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.

Medical Hypotheses 142 (2020) 109818

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Genetic predisposition models to COVID-19 infection

A wide range of disease severity among patients with coronavirus disease (COVID-19) has attracted scientists' attention worldwide. Development of severe symptoms in some adults without any underlying diseases is a challenge. Herein, we explain the potential "genetic predisposition models" to COVID-19 infection with particular emphasis on hypothesizing the possibility of moderately rare dominant variants in severe cases without any underlying medical conditions.

Three genetic-related models for predisposition to COVID-19 could be described: 1-Common variants in multiple loci that have weak effect through single contribution. However, they might manifest significant effect through additive contribution in specific individuals to increase infection risk and severity. 2-Moderately rare variants in limited genes are expected to have strong effects, and thus be highly penetrant and even dominant trait as long as COVID-19 infection is considered. These variants could underlie severe forms in young patients without any other medical conditions. 3-Gene-environment interactions define host predisposition. The concept of susceptibility to COVID-19 is getting more and more complex when gene interactions with environment factors, such as smoking, are considered (see Fig. 1).

In order to reach more specific and sensitive results of indecisive variants, the assessment of targeted genes could be preferred. The receptor-binding domain (RBD) of the COVID-19 spike-protein shows strong interaction with human angiotensin-converting enzyme 2 (ACE2) receptor. It is assumed that the virus binds to ACE2 to enter cells. Consequently, ACE2 genetic variants that could affect its gene expression, protein conformation, and protein stability are the one of most questionable underlying factors involving in genetic predisposition to COVID-19 infection [1]. ACE2 is an X-linked gene that harbours a strong variant with tendency to X-linked dominant inheritance pattern in severely affected patients. It might be a clue to the higher prevalence and severity of COVID-19 in men than in women [2].

The immune-related genetic variants involving the prior strain of coronavirus, namely SARS-CoV, are suspected to have roles in genetic predisposition of COVID-19 infection [3,4], since COVID-19 has 80% genetic identity to SARS-CoV [5]. Notably, Mannose-Biding Lectin, CD147, CCL2, Interleukin-12, and HLA genes should be considered [6–9].

COVID-19 appears to be less severe in children [10]. However, severe illness is seldom developed in children. Being detected DNA-driven interplay points and prospective rare dominant variants could shed light on this mystery.

Definitely, the outcome of genetic variants inspection will be a pivotal step to help personalized and predictive medicine in high-risk individuals for severe COVID-19 infection.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

https://doi.org/10.1016/j.mehy.2020.109818
Received 11 April 2020; Received in revised form 22 April 2020; Accepted 5 May 2020

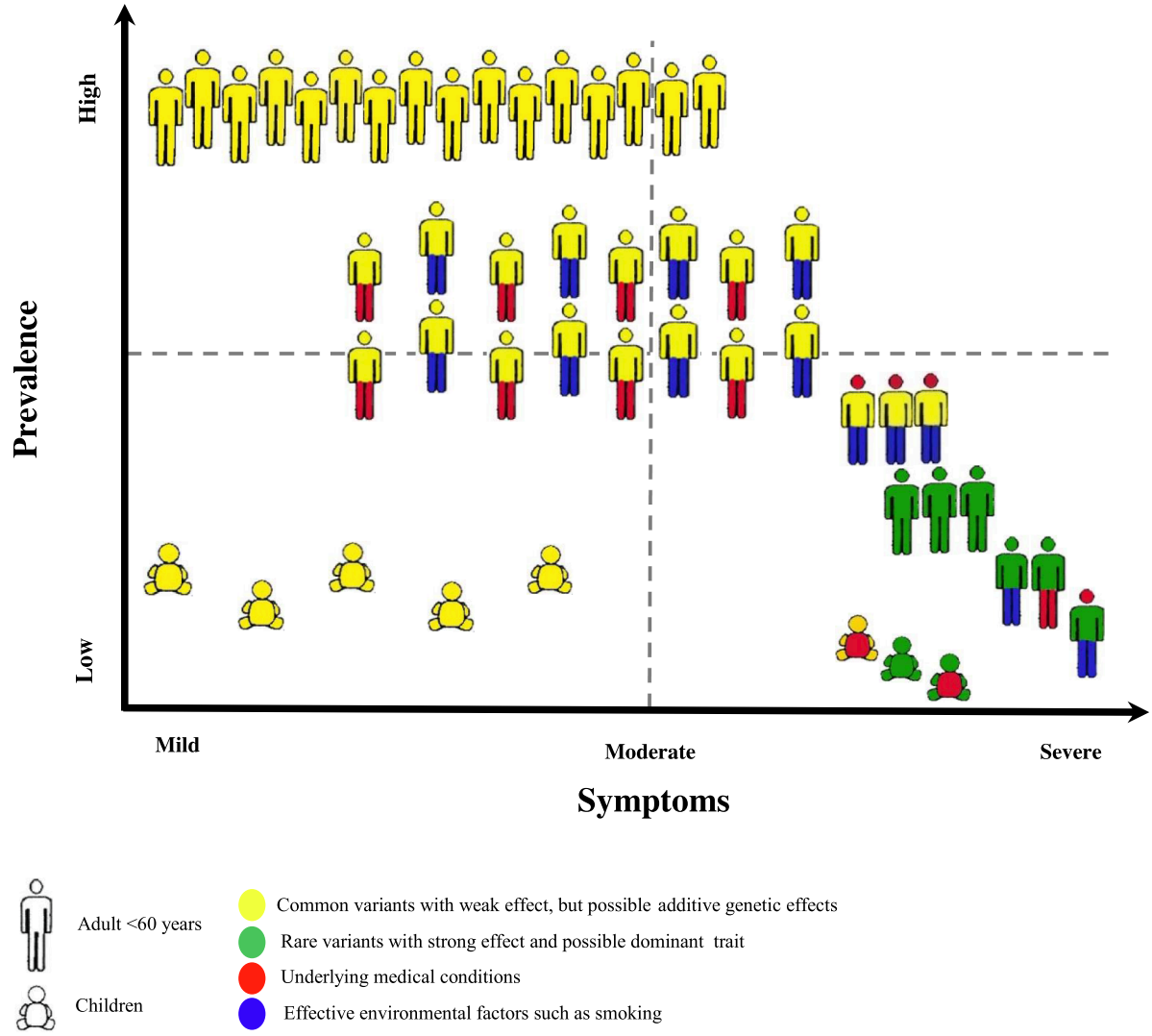

Fig. 1. Schematic visualization of genetic predisposition of COVID-19 infection. Risk of sex difference is not considered. The number of individuals is not to scale.

References

[1] Cao Y, Li L, Feng Z, Wan S, Huang P, Sun X, et al. Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations. Cell Discovery 2020;6(1):1–4.

[2] Cai H. Sex difference and smoking predisposition in patients with COVID-19. Lancet Respir Med 2020.

[3] Saghazadeh A, Rezaei N. Immune-epidemiological parameters of the novel coronavirus – a perspective. Expert Rev Clin Immunol 2020.

[4] Yousefzadegan S, Rezaei N. Death due to COVID-19 in three brothers. Am J Trop Med Hyg 2020.

[5] 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. The Lancet 2020;395(10224):565–74.

[6] Lin M, Tseng H-K, Trejaut JA, Lee H-L, Loo J-H, Chu C-C, et al. Association of HLA class I with severe acute respiratory syndrome coronavirus infection. BMC Med Genet 2003;4(1):9.

[7] Tang F, Liu W, Zhang F, Xin Z-T, Wei M-T, Zhang P-H, et al. IL-12 RB1 genetic variants contribute to human susceptibility to severe acute respiratory syndrome infection among Chinese. PloS one. 2008;3(5).

[8] Tu X, Chong WP, Zhai Y, Zhang H, Zhang F, Wang S, et al. Functional polymorphisms of the CCL2 and MBL genes cumulatively increase susceptibility to severe acute respiratory syndrome coronavirus infection. J Infect 2015;71(1):101–9.

[9] Wang K, Chen W, Zhou Y-S, Lian J-Q, Zhang Z, Du P, et al. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. bioRxiv. 2020.

[10] Rezaei N. COVID-19 affects Healthy Pediatricians more than Pediatric Patients. Infection Control & Hospital Epidemiology. 2020.

Farzaneh Darbeheshti[a,b], Nima Rezaei[c,d,e,*]

[a] *Department of Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[b] *Medical Genetics Network (MeGeNe), Universal Scientific Education and Research Network (USERN), Tehran, Iran*

[c] *Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran*

[d] *Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[e] *Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran*

E-mail address: rezaei_nima@tums.ac.ir (N. Rezaei).

[*] Corresponding author at: Research Center for Immunodeficiencies, Children's Medical Center Hospital, Dr. Qarib St, Keshavarz Blvd, Tehran 14194, Iran.