2 polymorphism is widely studied and the observed results are variable. Indeed, the effect of genetic polymorphisms might be affected by other confounding factors. For example, if one discusses the impact of severity and disease outcome, one should not forget to recognize the background treatment activity in each setting. Additionally, an

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The author declares that there are no conflicts of interest

Personal funding was used for the project.

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important concern is on the possible effect of combined genetic polymorphisms.

In many reports, only one genetic polymorphism is studied on its impact and there might be a hidden effect of non-studied genetic polymorphism. To evaluate the effect of genetic polymorphism is interesting. There should be a further multicentre study of the effect of genetic factors covering multiple important polymorphisms.

Finally, we should also discuss the effect of polymorphism in relationship with other important disease. For example, Arshad AR, *et al*<sup>10</sup> proposed the potential role of CD-147, and potential malaria-induced immunity and polymorphisms in COVID-19 patients. When an antimalarial drug is used for prophylaxis of COVID-19, the change of malarial parasite polymorphism resistant to the drug occurs<sup>11</sup>.

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