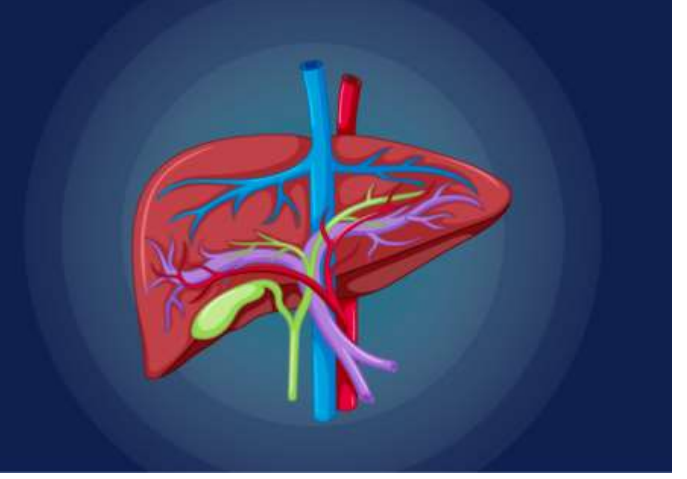


KLİMİK
HEPATİT AKADEMİSİ
2025

14-16 ŞUBAT 2025
Anemon Grand Eskişehir Otel / Eskişehir

 **VHÇG** KLİMİK DERNEĞİ VİRAL
HEPATİT ÇALIŞMA GRUBU



Hepatit E: Gözden Geçirme

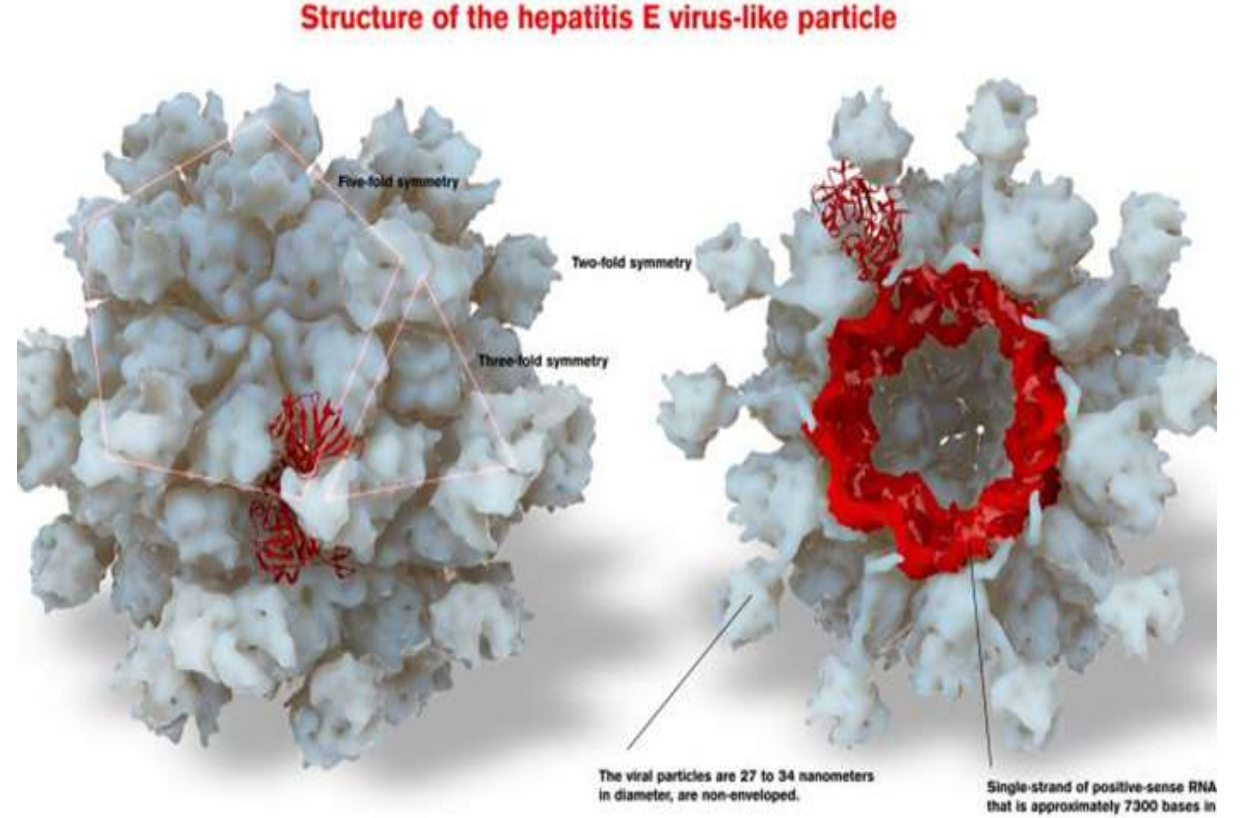
Doçent Dr. Zeynep TÜRE YÜCE

Özel Gürlife Hastanesi Enfeksiyon Hastalıkları Kliniği, Eskişehir

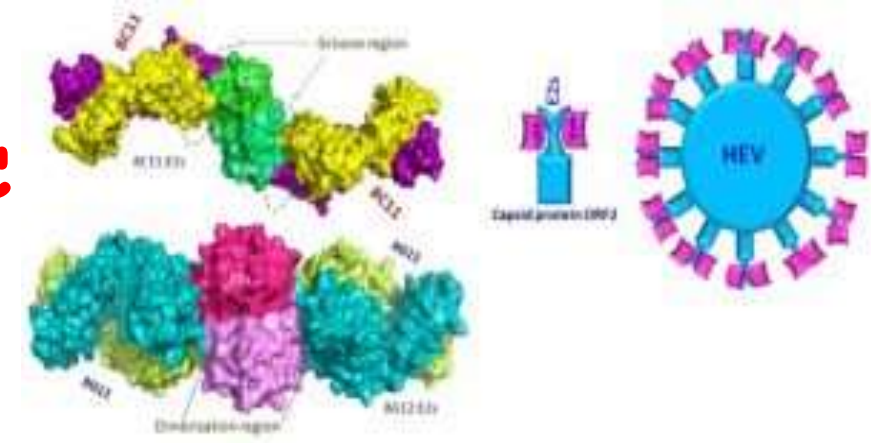
16.02.2025

Sunum Planı

- Virolojik Özellikler
- Epidemiyoloji
- Bulaşma yolları
- Klinik Tablolar
- Özel hasta grupları
- Tedavi yönetimi
- Korunma



Hepatit E: Gözden Geç



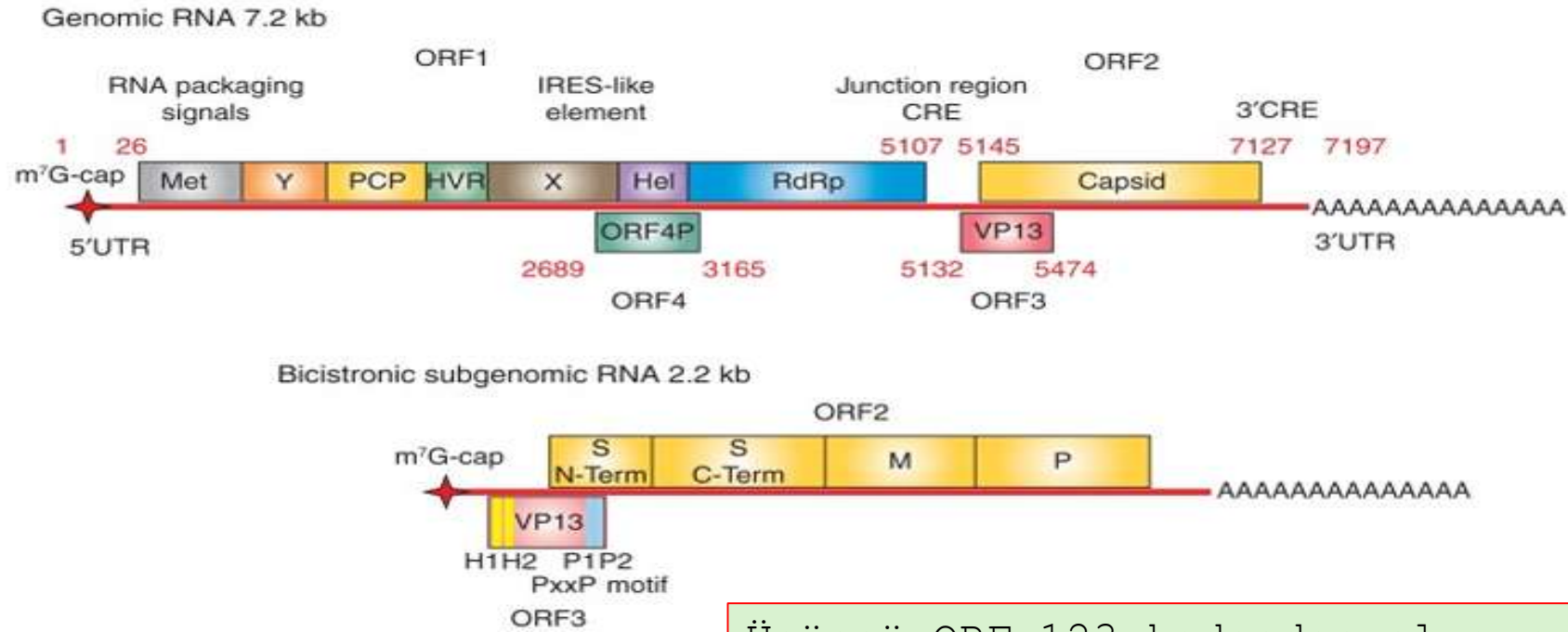
- Hepatit E infeksiyonu, karaciğerde Hepatit E virüsüne bağlı oluşan inflamasyon
- Her yıl dünyada 20 milyon yeni olgu, 3.3 milyon semptomatik olgu
- DSÖ verilerine göre 2015 yılında 44000 ölüm
- HEV insanlar yanında evcil ve vahşi domuzlarda, geyiklerde ve kemiricilerde infeksiyona yol açar

Virolojik Özellikleri

- Hepeviridae ailesinde yer alan Hepevirus genusundadır
- 27-34 nm çapında, ikozahedral yapıda, zarfsız RNA virusu
- Pozitif sarmal RNA sında 3 büyük açık okuma bölgesi

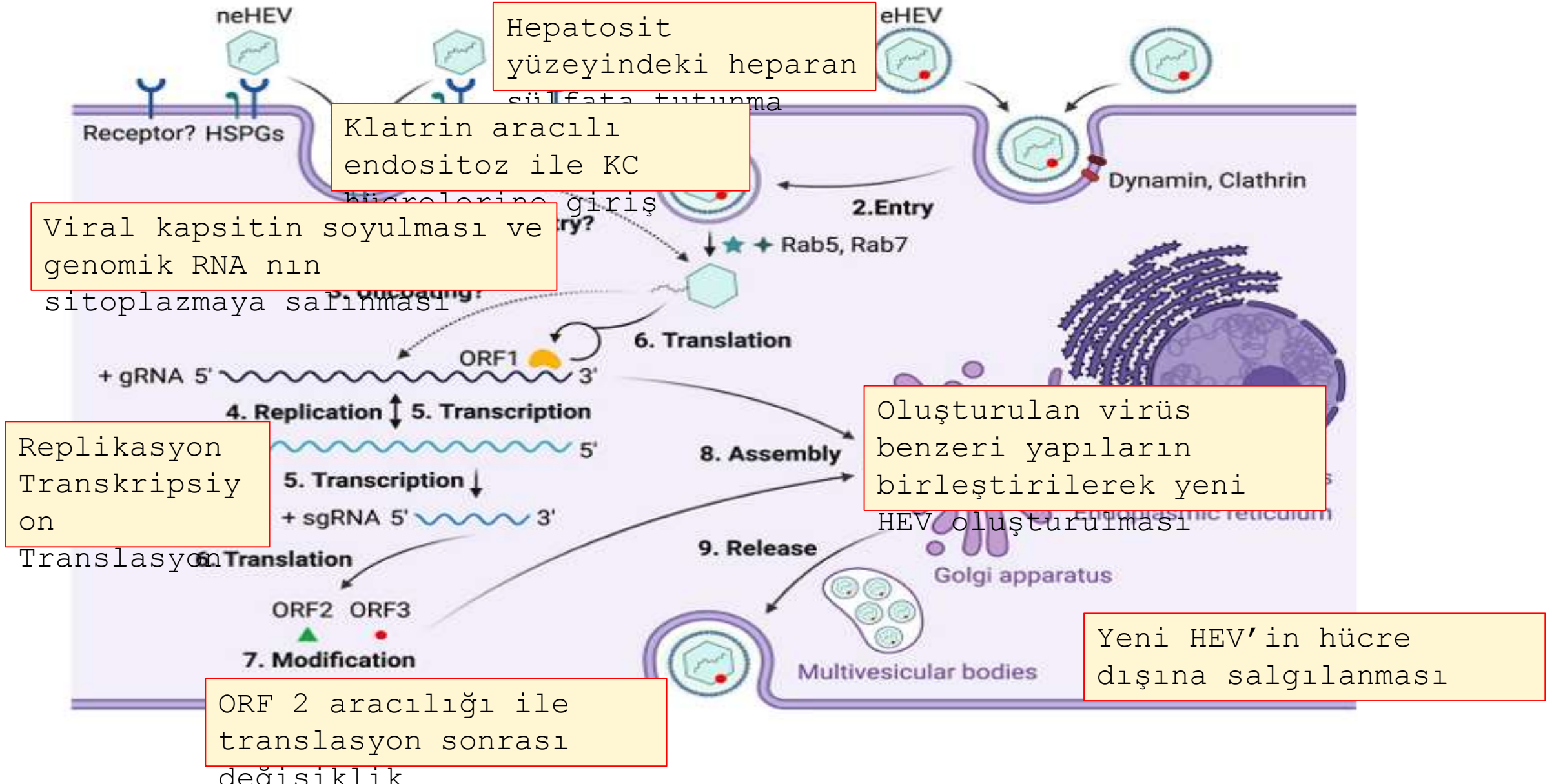
En büyük ORF 1693 kodondan oluşur.
Virüsün işlenmesi ve replikasyonundan sorumludur (metil transferaz, RNA helikaz, sistein proteaz, RNA polimeraz)

İkinci ORF 660 kodondan viral kapsit proteinini kodlar



Üçüncü ORF 123 kodondan oluşur; enfekte hücrelerden enfeksiyöz virionların salınımını kolaylaştırabilecek bir viroporin gibi davranır

Virolojik Özellikleri



Virolojik Özellikleri

- Yapılan genomik dizi analizlerine göre HEV' in insanlarda infeksiyona neden olan 4 genotipi bulunmaktadır

Her bir HEV genotipi farklı coğrafyada dağılım gösterir

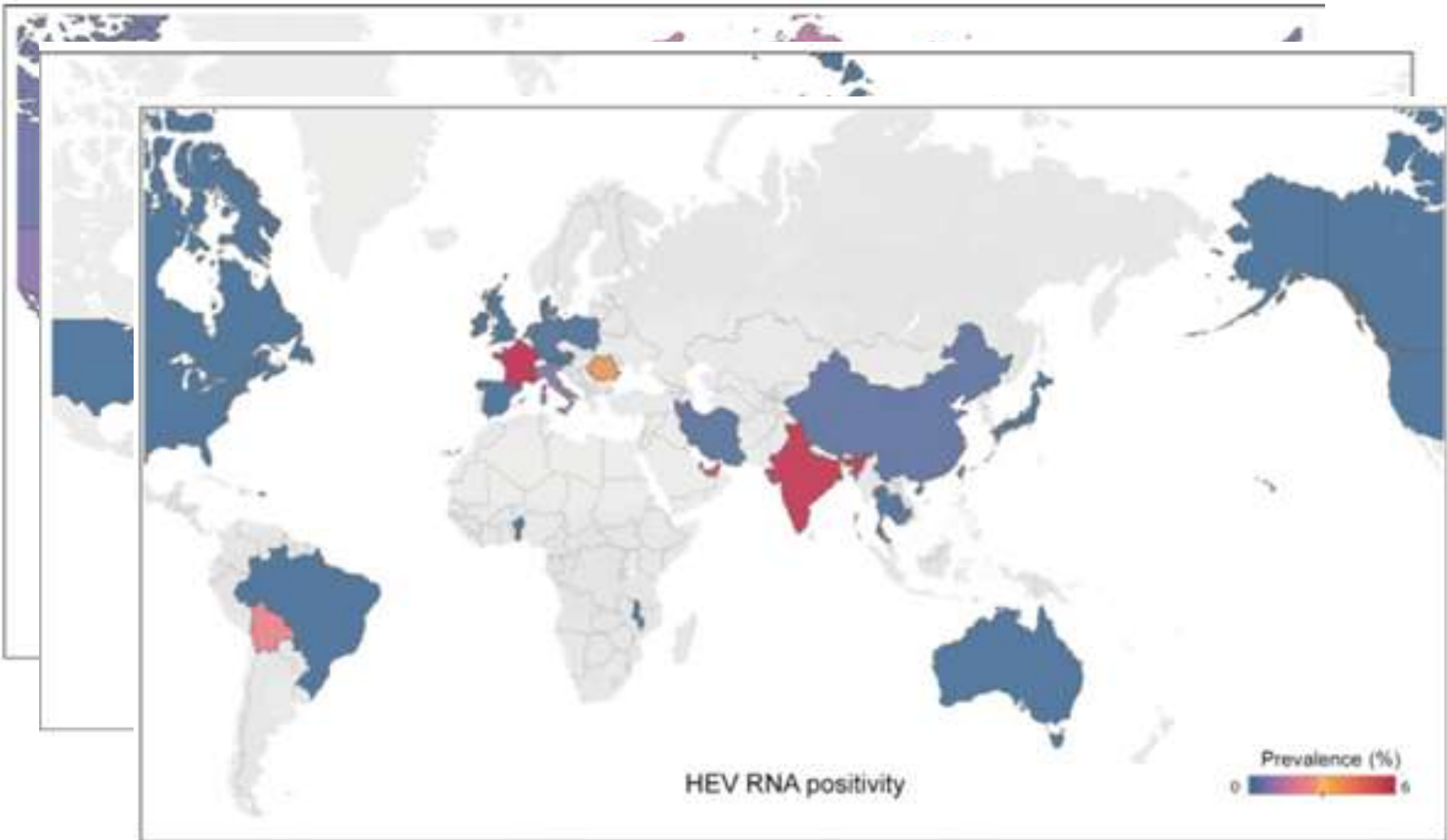
- **Genotip 1 ve 2:** Asya ve Afrika ülkeleri ile Meksika'daki bir çok salgından sorumludur
- **Genotip 3 ve 4:** ABD, Arjantin, Avrupa ülkeleri, Japonya ve Çin'den izole edilen yerel vakalardan sorumludur

Epidemiyoloji

- Gelişmiş ülkelerde prevalans %1-21
- Az gelişmiş ülkelerde %10-70
- Ülkemizde HEV prevalansı bölgelere göre değişkenlik göstermekle birlikte (%0-73), genel seroprevalansı %6,3 olarak saptanmıştır

https://www.uptodate.com/contents/hepatitis-e-virus_infection?source=history_widget. Erişim tarihi: 03.02.2025

https://hsgm.saglik.gov.tr/depo/Yayinlarimiz/Programlar/Turkiye_Viral_Hepatit_Onleme_ve_Kontrol



Li P. The global epidemiology of hepatitis E virus infection: A systematic review and meta-analysis. *Liver Int.* 2020 Jul;40(7):1516-1528.

Hepatitis E Infection in Solid Organ Transplant Recipients in Turkey

Seval Ögüt¹, Ayça Arzu Sayiner¹, Barış Otlu², Gülendamar Bozdayı³, Aysın Zeytinođlu⁴, Sebahat Aksaray⁵, Dilek Çolak⁶, Selma Gökahmetođlu⁷, Murat Aysin⁸

ABSTRACT

Background: Hepatitis E virus infection in immunosuppressed patients receiving solid organ transplantation, especially kidney transplantation, is an emerging concern.

Methods: A total of 485 sera samples of solid organ recipients were collected from 7 transplantation centers in Turkey. Samples were tested for anti-hepatitis E virus (HEV) IgM, IgG, and HEV RNA. Risk factors were evaluated.

Results: Samples of 472 patients and 13 (2.7%) were positive for HEV IgM and/or HEV IgG, respectively. Seropositivity for HEV IgM was higher in the Central region.

Conclusion: This is the first prevalence study of hepatitis E virus infection in solid organ recipients in Turkey. Anti-hepatitis E virus immunoglobulin G prevalence was 17.3% which was higher than the previously reported rate in blood donors. Seropositivity was significantly higher in liver recipients. Despite the high antibody prevalence, none of the patients were viremic.

Keywords: Hepatitis antibodies, hepatitis E virus, kidney transplantation, liver transplantation, organ transplantation

7 SOT merkezinden 485 serum örneđinden

Anti HEV IgM, IgG, HEV RNA

Risk Faktörleri açısından bir anket

300 böbrek, 185 KC nakil hastası

IgM: 3 hasta (%0.3)

IgG: 84 (%17.3)

infection in immunosuppressed patients receiving solid organ transplantation, especially kidney transplantation, is an emerging concern.

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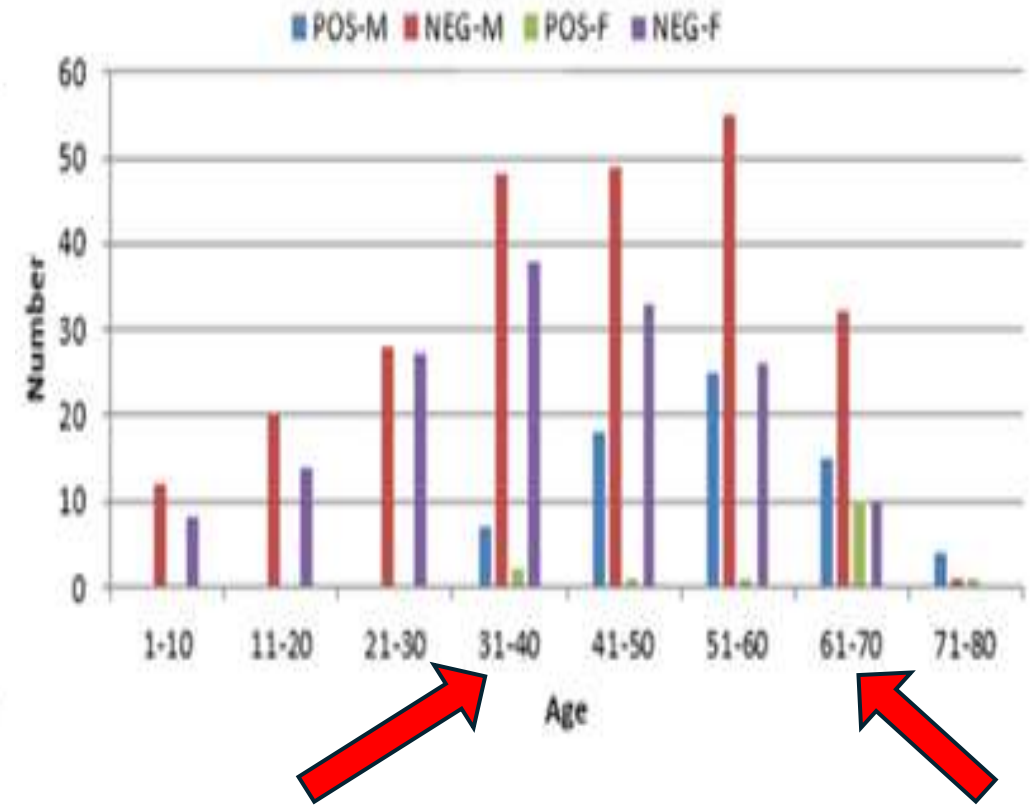
Hepatitis E Infection in Solid Organ Transplant Recipients in Turkey

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Region	Tested Samples (n)*	Anti-HEV IgG Positive Samples, n (%)
Central East Anatolia	28	12 (42.9)
Southeast Anatolia Region	51	15 (31.4)
Mediterranean Region	36	8 (22.2)
Aegean region	190	29 (15.3)
West Black Sea Region	15	2 (13.3)
İstanbul region	28	3 (10.7)
Central Anatolia Region	39	4 (10.3)
West Anatolia Region	66	6 (9.1)
Total	453	79 (17.4)

*Four regions with a number of patients lower than 10 and 5 patients living abroad are not shown on the table.

Anti-HEV IgG, anti-hepatitis E virus immunoglobulin G.



Ögüt S, Sayiner AA, Otlu B, et al. Hepatitis E infection in solid organ transplant recipients in Turkey. Turk J Gastroenterol. 2022; 33(1): 68-73.

Hepatitis E Infection in Solid Organ Transplant Recipients in Turkey

Seval Öğüt¹, Ayça Arzu Sayiner¹, Barış Otlu², Gülendam Bozdayı³, Aysin Zeytinoğlu⁴, Sebahat Aksaray⁵, Dilek Çolak⁶, Selma Gökahmetoğlu⁷, Murat Aysin⁸

Seropozitifliğin:

- İleri yaş
- Erkek cinsiyet
- Karaciğer alıcısı olma
- Hepatit B virüsü ve/veya hepatit C virüsü ile infekte olmak

Öğüt S, Sayiner AA, Otlu B, et al. Hepatitis E infection in solid organ transplant recipients in Turkey. Turk J Gastroenterol. 2022; 33(1): 68-73.

Epidemiology of hepatitis E virus in children in the province of Van, Turkey

Gülsüm İclal Bayhan¹, Kaan Demiören², Hüseyin Güdücüoğlu³

¹Department of Pediatrics, Pediatric Infection Clinic, Yüzüncü Yıl University School of Medicine, Van, Turkey

²Clinic of Gastroenterology, Dörtçelik Children's Hospital, Bursa, Turkey

³Department of Microbiology, Yüzüncü Yıl University School of Medicine, Van, Turkey

408 çocuk ve adölesanda (2 ay-18 yaş)

Abstract

Aim: Hepatitis E virus is an etiological agent of hepatitis which is transmitted enterically and may lead to water-borne outbreaks. Although it is mainly transmitted by the fecal-oral route, it is estimated that many cases are associated with zoonotic transmission in developing countries. In this study, we aimed to investigate the seroprevalence of hepatitis E in the childhood age group in the province of Van and to demonstrate the relationship between seroprevalence and demographic properties, residential house/region, water supply used at home, dealing with livestock and history of surgery.

Material and Methods: In this study, hepatitis E virus IgG antibody was studied by ELISA method in children aged between 2 months and 18 years between June 2014 and September 2014 in the province of Van.

Results: A total of 408 children and adolescents were enrolled in the study. Hepatitis E IgG was found to be positive in 4.2% of the subjects. 179 (43.8%) of the subjects were female and 229 (56.2%) were male. The mean age was 123 months±56.6 months (minimum 2 months, maximum 214 months). When the seropositivity rates were compared by age groups and gender, no difference was found. No correlation was found between hepatitis E seropositivity and the variables of residence, dealing with livestock and water resources. No correlation was found between anti-hepatitis E virus seropositivity and parental education level, number of cohabitants and history of surgery.

Conclusion: In our study, hepatitis E virus seropositivity was found to be lower compared to the mean seropositivity in Turkey. Hepatitis E infection does not constitute a serious problem in children in the province of Van in accordance with the results reported from different parts of our country. Livestock dealing and usage of well water are not considered risk factors for Hepatitis E infection. (Turk Pediatri Ars 2016; 51: 148-51)

Keywords: Adolescent, child, hepatitis E, Turkey, Van

The Prevalence of Hepatitis E Virus Infection in the Adult Turkish Population: A Systematic Review of the Literature and Prevalence Study in Blood Donors in Mersin Province

Orhan Sezgin¹, Serkan Yaraş¹, Seda Tezcan Ülger², Gönül Aslan², Eyyüp Naci Tiftik³

ABSTRACT

Background: The hepatitis E virus (HEV) is an RNA virus that causes acute hepatitis, and can become chronic in immunocompromised patients, though this is rare. The frequency of HEV infection varies, depending on factors such as geographical region, socioeconomic level, and age. Despite limited studies on the adult population in Turkey, there is no current information about HEV frequency in our country. Therefore, we aimed to determine the prevalence of HEV infection in blood donors in Mersin province.

Methods: A total of 900 voluntary blood donors from the Mersin Provincial Blood Center and accepted the use of their blood for research purposes. The data were enrolled in the study. The donors' location, occupation, and age were recorded. The prevalence of HEV infection was determined by enzyme-linked immunosorbent assays method. A systematic review of the literature on HEV infection, we evaluated the full text and conference abstracts published between 1990 and 2020, investigating the adult population.

Results: The average age of the donors was 32.8 years, and 889 (98.7%) were men. Anti-HEV IgG was positive in 12.8% of the seropositive was 40.40 ± 9.72 years, and 98.2% were men. No association was found between HEV IgG positivity and occupation, place of residence, and contact with animals. An evaluation of the studies conducted in Turkey reveals that the average HEV infection seroprevalence is 9.52% in the healthy population, and the prevalence is increased in the region of Southeastern Anatolia. Patients with acute hepatitis and hemodialysis also had increased rates.

Conclusion: The anti-HEV IgG seropositivity rate in healthy blood donors in Mersin province was 12.8%, and was similar to the rates reported earlier in our country. However, this rate, found in a sample of individuals from a healthy society, causes concern about what the frequency may be in sick people. Wide-ranging community screening is needed.

Keywords: Hepatitis E virus, anti-HEV IgG, Turkey, Mersin

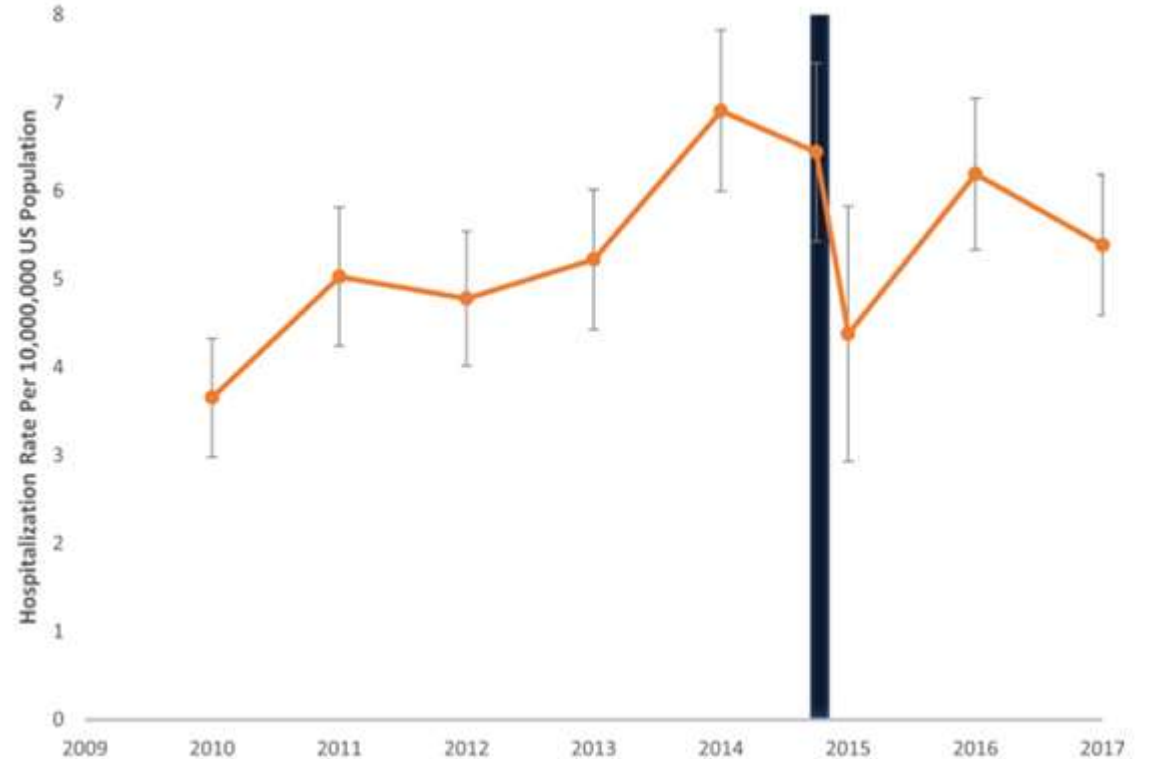
900 sağlıklı kan
bağışçısı
Anti HEV IgG
Yaş ortalaması 32
Anti HEV
seropozitifliği:

%12.8

Hepatitis E-Associated Hospitalizations in the United States: 2010–2015 and 2015–2017

Paul Wasuwanich^{1,2} | Thammasin Ingviya^{3,4} | Supharek Thawillarp⁵ |
Eyasu H. Teshale⁶ | Saleem Kamili⁶ | Jude P. Crino⁷ | Ann O. Scheimann¹ |
Cynthia Argani⁸ | Wikrom Karnsakul¹

- 2010 ve 2015 yıllarında ICD-9 ve ICD-10 koduna dayalı hospitalizasyonlar
- 2010 yılında 10 milyonda 3.7
- 2015 yılında 10 milyonda 6.4
- Hospitalize edilen hastalarda mortalite %4
- Kronik KC hastalığı üzerine akut KC yetmezliği oranı %9
- Maternal ya da fetal ölüm bildirilmemiş



Hepatitis E in Bangladesh: Insights From a National Serosurvey

Andrew S. Azman,^{1,2} Kishor Kumar Paul,³ Taufiqur Rahman Bhuiyan,³ Aybüke Koyuncu,¹ Henrik Salje,^{1,4} Firdausi Qadri,³ and Emily S. Gurley¹

Background. Hepatitis E virus (HEV) genotypes 1 and 2 are a major cause of avoidable morbidity and mortality in South Asia. Despite the high risk of death among infected pregnant women, scarce incidence data has been a contributing factor to global policy recommendations.

Methods. We conducted a national serosurvey in Bangladesh, identifying 70 districts and testing 2924 serum samples for anti-HEV IgG. We used logistic regression to estimate seroprevalence by age, sex, and district. We also examined the association between seroprevalence and demographic factors.

- Bangladeş'te 70 bölgeden örnekler
- 2924 serum örneğinden anti HEV IgG çalışılmış
- Ulusal seroprevelans %20
- İleri yaş, erkek cinsiyette seropozitiflik oranı yüksek

Conclusions. Hepatitis E infections are common throughout Bangladesh. Strengthening surveillance for hepatitis E, especially in urban areas, can provide additional evidence to appropriately target interventions.

Keywords. hepatitis E; hepatitis E virus (HEV); seroprevalence.

Bulaşma Yolları

1. HEV genotip 1 ve 2 enfeksiyonları, endemik bölgelerde dışkıyla kontamine olmuş su yoluyla yayılır

2. HEV genotipleri 3 ve 4 genellikle kontamine gıda tüketimi nedeniyle enfeksiyonlara neden olur



Vertikal bulaşma



Khuroo MS, Khuroo MS, Khuroo NS. Transmission of Hepatitis E Virus in Developing Countries. *Viruses*. 2016; 8(9):253.

Klinik Tablo

Akut HEV infeksiyonu

- İnkübasyon süresi 15-60 gün
- Genellikle asemptomatik ya da hafif semptomatik
- %5-30 ikterik hepatit tablosu
- Halsizlik, yüksek ateş, kas eklem ağrısı, bulantı, kusma 1. hafta görülebilir
- Koyu renkli idrar ve sarılık

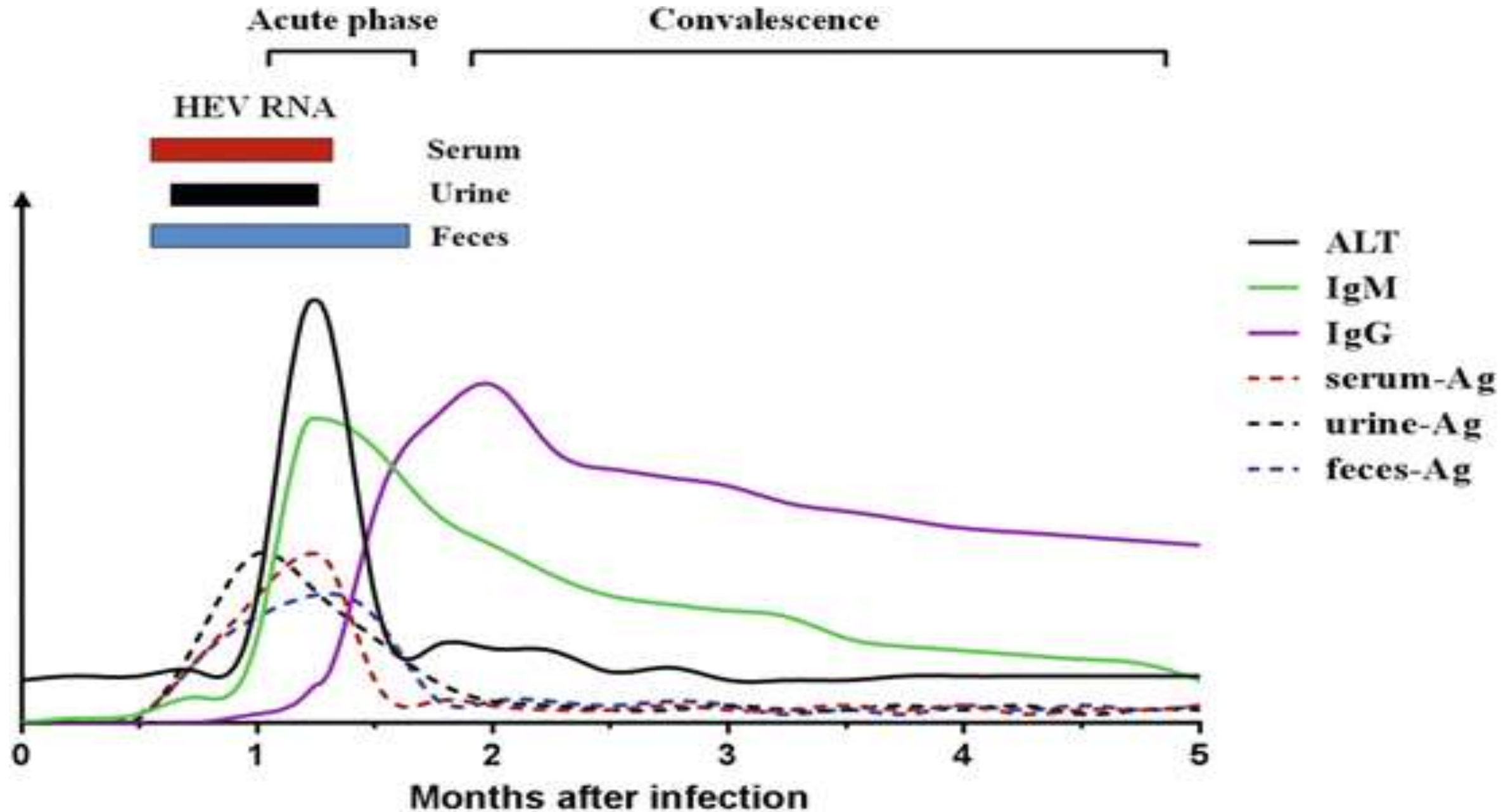
Klinik Tablo

Ekstrahepatik Bulguları

- Trombositopeni, hemoliz ve aplastik anemi dahil hematolojik anormallikler
- Akut tiroidit
- Membranöz glomerülonefrit
- Akut pankreatit

Nörolojik hastalıklar:

- Akut transvers miyelit
- Akut meningoensefalit
- Aseptik menenjit
- Nöraljik amiyotrofi
- Psödotümör serebri
- Bilateral piramidal sendrom
- Guillain-Barré sendromu
- Kranial sinir felçleri
- Periferik nöropati
- Myasthenia gravis



Klinik tablo (Komplikasyonlar)

Akut Hepatik Yetmezlik

- Akut HEV li hastaların %0.5-4 ünde görülür
- Özellikle gebelik ve malnütrisyonunda görülme oranı yüksek
- Hepatik ensefalopati
- Aminotransferazlarda yükseklik (bilirubin ve alkalen fosfataz dahil)
- INR > 1.5
- YBÜ desteği ve KC nakli olmadığı durumlarda mortalite %3

Role of Hepatitis E Virus Infection in Acute-on-Chronic Liver Failure

Mario Frias , Pedro López-López , Antonio Rivero, and Antonio Rivero-Juarez 

Country	Region/City	Population	Number of patients	Cases of decompensation due to HEV infection, n (%)
ASIA				
India	New Delhi	Cirrhotic patients with liver decompensation	CHD = 31 ACLF = 42	CHD = 6 (19.3%) ACLF = 21 (50%)
India	Lucknow	ACLF patients	121	80 (66.1%)
India	New Delhi	ACLF patients	91	14 (15.3%)
India	New Delhi	ACLF patients	48	7 (14.5%)
India	New Delhi	CHBV patients with acute hepatitis	43	8 (18.6%) ¹
India	New Delhi	Cirrhotic patients with liver decompensation	10	10 (100%)
India	Vellore	ACLF patients	9	9 (100%)
India	New Delhi	CHBV patients with liver decompensation	72	6 (8.3%)
India	Jaipur	ACLF patients	52	5 (9.6%)
India	Chandigarh	ACLF patients	100	8 (8%)
India	Chandigarh	ACLF patients	102	4 (3.9%)
India	Lucknow	ACLF pediatric patients	36	23 (63.8%)
India	Chandigarh	ACLF patients	31	3 (9.6%)
China	Guangzhou	CHBV infected with HEV infection	136	54 (39.7%)
China	Guangzhou	ACLF patients	107	80 (74.7%)
China	Shanghai	ACLF patients	301	34 (11.3%)
Bangladesh	Dhaka	ACLF patients	69	15 (21.7%)

Klinik tablo (Komplikasyonlar)

Kolestatik hepatit

- 3 aydan uzun süren sarılık
- Hastaların %60 ına kadar görülebilir
- Asemptomatik ya da kolestaza bağlı kaşıntı
- Genellikle haftalar içinde spontan geriler sekel bırakmaz
- İyileşme viral klerens, Anti HEV IgG düzeyinde yükselme, IgM düzeyinde gerileme

Klinik tablo (Komplikasyonlar)

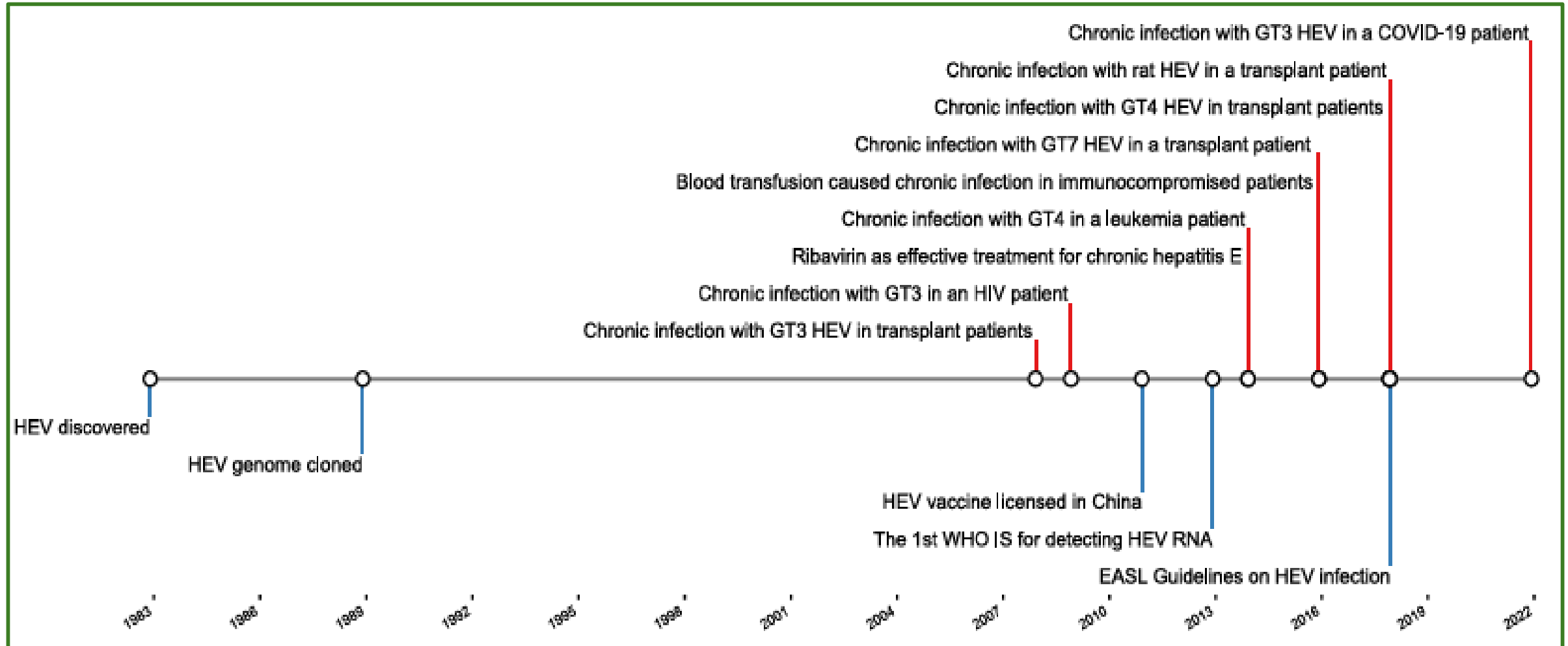
Kronik Hepatit E

- Serum ya da gayta örneğinde 3 aydan uzun süren HEV RNA pozitifliği
- Genellikle HIV infeksiyonu, solid organ nakli, ya da kemik iliği nakli alıcılarında
- Genellikle Genotip 3 te görülür; 4 ve 7 ile de bildirilmiş olgu serileri mevcut
- Genotip 1 ve 2 ile olgu bildirilmemiş



Chronic hepatitis E: Advancing research and patient care

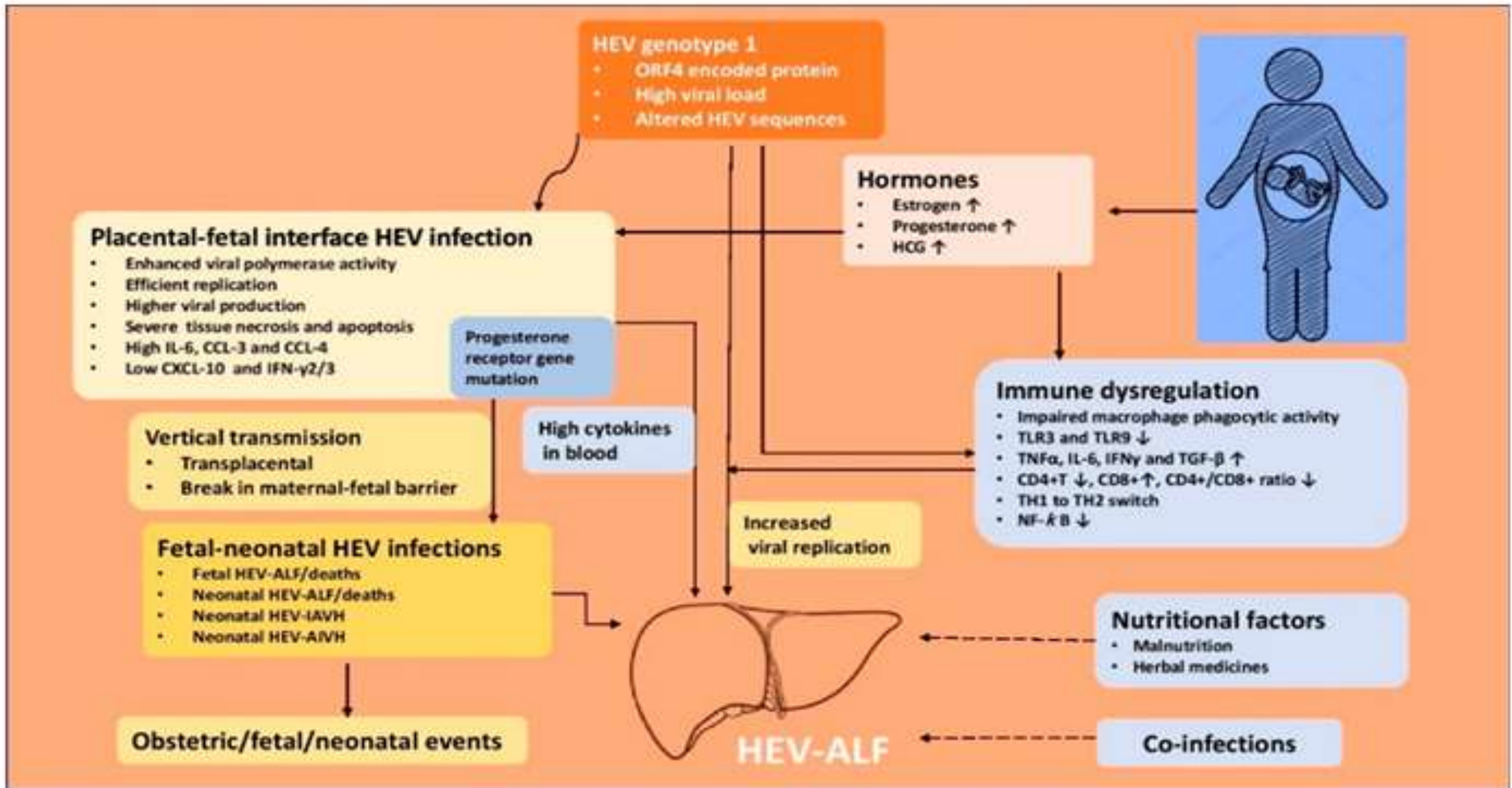
Zhongren Ma¹, Robert A. de Man², Nassim Kamar³, Qiuwei Pan^{2,*}



Özel Hasta Grubu

Gebelik

- HEV infeksiyonunun endemik olduğu bölgelerde akut KC yetmezliği gebelerde görülebilir
- Üçüncü trimesterde hepatik yetmezlik oranı daha fazla (%15-25)
- Nutrisyonel durumu kötü olan hastalarda prognoz daha kötü



A 5-year Single-Center Experience of Hepatitis E Virus Infection During Pregnancy



Rahul Karna*, Rajib K. Hazam*, Jayanta Borkakoti*, Ashok Kumar†, Premashis Kar*

*Department of Medicine, Maulana Azad Medical College, University of Delhi, New Delhi and †Department of Obstetrics and Gynaecology, Maulana Azad Medical College, University of Delhi, New Delhi

Table 1 The Comparative Analysis of Biochemical and Clinical Parameters in Patients With AVH and ALF.

Parameters	AVH pregnant (411)	AVH nonpregnant (357)	P value	ALF pregnant (139)	ALF nonpregnant (181)	P value
Hb	9.30 ± 3.11	11.21 ± 1.91	<0.001	10.42 ± 2.02	8.74 ± 2.21	<0.001
ALT IU/dl	471.18 ± 369.85	486.62 ± 502.81	0.62	806.31 ± 574.91	1124.00 ± 458.00	<0.001
AST IU/dl	557.82 ± 421.63	545.43 ± 615.64	0.74	663.15 ± 351.77	803.00 ± 375.00	<0.001
TBil	6.90 ± 2.32	5.70 ± 2.41	<0.001	11.75 ± 3.82	13.62 ± 7.34	<0.001
ALP	156.81 ± 142.82	187.23 ± 122.16	<0.001	247.5 ± 262.3	296.3 ± 322.3	<0.14
Fever	319 (77.6%)	197 (55.2%)	<0.001	124 (89.2%)	64 (35.3%)	<0.001
Pruritus	140 (34.1%)	153 (42.9%)	0.15	82 (59%)	95 (52.5%)	0.29
Anorexia	389 (94.6%)	313 (87.7%)	<0.001	139 (100%)	128 (70.7%)	<0.001
Pedal edema	335 (81.5%)	110 (30.8%)	<0.001	117 (84.2%)	85 (46.9%)	<0.001
IUD	103 (25.1%)	NA	NA	120 (86.33%)	NA	NA
Maternal mortality	13 (3.16%)	0	<0.001	116 (83.45%)	30 (16.6%)	<0.001
Preterm delivery	173 (42.1%)	NA	NA	102 (73.4%)	NA	NA

AVH, acute viral hepatitis; ALF, acute liver failure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; ALP, alkaline phosphatase; IUD, intrauterine death; NA, non applicable; hb, hepatitis B.

A 5-year Single-Center Experience of Hepatitis E Virus Infection During Pregnancy



Rahul Karna*, Rajib K. Hazam*, Jayanta Borkakoti*, Ashok Kumar†, Premashis Kar*

*Department of Medicine, Maulana Azad Medical College, University of Delhi, New Delhi and †Department of Obstetrics and Gynaecology, Maulana Azad Medical College, University of Delhi, New Delhi

Table 3 Prevalence of Hepatotropic Viruses in ALF.

Viral markers	ALF pregnant (139)	ALF nonpregnant (181)	P value
HAV IgM	5 (3.6%)	5 (2.76%)	0.91
HBsAg	13 (9.35%)	28 (15.47%)	0.14
Anti-HCV	1 (0.72%)	2 (1.10%)	0.81
HEV IgM	102 (73.38%)	111 (61.32%)	0.03
Non-A-E	18 (12.94%)	35 (19.34%)	0.17

Table 2 Prevalence of Hepatotropic Viruses in AVH.

Viral markers	AVH pregnant (411)	AVH nonpregnant (357)	P value
HAV IgM	13 (3.16%)	44 (12.32%)	<0.001
HBsAg	39 (9.48%)	77 (21.56%)	<0.001
Anti-HCV	11 (2.67%)	7 (1.96%)	0.67
HEV IgM	340 (82.72%)	155 (43.41%)	<0.001
Non-A-E	8 (1.94%)	74 (20.72%)	<0.001

AVH, acute viral hepatitis; HAV IgM, hepatitis A virus immunoglobulin M; HBsAg, hepatitis B's antigen; HCV, hepatitis C virus; HEV IgM, hepatitis E virus immunoglobulin M; non-A-E, non-adverse events.

Pregnancy mortality (129)

	AVH ¹³	ALF (116)	Total	P value
HEV	9	89	98	<0.001
Non-HEV	4	27	31	

Özel Hasta Grubu

Solid Organ Nakli

- Solid organ nakli hastalarında kronik HEV enfeksiyonu sıklığı fazladır
- Nakil sonrası kronikleşme oranı %70 e kadar yüksek oranlarda
- Kronik enfeksiyonlardan genellikle HEV spesifik T lenfosit yanıtındaki bozulma
- Kronik hepatit, daha düşük lenfosit ve CD2, CD3 ve CD4 T hücre sayısı
- Takrolimus kullanımı; HEV enfeksiyonunda tanı anında düşük trombosit sayısı; daha genç yaş; ve karaciğer nakli
- Nakil alıcılarında kronik KC hastalığında hızla siroza ilerleme

Ayırıcı Tanı

İnfeksiyöz: Hepatit A virüsü enfeksiyonu
Akut veya kronik hepatit B virüsü enfeksiyonu
Kronik hepatit C enfeksiyonu
Akut veya kronik hepatit D enfeksiyonu
Herpes simpleks virüsü enfeksiyonuna bağlı hepatit
Epstein-Barr virüsü enfeksiyonuna bağlı hepatit
Sitomegalovirüs enfeksiyonuna bağlı hepatit

Toksik Alkolik hepatit
Asetaminofen toksisitesi
İlaç kaynaklı karaciğer hasarı/kendine özgü ilaç reaksiyonları
Toksin kaynaklı hepatit (örneğin mantar zehirlenmesi, karbon tetraklorür)

Metabolik Non-Alkolik steatohepatit
Otoimmün hepatit
Wilson hastalığı
Hereditör hemokromatozis
Alfa-1 antitripsin eksikliği

Diğer İskemik hepatit
Budd-Chiari sendromu
HELLP Gebelikte akut yağlı karaciğer

Tedav

i

- Hastanın immünitesi ve infeksiyonun evresine göre değişir

Akut HEV infeksiyonu:

- Hafif ve kendi kendini sınırlayan immunokompetan hastalarda destek tedavisi
- Progrese olursa KC nakli
- Gebelerde ve kronik KC hastalığı olanlarda mortal seyredebilir
- Ribavirin...
- Kortikosteroid....

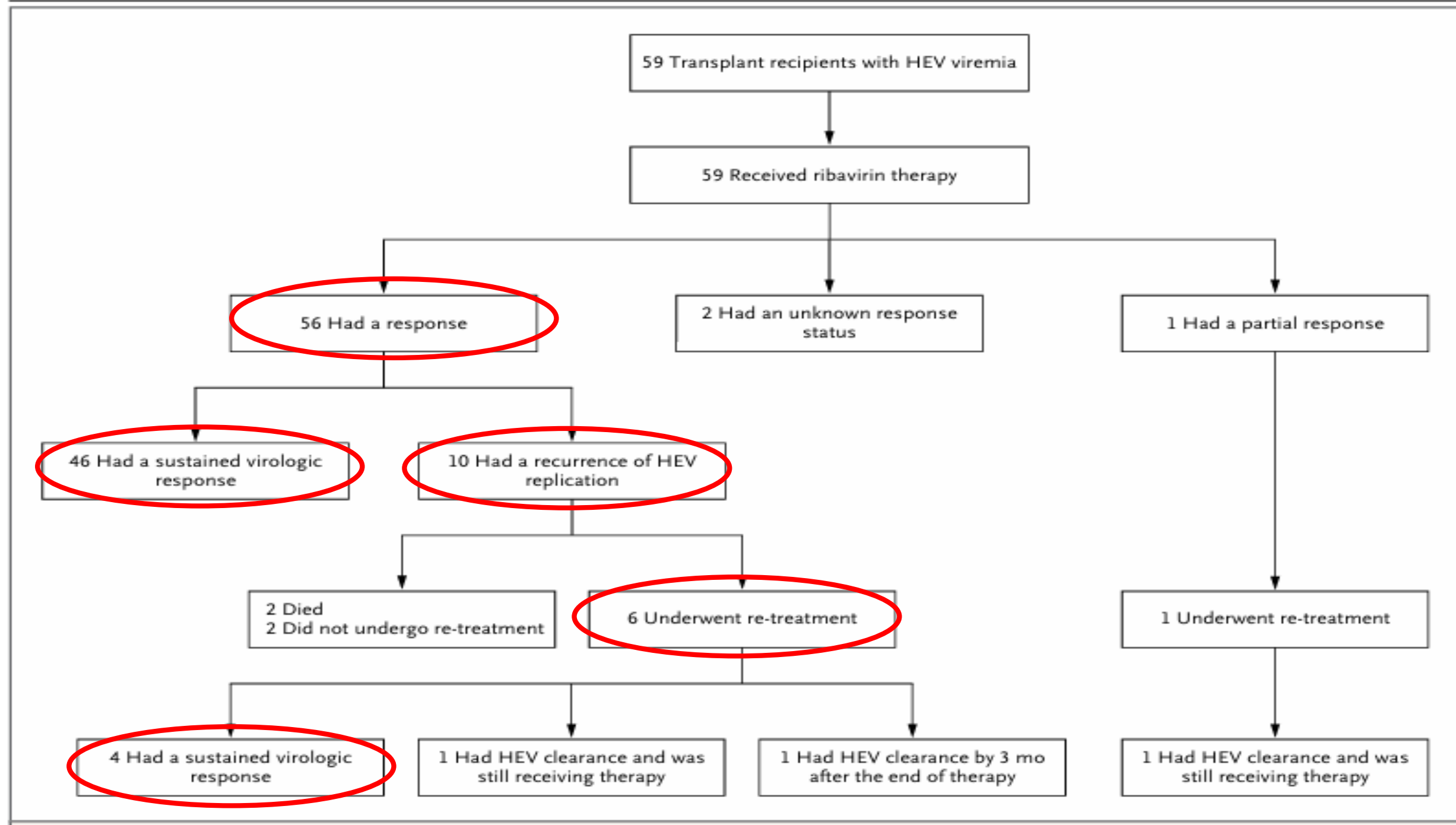
Tedav i

- Kronik HEV infeksiyonunda ilk basamak tedavi planı özellikle T lenfositleri hedefleyen immunosüpresif tedavileri azaltmak
- Hastaların üçte birinde viral klerens sağlanabilir
- Pegile interferon-alfa, ribavirin veya iki ilacın kombinasyonu ile tedavi edilebilir
- Sofosbuvir...

**Ribavirin for Chronic Hepatitis E
Virus Infection in Transplant Recipients**

Nassim Kamar, M.D., Ph.D., Jacques Izopet, Pharm.D., Ph.D., Simona Triponi, M.D.,

- Retrospektif, çok merkezli çalışma
- Uzamış HEV viremisi olan hastalarda ribavirinin etkinliğinin değerlendirilmesi
- 59 hasta (37 böbrek, 10 karaciğer, 5 kalp, 5 böbrek ve pankreas ve 2 akciğer)
- Ribavirin tedavisi, HEV enfeksiyonunun tanısından 9 ay sonra başlatıldı
- Hastalar medyan 3 ay boyunca ribavirin aldı
- %66'sı 3 ay veya daha fazla süreyle
- 54 hasta genotip 3





Sofosbuvir monotherapy fails to achieve HEV RNA elimination in patients with chronic hepatitis E – The HepNet SofE pilot study

Table 1. Baseline characteristics and medical history (organ transplantation and immunosuppressive medication).

Patient	P1	P2	P3	P4	P5	P6	P7	P8	P9	Mean ± SD, or median (IQR)
Age (years)	37	61	42	47	30	60	36	59	24	44.0 ± 13.7
Sex	Female	Male	Female	Male	Female	Male	Male	Male	Male	
Duration of infection (months)	14	58	17	3	5	25	44	89	7	29.1 ± 29.13
HEV RNA (IU/ml)	80,000	350,000	580,000	4,800,000	4,600,000	160,000	474,000	805,000	1,000,000	6E ⁵ (8E ⁴ –5E ⁶)
HEV genotype	3c	3c	3c	3 (na)	3c	3l	3c	3c	3c	
ALT (IU/L)	38	139	148	624	123	91	50	126	430	126 (38–624)
AST (IU/L)	33	88	81	349	72	88	41	93	238	88 (38–624)
Bilirubin (μmol/L)	5.0	6.0	8.6	5.1	6.8	10.3	6.0	10.6	19.0	6.8 (5–19)
Creatinine clearance (ml/min)	36.0	56.0	93.7	46.8	53.7	52.3	63.5	77.5	44.5	53.7 (36–93.7)
INR	1.0	0.9	1.0	0.9	1.0	1.1	1.0	1.1	1.2	1 (0.9–1.16)
Platelets (10 ³ /μl)	175	142	160	231	221	188	467	251	81	188 (81–467)
Fibroscan at screening LSM/IQR (kPa)	11.9/1.9	10.8/1.3	5.2/0.9	7.1/0.8	6.8/1.8	17.0/1.5	4.3/0.7	9.5/2.4	12.8/3.6	9.5 (4.3–17.0)
APRI score	0.5	1.2	1.4	3.0	0.9	0.9	0.2	0.7	5.9	
Cirrhosis ^a	No	Yes	Yes	No	No	Yes	No	No	Yes	
Duration of previous ribavirin therapy (days)	181	1,170 ^b	180	Contra-indication ¹	Contra-indication ²	567	450	1,380	126	
Mean dose of previous ribavirin (mg/d)	300	500	450	Contra-indication ¹	Contra-indication ²	200	800	800	250	
Response to previous RBV therapy	RL	RL NR	RL	Contra-indication ¹	Contra-indication ²	RL	NR	NR	NR	
Immune suppressive condition	Heart, kidney Tx	Kidney, kidney Tx	Stem cell Tx	Heart Tx	Kidney, pancreas Tx	Heart Tx	Multi-visceral	Kidney	CVID	
Immunosuppressive regimen										
Cortisone	x	x		x	x	x		x	x	
Everolimus/sirolimus	x			x	x	x	x			
Tacrolimus	x	x		x	x		x	x		
Mycophenolate mofetil		x		x		x		x		



Sofosbuvir monotherapy fails to achieve HEV RNA elimination in patients with chronic hepatitis E – The HepNet SofE pilot study

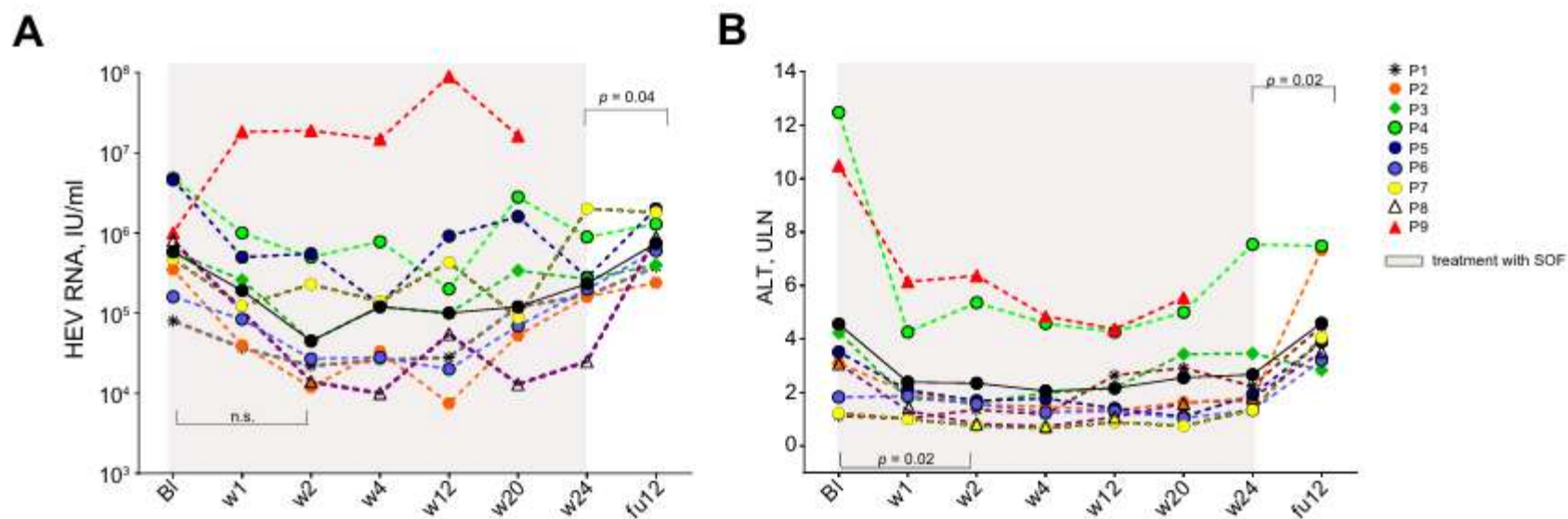
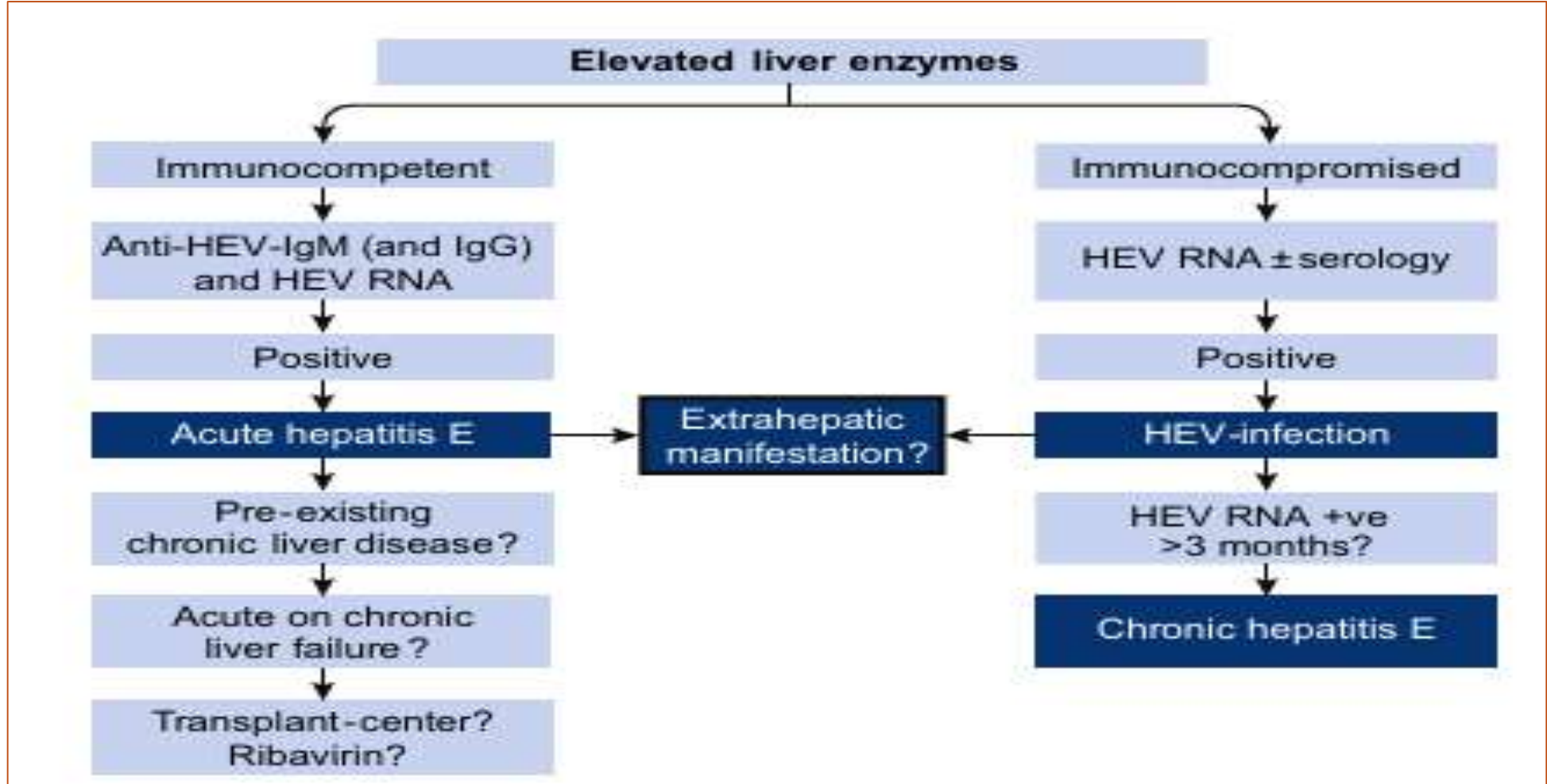


Fig. 1. Virological and biochemical response. (A) Individual and median HEV RNA (black line) from baseline until follow-up 12 weeks after the end of treatment. HEV RNA decreased between baseline and week 2 (not significant) and increased significantly after the end of treatment ($p = 0.04$ paired t test). (B) Individual and mean ALT (black line) values depicted as ULN. ALT decreased significantly between baseline and week 2 ($p = 0.02$ paired t test) and increased again after end of treatment ($p = 0.02$ paired t test). Treatment with the study medication (24 weeks sofosbuvir) is indicated in light grey in (A) and (B). ALT, alanine aminotransferase; ULN, upper limit of normal. (This figure appears in color on the web.)



EASL Clinical Practice Guidelines on hepatitis E virus infection[☆]

European Association for the Study of the Liver*





EASL Clinical Practice Guidelines on hepatitis E virus infection[☆]

European Association for the Study of the Liver*

- Akut hepatit tablosu olan bireylere HEV taraması (A1)
- Kronik KC hastalığı üzerine hepatik alevlenme olan hastalara HEV taraması (C2)
- Anormal KCFT si olan bütün immunosüpresiflere HEV taraması (A1)
- Kan ürünü alan hastalarda anormal KCFT varsa HEV taraması (A1)
- Akut Hepatit E tablosu ağır seyreden ya da kronik hepatit üzerine HEV infeksiyonlarında Ribavirin (C2)



EASL Clinical Practice Guidelines on hepatitis E virus infection[☆]

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- Solid organ nakil alıcılarında kronik HEV infeksiyonunda öncelikle mümkün ise immunosüpresiflerin azaltılması (B1)
- HEV RNA tespitinden 3 ay sonra pozitiflik devam eden hastalarda 12 haftalık ribavirin monoterapisi (B1)
- Serum ve dışkıda HEV RNA negatifleştikten sonra tedavi kesilebilir (B1)
- 12 haftadan sonra serumda ve/veya dışkıda HEV RNA'sı hala tespit edilebilen hastalarda, ribavirin monoterapisine ek üç ay daha devam edilebilir (toplamda altı aylık tedavi) (c2)
- Ribavirin'e yanıt vermeyen karaciğer nakli alıcıları PEG-interferon-a tedavisi düşünülebilir (C2)

Korunma ve Kontrol

- HEV'in endemik olduđu bölgelere (örneğin Asya, Afrika, Orta Doğu ve Orta Amerika) seyahat edenler, seyahat ishâlinin önlenmesi için kullanılan genel önlemleri takip etmelidir
- Saflığı bilinmeyen sudan, sokak satıcılarından alınan yiyeceklerden, çiğ veya az pişmiş deniz ürünlerinden, et veya domuz ürünlerinden ve çiğ sebzelerden kaçınmak
- Avrupa'ya seyahat edenler ayrıca, uygun şekilde ısıtılmamış çiğ ve az pişmiş domuz/yaban domuzu sosisi veya diğer vahşi hayvan etlerinden (örneğin tavşan) kaçınmalıdır

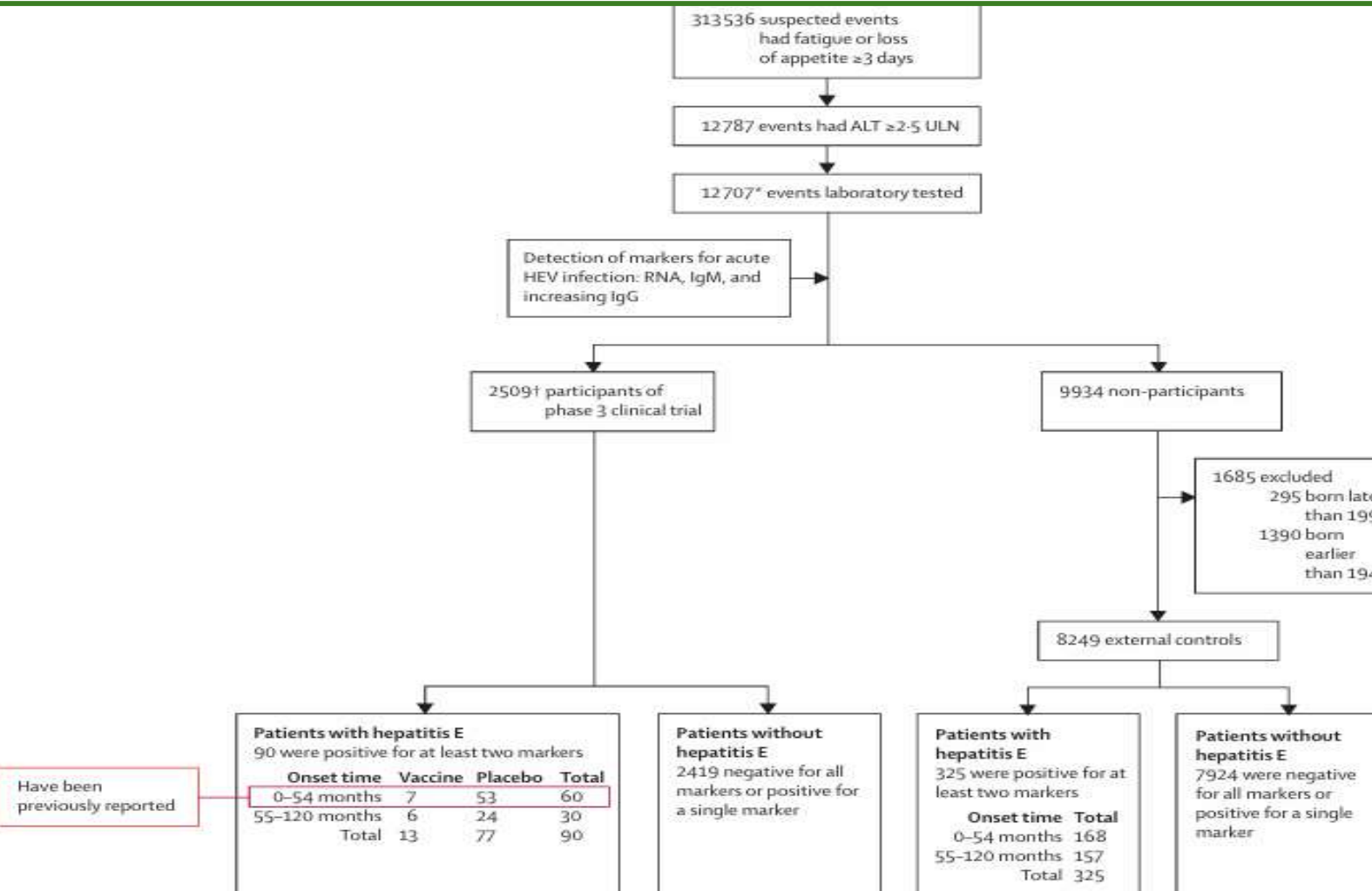
Korunma ve Kontrol

- Rekombinant aşılar HEV'e karşı etkililik göstermiştir
- Çin'de yapılan bir randomize çalışmada, 112.604 sağlıklı yetiştine üç doz HEV rekombinant aşısı
- Aşılamadan sonraki 12 aylık dönemde HEV'e karşı koruyucu etkinliği %96
- İlk aşılamadan 4,5 yıl sonra aşı etkinliği %87 idi
- Çin'de lisanslıdır

Long-term efficacy of a recombinant hepatitis E vaccine in adults: 10-year results from a randomised, double-blind, placebo-controlled, phase 3 trial



Shoujie Huang*, Xuefeng Zhang*, Yingying Su*, Chunlan Zhuang*, Zimin Tang*, Xingcheng Huang, Qi Chen, Kongxin Zhu, Xiaowen Hu, Dong Ying, Xiaohui Liu, Hanmin Jiang, Xia Zang, Zhongze Wang, Changlin Yang, Donglin Liu, Yijun Wang, Quan Tang, Wentong Shen, Huanhuan Cao, Huirong Pan, Shengxiang Ge, Yue Huang, Ting Wu†, Zizheng Zheng†, Fengcai Zhu†, Jun Zhang†, Ningshao Xia†

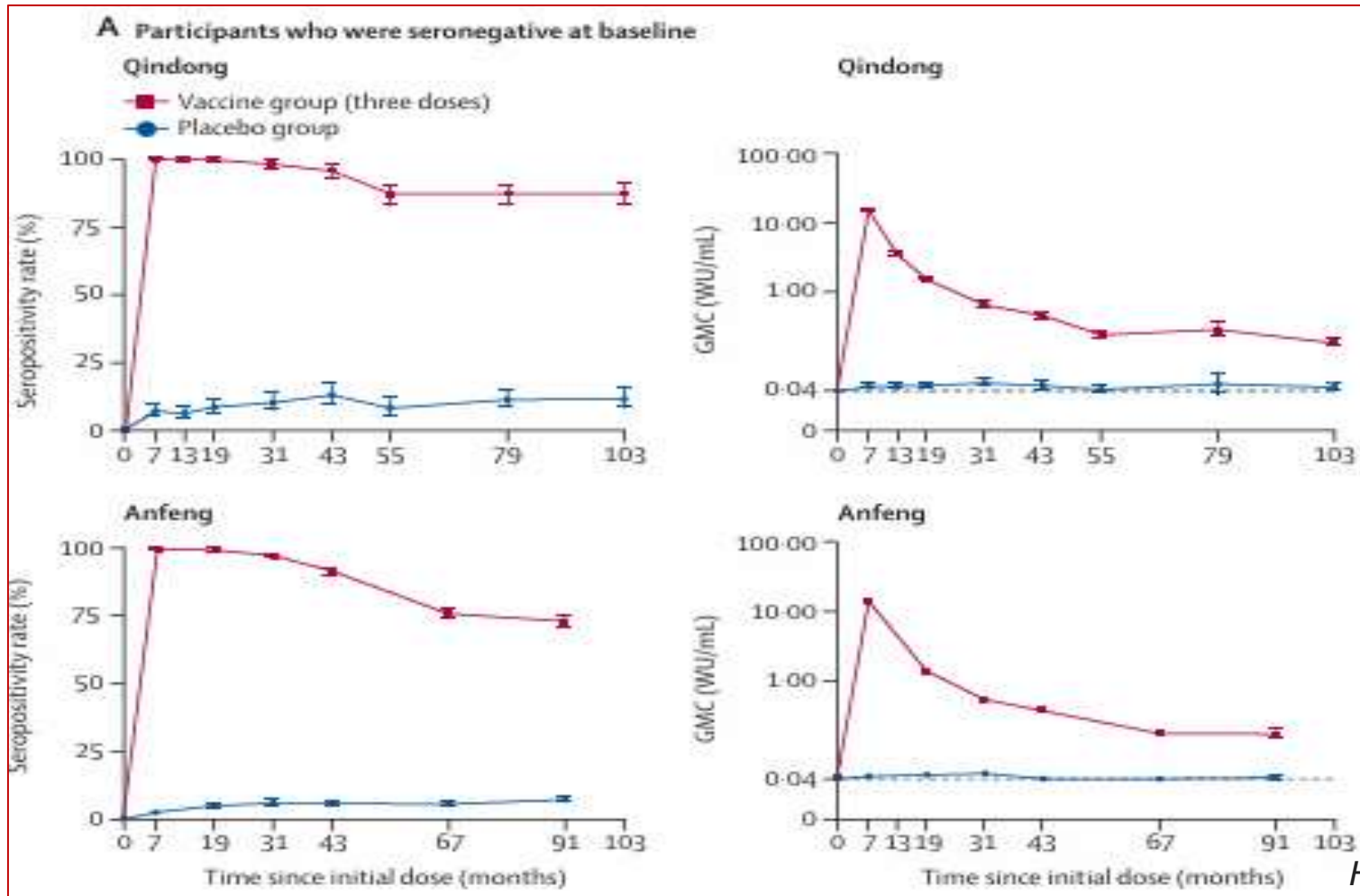


- Randomize çift kör, plasebo kontrollü, faz 3
- İlk çalışmaya 112 604 katılımcı dahil oldu
- 0,1,6. aylarda HEV aşısı
- 10 yıllık süreçte 90 hastada HEV infeksiyonu gelişti
- 13 aşı grubunda, 77 plasebo grubunda

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- Seronegatif bireylerde 7.5 yıl sonunda %87 (Qindong)
- Anfeng 8.5 yıl sonunda (%73)

Long-term efficacy of a recombinant hepatitis E vaccine in adults: 10-year results from a randomised, double-blind, placebo-controlled, phase 3 trial



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	Vaccine group (n=13)	Placebo group (n=77)	External control* (n=325)	Vaccine group vs placebo group, p value	Vaccine group vs external control, p value
Age at onset of hepatitis E in years, median (IQR)	54.0 (43.0-58.0)	57.0 (48.0-63.0)	55.0 (47.0-63.0)	0.15	0.20
Sex, number of participants					
Male	7	51	221	0.58	0.44
Female	6	26	104
HEV genotype, number of participants					
Genotype 1	1	2	6	0.28	0.26
Genotype 4	3	34	89
Coinfection, number of participants					
Positive HAV IgM	0	2	8	>0.99	>0.99
Positive HBsAg	3	17	76	>0.99	>0.99
Positive HBcAb	2	4	35	0.45	0.94
Positive HCV IgG	0	1	0	>0.99	NA
Peak alanine aminotransferase, † GM (SD), multiples of the ULN	8.8 (2.9)	22.9 (2.7)	16.5 (3.2)	0.0020	0.056
Length of symptomatic course in days, median (IQR)	35.0 (22.0-43.0)	45.0 (34.0-62.0)	43.0 (25.0-69.0)	0.038	0.18
Peak concentrations of IgM antibodies against HEV, GM (95% CI), signal to cutoff	4.1 (2.2-7.3)	8.7 (7.4-10.1)	5.8 (5.2-6.5)	0.0010	0.22
Peak concentrations of IgG antibodies against HEV in WU/mL, GMC (95% CI)	11.9 (2.4-60.6)	61.0 (41.9-88.7)	27.4 (21.3-35.2)	0.053	0.21
Avidity of IgG antibodies in samples obtained during the acute phase, ‡ median (IQR)	69.8% (49.4-82.4)	5.5% (1.6-9.8)	NA	<0.0001	NA

- Pik ALT dizeyleri ortalaması plasebo grubunda daha yüksek
- Semptomatik gün sayısı plasebo grubunda daha fazla
- IgG avidite düzeyi aşı grubunda daha yüksek

Sonuç...

- Gelişmekte olan su kaynaklı epidemilere neden olmakta ve daha çok Genotip 1,2 infeksiyonları
- Gelişmiş ülkelerde sporadik olgular şeklinde Genotip 3 ve 4'e bağlı zoonotik gıda kaynaklı (özellikle domuz eti) infeksiyonlar
- Gebelikte özellikle 2.-3. trimesterde hormonal ve immunolojik nedenlere bağlı fulminan hepatit gelişme ve ölüm oranı yüksek
- İmmünespresif tedavi alan ve solid organ alıcılarında özellikle HEV Genotip 3 infeksiyonları kronikleşebilmektedir
- Ribavirin tedavisi rehberlerde bulunuyor
- İmmün yeterli bireylerde akut hepatit E için yalnızca semptomatik tedavi yeterli
- Rekombinant aşıda uzun dönem sonuçları iyi

