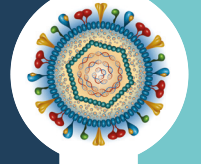


BÖLÜM 5

Flaviviridae



Oğuzhan AVCI¹

GENEL BİLGİLER

İnsanoğlunun diğer canlılarla birlikte yaşamını paylaştığı dünya üzerinde bugüne kadar yaklaşık 6.400 memeli türü tanımlanmış durumdadır. Bunlardan yaklaşık 200 kadarı Avrupa ülkelerinde görülebilirken ülkemizde ise yaklaşık 170 memeli türünün yaşadığı bilinmektedir.

Esas olarak memeliler ve kuşları enfekte eden virusların bulunduğu bu ailedeki viruslar 9.0-13 kb uzunluğunda pozitif polariteli linear tek iplikçikli RNA (ssRNA) içermektedir 'Flaviviridae' ismini (flavus, Latince 'sarı' anlamına gelmektedir) Sarıhumma virus'undan almıştır. Genellikle 45-60 nm virion büyüklüğüne sahip viruslar kübik simetriye sahiptirler. Zarlı viruslardır ve zar üzerinde bulunan E2 glikoproteini virusun dominant proteini olarak bilinmektedir. Viral replikasyon sitoplazmada gerçekleşmektedir. Virion, hücre içi zarlardan tomurcuklanarak ekzositoz yoluyla konak hücreden çıkmaktadır. *Flaviviridae* ailesindeki viruslar çevre şartlarında ve dezenfektanlara maruz kalmaları durumunda hızla inaktif olmaktadır. Bu ailedeki viruslar genellikle vektör (kene, sokucu sinekler) aracılığıyla bulaşmaktadır ayrıca bu aile içinde zoonoz karakter gösteren viruslar yer almaktadır. Hem horizontal hem de vertikal yolla bulaşabilen virusların yanı sıra kan ve cinsel yolla bulaşan viruslar da bulunmaktadır.

Bu bölümde *Flaviviridae* ailesinde (Şekil 5.1) *Orthoflavivirus* genusunda yer alan Louping ill; West-nile enfeksiyonu; Domuzların Japon Ensephalitisi Virus; *Pestivirus* genusunda yer alan Bovine Viral Diarrhea-Mucosal Disease; Border Disease; Avrupa Domuz Vebası; Atipik Domuz Pestivirus, *Hepacivirus* genusunda yer alan Bovine Hepacivirus ve *Pegivirus* genusunda yer alan Porcine Pegivirus enfeksiyonları hakkında kısa ve temel bilgiler sunulmuş olup güncel veriler aktarılmaya çalışılmıştır.

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KAYNAKLAR

1. Albayrak H, Özcan E, Çavunt A. A serological survey of selected pathogens in wild boar (*Sus scrofa*) in northern Turkey. *European Journal of Wildlife Research*. 2013;59(6): 893-897.
2. Arnal M, Fernandez de Luco D, Riba L, et al. A novel pestivirus associated with deaths in Pyrenean chamois. *Journal of General Virology*. 2004;85: 3653-3657.
3. Arruda BL, Arruda PH, Magstadt DR, et al. Identification of a divergent lineage porcine pestivirus in nursing piglets with congenital tremors and reproduction of disease following experimental inoculation. *PLoS ONE*. 2016;11: e0150104.
4. Avalos-Ramirez R, Orlich M, Thiel HJ, et al. Evidence for the presence of two novel pestivirus species. *Virology*. 2001;286: 456-465.
5. Avcı O, Bulut O, Yapıcı O, et al. Effect of different storage temperatures on the stability of Bovine Viral Diarrhea Virus RNA in blood samples. *Pakistan Veterinary Journal*. 2015;35(4): 528-530.
6. Baba SS. Virological and immunological studies of Wesselsbron virus in experimentally infected red Sokoto (Maradi) goats. *Veterinary Microbiology*. 1993;34(4): 311-320.
7. Baba SS, Fagbami AH, Ojeh CK. Preliminary studies on the use of solid-phase immunosorbent techniques for the rapid detection of Wesselsbron virus (WSLV) IgM by haemagglutination-inhibition. *Comparative Immunology, Microbiology and Infectious Diseases*. 1999;22(1): 71-79.
8. Baechlein C, Fischer N, Grundhoff A, et al. Identification of a Novel Hepacivirus in Domestic Cattle from Germany. *Journal of Virology*. 2015;89(14): 7007-7015.
9. Baechlein C, Grundhoff A, Fischer N, et al. Pegivirus infection in domestic pigs, Germany. *Emerging Infectious Diseases*. 2016;22: 1312-1314.
10. Becher P, Shannon AD, Tautz N, et al. Molecular characterization of Border Disease Virus, a pestivirus from sheep. *Virology*. 1994;198: 542-551.
11. Becher P, Schmeiser S, Oguzoglu TC, et al. Complete genome sequence of a novel pestivirus from sheep. *Journal of Virology*. 2012;86: 11412.
12. Bielefeldt-Ohmann H. Special Issue: Bovine Viral Diarrhea Virus and related Pestiviruses. *Viruses*. 2020;12(10): 1181.
13. Blome S, Beer M, Wernike K. New leaves in the growing tree of Pestiviruses. *Advances in Virus Research*. 2017;99: 139-160.
14. Blome S, Staubach C, Henke J, et al. Classical Swine Fever-An updated review. *Viruses*. 2017;9(4): 86.
15. Blomstrom AL, Fossum C, Wallgren P, et al. Viral metagenomic analysis displays the co-infection situation in healthy and PMWS affected pigs. *PLoS One*. 2016;11: e0166863.
16. Blomström AL, Ley C, Jacobson M. Astrovirus as a possible cause of congenital tremor type All in piglets? *Acta Veterinaria Scandinavica*. 2014;56: 82.
17. Braun U, Hilbe M, Peterhans E, et al. Border disease in cattle. *The Veterinary Journal*. 2019;246: 12-20.
18. Breitfeld J, Fischer N, Tsachev I, et al. Expanded diversity and host range of Bovine Hepacivirus-Genomic and serological evidence in domestic and wild ruminant species. *Viruses*. 2022;30: 14(7), 1457.
19. Burgu I, Öztürk F, Akca Y, et al. Investigations on the occurrence and impact of bovine viral diarrhoea (BVD) virus infections in sheep in Turkey. *Deutsche Tierärztliche Wochenschrift*. 1987;94: 292-294.
20. Cagatay GN, Meyer D, Wendt M, et al. Characterization of the humoral immune response induced after infection with Atypical Porcine Pestivirus (APPV). *Viruses*. 2019;11: 880.
21. Chen F, Knutson TP, Braun E, et al. Semi-quantitative duplex RT-PCR reveals the low occurrence of Porcine Pegivirus and Atypical Porcine Pestivirus in diagnostic samples from the United States. *Transboundary and Emerging Diseases*. 2019;66: 1420-1425.
22. Chethan Kumar HB, Dhanze H, Bhilegaonkar KN, et al. Reply to commentary on serological evidence of Japanese encephalitis virus infection in pigs in a low human incidence state, Goa, India. *Preventive Veterinary Medicine*. 2020;77: 104945.
23. Dall Agnol AM, Alfieri AF, Alfieri AA. Pestivirus K (Atypical Porcine Pestivirus): Update on the virus, viral infection, and the association with congenital tremor in newborn piglets. *Viruses*. 2020;12(8): 903.
24. Dastjerdi A, Strong R, La Rocca SA, et al. Investigation into an outbreak of Border disease virus in pigs in England. *Transboundary and Emerging Diseases*. 2022;69(4): 1698-1706.
25. de Arce HD, Ganges L, Barrera M, et al. Origin and evolution of viruses causing classical swine fever in Cuba. *Virus Research*. 2005;112: 123-131.
26. De Mia GM, Greiser-Wilke I, Feliziani F, et al. Genetic characterization of a caprine pestivirus as the first member of a putative novel pestivirus subgroup. *Journal of Veterinary Medicine B*. 2005;52: 206-210.
27. de Oliveira LG, Mechler-Dreibl ML, Almeida HMS, et al. Bovine Viral Diarrhoea Virus: Recent findings about its occurrence in pigs. *Viruses*. 2020;12(6): 600.
28. Diagne MM, Faye M, Faye O, et al. Emergence of Wesselsbron virus among black rat and humans in Eastern Senegal in 2013. *One Health*. 2017;3: 23-28.
29. Diao NC, Gong QL, Li JM, et al. Prevalence of Bovine Viral Diarrhoea Virus (BVDV) in yaks between 1987 and 2019 in mainland China: A systematic review and meta-analysis. *Microbial Pathogenesis*. 2020;144: 104185.
30. Dong XN, Chen YH. Marker vaccine strategies and candidate CSFV marker vaccines. *Vaccine*. 2007;25: 205-230.
31. Edwards S. Survival and inactivation of classical swine fever virus. *Veterinary Microbiology*. 2000;73: 175-181.
32. Faye M, Seye T, Patel P, et al. Development of Real-Time molecular assays for the detection of Wesselsbron Virus in Africa. *Microorganisms*. 2022;10: 550.
33. Floegel G, Wehrend A, Depner KR, et al. Detection of classical swine fever virus in semen of infected boars. *Veterinary Microbiology*. 2000;77(1-2): 109-116.
34. Fritzemeier J, Haas L, Liebler E, et al. The development of early vs. late onset mucosal disease is a consequence of two different pathogenic mechanisms. *Archives of Virology*. 1997;142(7): 1335-1350.
35. Ganges L, Crooke HR, Bohórquez JA, et al. Classical swine fever virus: the past, present and future. *Virus Research*. 2020;289: 198151.
36. Gather T, Walter S, Todt D, et al. Vertical transmission of he-

- patitis C virus-like non-primate hepacivirus in horses. *Journal of General Virology*. 2016;97(10): 2540-2551.
37. Gatto IRH, Sonálio K, de Oliveira LG. Atypical Porcine Pestivirus (APPV) as a new species of pestivirus in pig production. *Frontiers in Veterinary Science*. 2019;6: 35.
 38. Givens MD, Newcomer BW. Perspective on BVDV control programs. *Animal Health Research Reviews*. 2015;1: 78-82.
 39. Gómez-Romero N, Basurto-Alcántara FJ, Verdugo-Rodríguez A, et al. Detection of border disease virus in Mexican cattle. *Transboundary and Emerging Diseases*. 2018;65(1): 267-271.
 40. Gomez-Romero N, Ridpath JF, Basurto-Alcantara FJ, et al. Bovine Viral Diarrhea Virus in cattle from Mexico: Current Status. *Frontiers in Veterinary Science*. 2021;8: 673577.
 41. Gould EA, Moss SR, Turner SL. Evolution and dispersal of encephalitic flaviviruses. *Arch Virol Suppl*. 2004;18: 65-84.
 42. İssi M, Gül Y, Özçelik M, et al. Bovine Viral Diarrhea Virus enfeksiyonlu bir buzağda görülen bukleli kıl örtüsü. *Fırat Üniversitesi Sağlık Bilimleri Veteriner Dergisi*. 2014;28(1): 45-48.
 43. Jeffries CL, Mansfield KL, Phipps LP, et al. Louping ill virus: an endemic tick-borne disease of Great Britain. *Journal of General Virology*. 2014;95(Pt 5): 1005-1014.
 44. Jokar M, Rahmanian V, Farhoodi M, et al. Seroprevalence of Bovine Viral Diarrhea Virus (BVDV) infection in cattle population in Iran: A systematic review and meta-analysis. *Tropical Animal Health and Production*. 2021;53(5): 449.
 45. Kennedy J, Pfankuche VM, Hoeltig D, et al. Genetic variability of porcine pegivirus in pigs from Europe and China and insights into tissue tropism. *Scientific Reports*. 2019;9: 8174.
 46. Kikuchi F, Hayashi A, Yamada K, et al. The role of wild boar as host of Japanese Encephalitis Virus in the absence of domestic pigs. *Viruses*. 2024;8: 1273.
 47. Kirkland PD, Frost MJ, Finlaison DS, et al. Identification of a novel virus in pigs-Bungowannah virus: A possible new species of pestivirus. *Virus Research*. 2007;129: 26-34.
 48. Ladreyt H, Durand B, Dussart P, et al. How central is the domestic pig in the epidemiological cycle of Japanese encephalitis virus? A review of scientific evidence and implications for disease control. *Viruses*. 2019;11(10): 949.
 49. Lamp B, Schwarz L, Högl S, et al. Novel pestivirus species in pigs, Austria, 2015. *Emerging Infectious Diseases*. 2017;23: 1176-1179.
 50. Le Flohic G, Porphyre V, Barbazan P, et al. Review of climate, landscape, and viral genetics as drivers of the Japanese encephalitis virus ecology. *PLOS Neglected Tropical Diseases*. 2013;7(9): e2208.
 51. Loeffelholz MJ, Fenwick BW. Taxonomic changes for human and animal viruses, 2018 to 2020. *Journal of Clinical Microbiology*. 2021;59(2): e01932-20.
 52. Lord JS. Changes in rice and livestock production and the potential emergence of Japanese encephalitis in Africa. *Pathogens*. 2021;10(3): 294.
 53. Lu G, Chen C, Shao R, et al. Identification and genetic characterization of bovine hepacivirus in China: A large scale epidemiological study. *Virologica Sinica*. 2022;37(2): 223-228.
 54. Mackenzie J, Williams D, Smith D. Japanese encephalitis virus: the geographic distribution, incidence, and spread of a virus with a propensity to emerge in new areas. *Perspectives in Medical Virology*. 2006;16: 201-268.
 55. Malik YS, Bhat S, Kumar ORV, et al. Classical Swine Fever Virus biology, clinicopathology, diagnosis, vaccines and a meta-analysis of prevalence: A review from the Indian perspective. *Pathogens*. 2020;9(6): 500.
 56. Marriott L, Willoughby K, Chianini F, et al. Detection of Louping ill virus in clinical specimens from mammals and birds using TaqMan RT-PCR. *Journal of Virological Methods*. 2006;137(1): 21-28.
 57. Moennig V, Floegel-Niesmann G, Greiser-Wilke I. Clinical signs and epidemiology of Classical Swine Fever: A review of new knowledge. *Veterinary Journal*. 2003;165(1): 11-20.
 58. Mohd Hanafiah K, Groeger J, Flaxman AD, et al. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology*. 2013;57: 1333-1342.
 59. Monies RJ, Paton DJ, Vilcek S. Mucosal disease like lesions in sheep infected with Border disease virus. *Veterinary Record*. 2004;155: 765-769.
 60. Neill JD, Ridpath JF, Fischer N, et al. Complete genome sequence of pronghorn virus, a pestivirus. *Genome Announcements*. 2014; 2.
 61. Oguzoglu TC, Floegel-Niesmann G, Frey H-R, et al. Differential diagnosis of classical swine fever and border disease: seroepidemiological investigation of a pestivirus infection on a mixed sheep and swine farm. *Deutsche Tierärztliche Wochenschrift*. 2001;108: 210-213.
 62. Oguzoglu TC, Tan MT, Toplu N, et al. Border Disease Virus (BDV) infections of small ruminants in Turkey: a new BDV subgroup? *Veterinary Microbiology*. 2009;135(3-4): 374-379.
 63. Oğuzoğlu TC, Muz D, Yılmaz D, et al. Molecular characteristics of Bovine Virus Diarrhoea Virus 1 isolates from Turkey: Approaches for an eradication programme. *Transboundary and Emerging Diseases*. 2012;59: 303-310.
 64. Oğuzoğlu TÇ, Koç BT, Coşkun N, et al. Endless variety for bovine virus diarrhoea viruses: new members of a novel subgroup into Pestivirus A from Turkey. *Tropical Animal Health and Production*. 2019;51(5): 1083-1087.
 65. Oymans J, van Keulen L, Wichgers Schreur PJ, et al. Early pathogenesis of Wesselsbron Disease in pregnant ewes. *Pathogens*. 2020;9(5): 373.
 66. Pang F, Long Q, Wei M. Immune evasion strategies of Bovine Viral Diarrhea Virus. *Frontiers in Cellular and Infection Microbiology*. 2023;13: 1282526.
 67. Park SL, Huang YS, Lyons AC, et al. Infection of feral phenotype swine with Japanese Encephalitis Virus. *Vector-Borne and Zoonotic Diseases*. 2023;23(12): 645-652.
 68. Pfankuche VM, Hahn K, Bodewes R, et al. Comparison of different in situ hybridization techniques for the detection of various RNA and DNA viruses. *Viruses*. 2018;10: 384.
 69. Possatti F, Headley SA, Leme RA, et al. Viruses associated with congenital tremor and high lethality in piglets. *Transboundary and Emerging Diseases*. 2018;65: 331-337.
 70. Postel A, Austermann-Busch S, Petrov A, et al. Epidemiology, diagnosis and control of Classical Swine Fever: recent developments and future challenges. *Transboundary and Emerging Diseases*. 2018;65: 248-261.
 71. Presi P, Struchen R, Knight-Jones T, et al. Bovine viral diarrhoea (BVD) eradication in Switzerland—Experiences of the first two years. *Preventive Veterinary Medicine*. 2011;99: 112-

- 121.
72. Ran X, Chen X, Ma L, et al. A systematic review and meta-analysis of the epidemiology of bovine viral diarrhoea virus (BVDV) infection in dairy cattle in China. *Acta Tropica*. 2019;190: 296-303.
73. Richter V, Kattwinkel E, Firth CL, et al. Mapping the global prevalence of bovine viral diarrhoea virus infection and its associated mitigation programmes. *Veterinary Record*. 2019;184(23): 711.
74. Ridpath JF, Bolin SR. Comparison of the complete genomic sequence of the Border Disease Virus, BD31 to other pestiviruses. *Virus Research*. 1997;50: 237-243.
75. Ross HM, Evans CC, Spence JA, et al. Louping ill in free-ranging pigs. *Veterinary Record*. 1994;134(4): 99-100.
76. Rüfenacht J, Schaller P, Audigé L, et al. The effect of infection with Bovine Viral Diarrhoea Virus on the fertility of Swiss dairy cattle. *Theriogenology*. 2001;56: 199-210.
77. Saltik HS, Kale M, Atli K. First molecular evidence of Border Disease Virus in wild boars in Turkey. *Veterinary Research Communications*. 2022;46(1): 243-250.
78. Simmonds P, Becher P, Bukh J, et al. ICTV virus taxonomy profile: Flaviviridae. *Journal of General Virology*. 2017;98: 2-3.
79. Smith DB, Becher P, Bukh J, et al. Proposed update to the taxonomy of the genera hepacivirus and pegivirus with in the Flaviviridae family. *Journal of General Virology*. 2016;97: 2894-2907.
80. Smith DB, Meyers G, Bukh J, et al. Proposed revision to the taxonomy of the genus Pestivirus, family Flaviviridae. *Journal of General Virology*. 2017;98: 2106-2112.
81. Smith DR. Waiting in the wings: The potential of mosquito transmitted flaviviruses to emerge. *Critical Reviews in Microbiology*. 2017;43(4): 405-422.
82. Sozzi E, Lavazza A, Gaffuri A, et al. Isolation and full-length sequence analysis of a pestivirus from aborted lamb fetuses in Italy. *Viruses*. 2019;11: 744.
83. Stalder HP, Meier Ph, Pfaffen G, W et al. Genetic heterogeneity of pestiviruses of ruminants in Switzerland. *Preventive Veterinary Medicine*. 2005;72: 37-41.
84. Stenberg H, Leveringhaus E, Malmsten A, et al. Atypical porcine pestivirus-A widespread virus in the Swedish wild boar population. *Transboundary and Emerging Diseases*. 2022;69(4): 2349-2360.
85. Tarradas J, de la Torre ME, Rosell R, et al. The impact of CSFV on the immune response to control infection. *Virus Research*. 2014;185: 82-91.
86. Timurkan MÖ, Aydın H. Increased genetic diversity of BVDV strains circulating in Eastern Anatolia, Turkey: first detection of BVDV-3 in Turkey. *Tropical Animal Health and Production*. 2019;51(7): 1953-1961.
87. van den Hurk A, Ritchie S, Mackenzie J. Ecology and geographical expansion of Japanese encephalitis virus. *Annual Review of Entomology*. 2009;54: 17-35.
88. van der Lugt JJ, Coetzer JA, Smit MM, et al. The diagnosis of Wesselsbron disease in a new-born lamb by immunohistochemical staining of viral antigen. *Onderstepoort Journal of Veterinary Research*. 1995;62(2): 143-146.
89. Vilcek S, Ridpath JF, Van Campen H, et al. Characterization of a novel pestivirus originating from a pronghorn antelope. *Virus Research*. 2005;108: 187-193.
90. Xie Y, Wang X, Feng J, et al. The Prevalence, Genetic Characterization, and Evolutionary Analysis of Porcine Pegivirus in Guangdong, China. *Virologica Sinica*. 2021;36(1): 52-60.
91. Yang C, Wang L, Shen H, et al. Detection and genetic characterization of Porcine Pegivirus in pigs in the United States. *Transboundary and Emerging Diseases*. 2018;65: 618-626.
92. Yesilbag K, Förster C, Bank-Wolf B, et al. Genetic heterogeneity of Bovine Viral Diarrhoea Virus (BVDV) isolates from Turkey: Identification of a new subgroup in BVDV-1. *Veterinary Microbiology*. 2008;130: 258-267.
93. Yesilbag K, Alpaz G, Karakuzulu HA. Serologic survey of viral infections in captive ungulates in Turkish zoos. *Journal of Zoo and Wildlife Medicine*. 2011;42: 44-48.
94. Yesilbag K, Forster C, Ozyigit MO, et al. Characterisation of Bovine Viral Diarrhoea Virus (BVDV) isolates from an outbreak with haemorrhagic enteritis and severe pneumonia. *Veterinary Microbiology*. 2014; 169(1-2): 42-49.
95. Yeşilbağ K, Alpaz G, Becher P. Variability and global distribution of subgenotypes of Bovine Viral Diarrhoea Virus. *Viruses*. 2017;9(6): 128.
96. Yesilbag K, Baechlein C, Kadiroğlu B, et al. Presence of Bovine Hepacivirus in Turkish cattle. *Veterinary Microbiology*. 2018;225: 1-5.
97. Yıldız R, Ok M. Koyunların Ensefalomyelitisi Louping ill. *Türkiye Klinikleri Veterinary Sciences – Internal Medicine-Special Topics*. 2016;2(1): 33-36.
98. Yılmaz H, Altan E, Ridpath J, et al. Genetic diversity and frequency of Bovine Viral Diarrhoea Virus (BVDV) detected in cattle in Turkey. *Comparative Immunology, Microbiology and Infectious Diseases*. 2012;35: 411-416.
99. Zirra-Shallangwa B, González Gordon L, Hernandez-Castro LE, et al. The epidemiology of Bovine Viral Diarrhoea Virus in Low – and Middle-Income Countries: A systematic review and meta-analysis. *Frontiers in Veterinary Science*. 2022;9: 947515.