BÖLÜM 5

COVID-19 KOENFEKSİYONLARI: VİRAL ETKENLER

Sibel AYDOĞAN[1]

GİRİŞ

Konakçının aynı anda veya art arda birden fazla patojenle enfeksiyonu yaygındır ve bu fenomen koenfeksiyon olarak tanımlanır. Doğada viral koenfeksiyonlar tek etkenle gelişen viral enfeksiyonlar kadar yaygın görülmektedir. Virolojide koenfeksiyon bir hücrenin veya organizmanın ayrı virüsler tarafından eş zamanlı enfeksiyonu anlamına gelmektedir. Viral koenfeksiyonlar sıklıkla viral patojenitede değişiklik, konak savunmasında bozulma ve karışık klinik semptomlara neden olurlar ve bunların tümü tanı ve tedavide olumsuz etki yaratır (1).

Enfekte bir hücrede virüsler, virüs replikasyonunu destekleyebilecek veya inhibe edebilecek çok sayıda hücresel proteinle (virüs-konakçı interaktomu) etkileşime girebilir. Viral koenfeksiyonlardaki etkileşimler öncelikle virüs replikasyon döngülerindeki (viral faktörler) ve replikasyon ortamındaki (konakçı faktörleri) değişikliklerden kaynaklanır. Konakçı faktörleri çevresel değişiklikler ile virüslerin bulaşmasını ve patojenitesini etkiler (2).

KOENFEKSİYONLARDA GÖRÜLEN ETKİLEŞİMLER

Koenfeksiyonların diğer koenfeksiyon oluşturan ajanlar ve konakçıya olan etkileriyle ilgili çok az bilgi vardır. En yaygın bilinen etkileşim olan viral interferenste, bir virüs koenfeksiyondaki diğer virüsün replikasyonunu yarışmalı olarak bastırır. İnterferensin yanı sıra bazı virüsler diğer virüsün replikasyonunda

[1] Doç. Dr., Sağlık Bilimleri Üniversitesi Ankara Bilkent Şehir Sağlık Uygulama ve Araştırma Merkezi, drsaydogan72@gmail.com

KAYNAKLAR

1. Du Y, Wang C, Zhang Y. Viral coinfections. *Viruses* 2022; 14(12):2645. doi: 10.3390/v14122645.
2. Kumar N, Sharma S, Barua S, et al. Virological and immunological outcomes of coinfections. *Clinical Microbiology Reviews* 2018;31(4):e00111-17. doi: 10.1128/CMR.00111-17.
3. Essaidi-Laziosi, M., Geiser, J., Huang, S. *et al.* Interferon-dependent and respiratory virus-specific interference in dual infections of airway epithelia. *Scientific Reports* 2020; 10:10246. https://doi.org/10.1038/s41598-020-66748-6.
4. Cheng X, Uchida T, Xia Y, et al. Diminished hepatic IFN response following HCV clearance triggers HBV reactivation in coinfection. *The Journal of Clinical Investigation* 2020;130(6):3205-3220. doi: 10.1172/JCI135616.
5. Goto H, Ihira H, Morishita K, et al. Enhanced growth of influenza A virus by coinfection with human parainfluenza virus type 2. *Medical Microbiology and Immunology* 2016;205(3):209-218. doi: 10.1007/s00430-015-0441-y.
6. Bellecave P, Gouttenoire J, Gajer M, et al. Hepatitis B and C virus coinfection: a novel model system reveals the absence of direct viral interference. *Hepatology* 2009;50(1):46-55. doi: 10.1002/hep.22951.
7. Goka EA, Vallely PJ, Mutton KJ, et al. Single, dual and multiple respiratory virus infections and risk of hospitalization and mortality. *Epidemiology and Infection* 2015;143(1):37-47. doi: 10.1017/S0950268814000302.
8. Shannon KL, Osula VO, Shaw-Saliba K, et al. Emergency Department National Influenza Network Investigators. Viral co-infections are associated with increased rates of hospitalization in those with influenza. *Influenza and Other Respiratory Viruses* 2022;16(4):780-788. doi: 10.1111/irv.12967.
9. Mavilia MG, Wu GY. HBV-HCV Coinfection: Viral interactions, management, and viral reactivation. *Journal of Clinical and Translational Hepatology* 2018;6(3):296-305. doi: 10.14218/JCTH.2018.00016.
10. Harapan H, Michie A, Sasmono RT, et al. Dengue: A Minireview. *Viruses* 2020;12(8):829. doi: 10.3390/v12080829.
11. González-Candelas F, López-Labrador FX, Bracho MA. Recombination in hepatitis C virus. *Viruses* 2011;3(10):2006-2024. doi: 10.3390/v3102006.
12. Urbaniak K, Markowska-Daniel I. In vivo reassortment of influenza viruses. *Acta Biochimica Polonica* 2014;61(3):427-431.
13. Hoque MN, Akter S, Mishu ID, et al. Microbial co-infections in COVID-19: Associated microbiota and underlying mechanisms of pathogenesis. *Microbial Pathogenesis* 2021;156:104941. doi: 10.1016/j.micpath.2021.104941.
14. Cimolai N. The complexity of co-Infections in the era of COVID-19. *SN Comprehensive Clinical Medicine* 2021;3(7):1502-1514. doi: 10.1007/s42399-021-00913-4.
15. Aghbash PS, Eslami N, Shirvaliloo M, et al. Viral coinfections in COVID-19. *Journal of Medical Virology* 2021;93(9):5310-5322. doi: 10.1002/jmv.27102.
16. Swets MC, Russell CD, Harrison EM, et al. SARS-CoV-2 co-infection with influenza viruses, respiratory syncytial virus, or adenoviruses. *Lancet* 2022;399(10334):1463-1464. doi: 10.1016/S0140-6736(22)00383-X.
17. Alhumaid S, Alabdulqader M, Al Dossary N, et al. Global coinfections with bacteria, fungi, and respiratory viruses in children with SARS-CoV-2: A Systematic review and meta-Analysis. *Tropical Medicine and Infectious Disease* 2022;7(11):380. doi: 10.3390/tropicalmed7110380.
18. Cong B, Deng S, Wang X, Li Y. The role of respiratory co-infection with influenza or respiratory syncytial virus in the clinical severity of COVID-19 patients: A systematic review and meta-analysis. *Journal of Global Health* 2022;12:05040. doi: 10.7189/jogh.12.05040.
19. Wishaupt JO, van der Ploeg T, de Groot R, et al. Single- and multiple viral respiratory infe-

ctions in children: disease and management cannot be related to a specific pathogen. *BMC Infectios Diseases* 2017; 17(1):62.
20. Lansbury L, Lim B, Baskaran V, et al. Co-infections in people with COVID-19: a systematic review and meta-analysis. *Journal of Infection* 2020; 81(2):266-275. doi: 10.1016/j.jinf.2020.05.046.
21. Zandi M, Soltani S, Fani M, et al. Severe acute respiratory syndrome coronavirus 2 and respiratory syncytial virus coinfection in children. *Osong Public Health and Research Perspectives* 2021;12(5):286-292. doi: 10.24171/j.phrp.2021.0140.
22. Krumbein H, Kümmel LS, Fragkou PC, et al. Respiratory viral co-infections in patients with COVID-19 and associated outcomes: A systematic review and meta-analysis. *Reviewes in Medical Virology* 2023;33(1):e2365. doi: 10.1002/rmv.2365.
23. Trifonova I, Christova I, Madzharova I, et al. Clinical significance and role of coinfections with respiratory pathogens among individuals with confirmed severe acute respiratory syndrome coronavirus-2 infection. *Frontiers in Public Health* 2022;10:959319. doi: 10.3389/fpubh.2022.959319.
24. Alosaimi B, Naeem A, Hamed ME, et al. Influenza co-infection associated with severity and mortality in COVID-19 patients. *Virology Journal* 2021;18(1):127. doi: 10.1186/s12985-021-01594-0.
25. Bai L, Zhao Y, Dong J, et al. Coinfection with influenza A virus enhances SARS-CoV-2 infectivity. *Cell Research*. 2021;31(4):395-403. doi: 10.1038/s41422-021-00473-1.
26. Dadashi M, Khaleghnejad S, Abedi Elkhichi P, et al. COVID-19 and influenza co-infection: A systematic review and meta-analysis. *Frontiers in Medicine (Lausanne)* 2021;8:681469. doi: 10.3389/fmed.2021.681469.
27. Chotpitayasunondh T, Fischer TK, Heraud JM, et al. Influenza and COVID-19: What does co-existence mean? *Influenza and Other Respiratory Viruses* 2021;15(3):407-412. doi: 10.1111/irv.12824.
28. Guan Z, Chen C, Li Y, et al. Impact of coinfection with SARS-CoV-2 and influenza on disease severity: A systematic review and meta-analysis. *Frontiers in Public Health* 2021;9:773130. doi: 10.3389/fpubh.2021.773130.
29. Qiu S, Zeng G, Li P, et al. Pneumonia patients caused by co-infection with SARS-CoV-2 and human adenovirus in China. *Frontiers in Medicine (Lausanne)* 2021;8:735779. doi: 10.3389/fmed.2021.735779.
30. Gesesew HA, Mwanri L, Stephens JH, et al. COVID/HIV Co-infection: A syndemic perspective on what to ask and how to answer. *Frontiers in Public Health* 2021;9:623468. doi: 10.3389/fpubh.2021.623468.
31. Kanwugu ON, Adadi P. HIV/SARS-CoV-2 coinfection: A global perspective. *Journal of Medical Virology* 2021;93(2):726-732. doi: 10.1002/jmv.26321.
32. Barbera LK, Kamis KF, Rowan SE, et al. HIV and COVID-19: review of clinical course and outcomes. *HIV Research and Clinical Practice* 2021;22(4):102-118.doi: 10.1080/25787489.2021.1975608.
33. CDC. What to know about HIV and COVID-19. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/need-extra precautions/hiv.html. Published 2020. Accessed October 1, 2020.
34. Suwanwongse K, Shabarek N. Clinical features and outcome of HIV/SARS-CoV-2 coinfected patients in The Bronx, New York city. *Journal of Medical Virology* 2020;92(11):2387-2389. doi: 10.1002/jmv.26077.
35. Gatechompol S, Avihingsanon A, Putcharoen O,et al. COVID-19 and HIV infection co-pandemics and their impact: a review of the literature. *AIDS Research and Therapy* 2021;18(1):28. doi: 10.1186/s12981-021-00335-1.
36. Xu L, Liu J, Lu M, et al. Liver injury during highly pathogenic human coronavirus infections. *Liver International* 2020;40(5):998-1004. doi: 10.1111/liv.14435.

37. Chen L, Huang S, Yang J, et al. Clinical characteristics in patients with SARS-CoV-2/HBV co-infection. *Journal of Viral Hepatitis* 2020;27(12):1504-1507. doi: 10.1111/jvh.13362.
38. Xiang TD, Zheng X. Interaction between hepatitis B virus and SARS-CoV-2 infections. *World Journal of Gastroenterology* 2021;27(9):782-793. doi: 10.3748/wjg.v27.i9.782.
39. He YF, Jiang ZG, Wu N, et al. Correlation between COVID-19 and hepatitis B: A systematic review. *World Journal of Gastroenterology* 2022;28(46):6599-6618. doi: 10.3748/wjg.v28.i46.6599.
40. Kadambari S, Klenerman P, Pollard AJ. Why the elderly appear to be more severely affected by COVID-19: The potential role of immunosenescence and CMV. *Reviews in Medical Virology* 2020;30(5):e2144. doi: 10.1002/rmv.2144.
41. Perera MR, Greenwood EJD, Crozier TWM, et al. Cambridge Institute of Therapeutic Immunology and Infectious Disease-National Institute of Health Research COVID BioResource Collaboration. Human cytomegalovirus infection of epithelial cells increases SARS-CoV-2 superinfection by upregulating the ACE2 receptor. *Journal of Infectious Disease* 2023;227(4):543-553. doi: 10.1093/infdis/jiac452.
42. Carll WC, Rady MY, Salomao MA, et al. Cytomegalovirus haemorrhagic enterocolitis associated with severe infection with COVID-19. *BMJ Open Gastroenterology* 2021;8(1):e000556. doi: 10.1136/bmjgast-2020-000556.
43. Molaei H, Khedmat L, Nemati E, et al. Iranian kidney transplant recipients with COVID-19 infection: Clinical outcomes and cytomegalovirus coinfection. *Transplant Infectious Disease* 2021;23(1):e13455. doi: 10.1111/tid.13455.
44. Roncati L, Lusenti B, Nasillo V, et al. Fatal SARS-CoV-2 coinfection in course of EBV-associated lymphoproliferative disease. *Annals of Hematology* 2020;99(8):1945-1946. doi: 10.1007/s00277-020-04098-z.
45. Tsheten T, Clements ACA, Gray DJ, et al. Clinical features and outcomes of COVID-19 and dengue co-infection: a systematic review. *BMC Infectious Disease* 2021;21(1):729. doi: 10.1186/s12879-021-06409-9.
46. Prapty CNBS, Rahmat R, Araf Y, et al. SARS-CoV-2 and dengue virus co-infection: Epidemiology, pathogenesis, diagnosis, treatment, and management. *Reviews of Medical Virology* 2023;33(1):e2340. doi: 10.1002/rmv.2340.
47. Huang YT, Hite S, Duane V, et al. CV-1 and MRC-5 mixed cells for simultaneous detection of herpes simplex viruses and varicella zoster virus in skin lesions. *Journal of Clinical Virology* 2002;24(1-2):37-43. doi: 10.1016/s1386-6532(01)00230-x.
48. LaSala PR, Bufton KK, Ismail N, et al. Prospective comparison of R-mix shell vial system with direct antigen tests and conventional cell culture for respiratory virus detection. *Journal of Clinical Virology* 2007;38(3):210-216. doi: 10.1016/j.jcv.2006.12.015.
49. Wu W, Tang YW. Emerging molecular assays for detection and characterization of respiratory viruses. *Clinics in Laboratory Medicine* 2009;29(4):673-693. doi: 10.1016/j.cll.2009.07.005.
50. Huang HS, Tsai CL, Chang J, et al. Multiplex PCR system for the rapid diagnosis of respiratory virus infection: systematic review and meta-analysis. *Clinical Microbiology and Infection* 2018;24(10):1055-1063. doi: 10.1016/j.cmi.2017.11.018.
51. Chen EC, Miller SA, DeRisi JL, Chiu CY. Using a pan-viral microarray assay (Virochip) to screen clinical samples for viral pathogens. *Journal of Visualized Experiments* 2011;(50):2536. doi: 10.3791/2536.
52. Fayyadh TK, Ma F, Qin C, et al. Simultaneous detection of multiple viruses in their co-infected cells using multicolour imaging with self-assembled quantum dot probes. *Mikrochimica Acta* 2017;184(8):2815–2824. doi: 10.1007/s00604-017-2300-6.
53. Peeling RW, Heymann DL, Teo YY, et al. Diagnostics for COVID-19: moving from pandemic response to control. *Lancet* 2022;399(10326):757-768. doi: 10.1016/S0140-6736(21)02346-1.