

HIV/COVID-19 Koenfeksiyonu

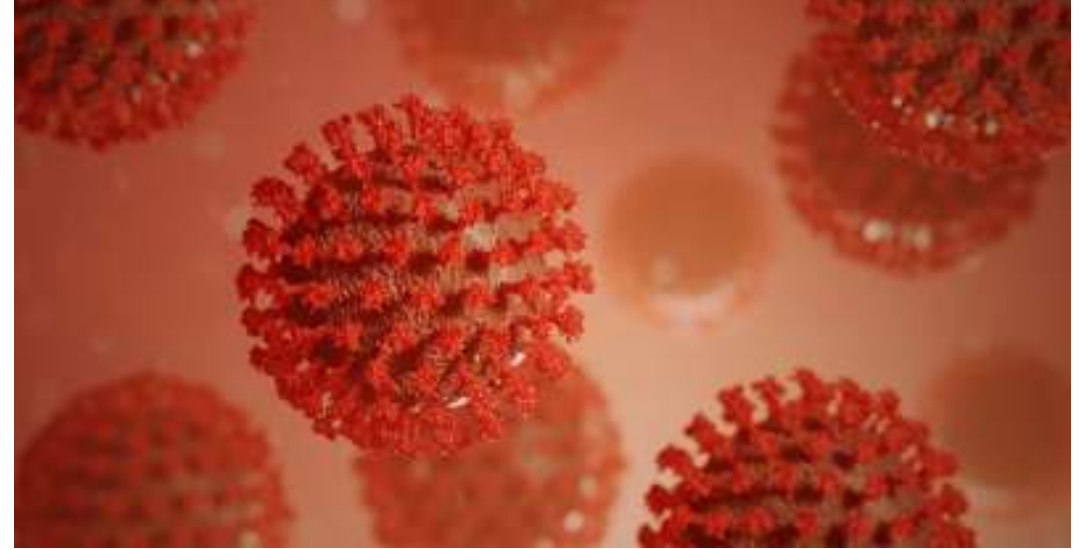
Dr. Alper Gündüz

Başakşehir Çam ve Sakura Şehir
SUAM

Enfeksiyon Hastalıkları ve Klinik
Mikrobiyoloji Kliniği

Zaman çizelgesi: Koronavirüsler

Virüs	Konak	Ortaya Çıkma
HCoV-NL63	İnsan	500-800 yıl
HCoV-229E	İnsan	200-300 yıl
HCoV-OC43	İnsan	~120 yıl
PEDV	Domuz	~25 yıl
PRRSV	Domuz	~25 yıl
rBCoV	Sığır	~25 yıl
SARS-CoV	İnsan	~16 yıl
MERS-CoV	İnsan	~7 yıl
SADS-CoV (HKU2)	Domuz	~2 yıl
SARS-CoV 2	İnsan	~7 ay



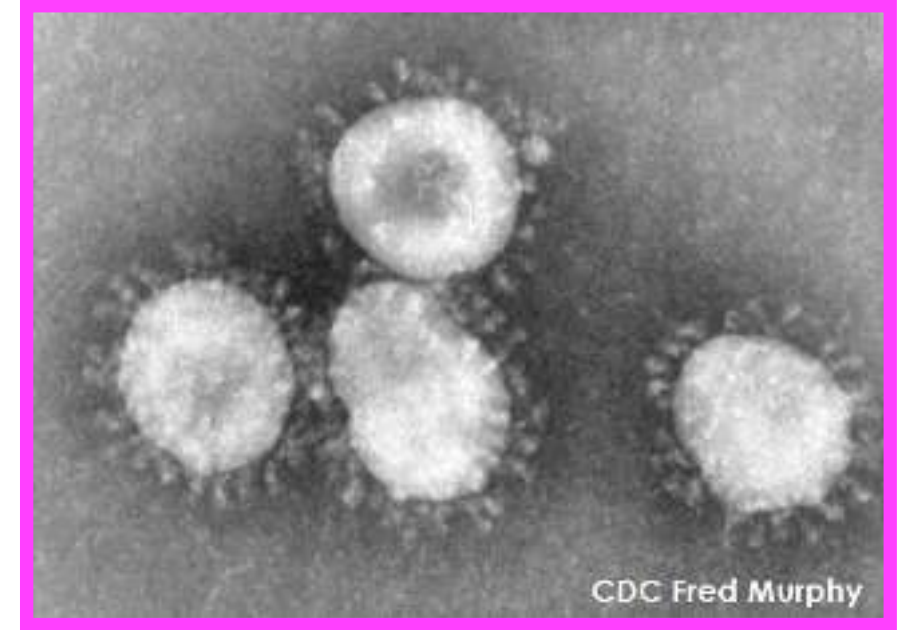
21. Yüzyılda
Türler arası geçiş hızlanmıştır

İnsan Koronavirüsleri (HCoV)

▪ Yaygın HCoVs (Düşük patojenite):

- HCoV-229E(alpha)
- HCoV-NL63(alpha)
- HCoV-OC43(beta)
- HCoV-HKU1(beta)

**Hafif Solunum Yolu
Enfeksiyonları**



▪ 21. Yüzyıl HCoVs (Yüksek patojenite):

- SARS-CoV(beta)
- MERS-CoV(beta)
- **SARS-CoV-2*(beta)**



Lai & Holmes, Fundamental Virology, 4th Edition 2001.

Epidemiyoloji

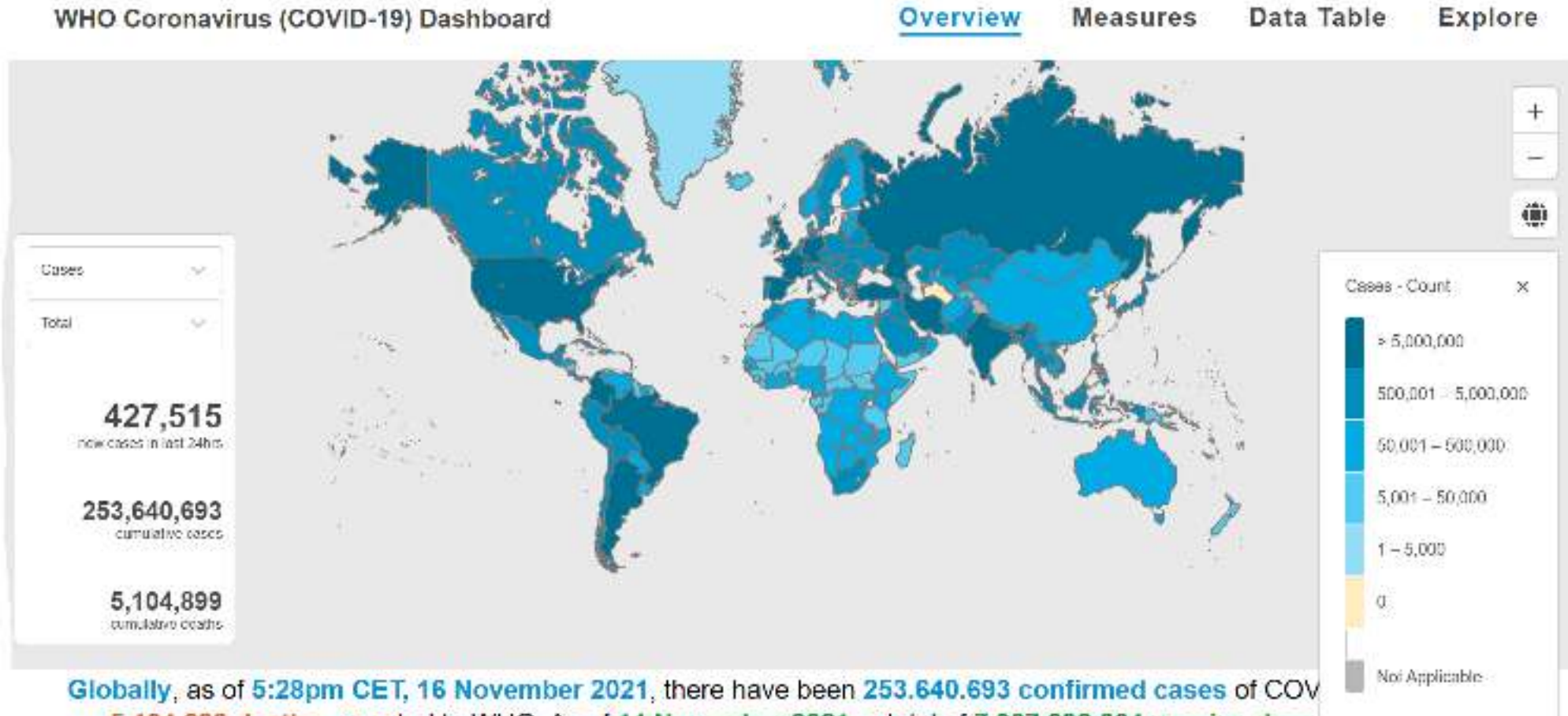
- **31 Aralık 2019 DSÖ:**
 - Çin Ülke Ofisi, Çin'in Hubei eyaletinin Wuhan şehrinde
 - Etiyolojisi bilinmeyen pnömoni vakalarını bildirimini
 - Wuhan Güney Çin Deniz Ürünleri Şehir Pazarında (farklı hayvan türleri satan bir toptan balık ve canlı hayvan pazarı) çalışanlarda kümelenme
- **7 Ocak 2020 Etkenin Tanımlanması:**
 - Daha önce insanlarda tespit edilmemiş
 - Yeni bir coronavirus olarak tanımlanmış
- **11 Mart 2020:**
 - Türkiye'de ilk vaka
 - DSÖ Pandemi ilan ediyor



Yeni Coronavirüs (SARS- CoV-2)

- Beta-coronavirus ailesi: SARS-CoV ve MERS-CoV da aynı aile içinde yer almakta olup ciddi solunum yetmezliği oluşturan virüslerdir.
- Fatalite hızı
 - SARS salgınında %11
 - MERS-CoV'da %35-50
 - 2019-nCoV %0,6-5,2 (*eldeki verilere göre*)

COVID-19 Olgu Sayısı (16 Kasım 2021)- DSÖ



Globally, as of **5:28pm CET, 16 November 2021**, there have been **253.640.693 confirmed cases** of COVID-19, **5.104.899 deaths**, reported to WHO. As of **14 November 2021**, a total of **7.307.892.664 vaccine doses** have been administered



COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Last Updated at (W/D/YYYY)
17.11.2021 19:21

Total Cases
254.659.963

Total Deaths
5.120.194

Total Vaccine Doses Administered
7.558.923.99

28-Day Cases
12.763.292

28-Day Deaths
199.715

28-Day Vaccine Doses Administered
791.452.684

Cases | Deaths by
Country/Region/Sovereignty

US
28-Day: **2.133.434** |
35.756
Totals: **47.331.191** | **766.232**

United Kingdom
28-Day: **1.105.085** |
4.333
Totals: **9.724.376** | **143.799**

Russia
28-Day: **1.054.950** |
31.695
Totals: **9.027.163** | **254.229**

Turkey
28-Day: **744.740** |



From: FAO, NOAA

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15 ay önce

Total mortalite %5,2

-İtalya %14,5

-ABD %5,2

-Türkiye %2,6

Şu anda

Total mortalite %2

-İtalya %2,7

-ABD %1,6

-Türkiye %0,9

COVID HIV ile yařayan kiřiye nasıl etkiler?

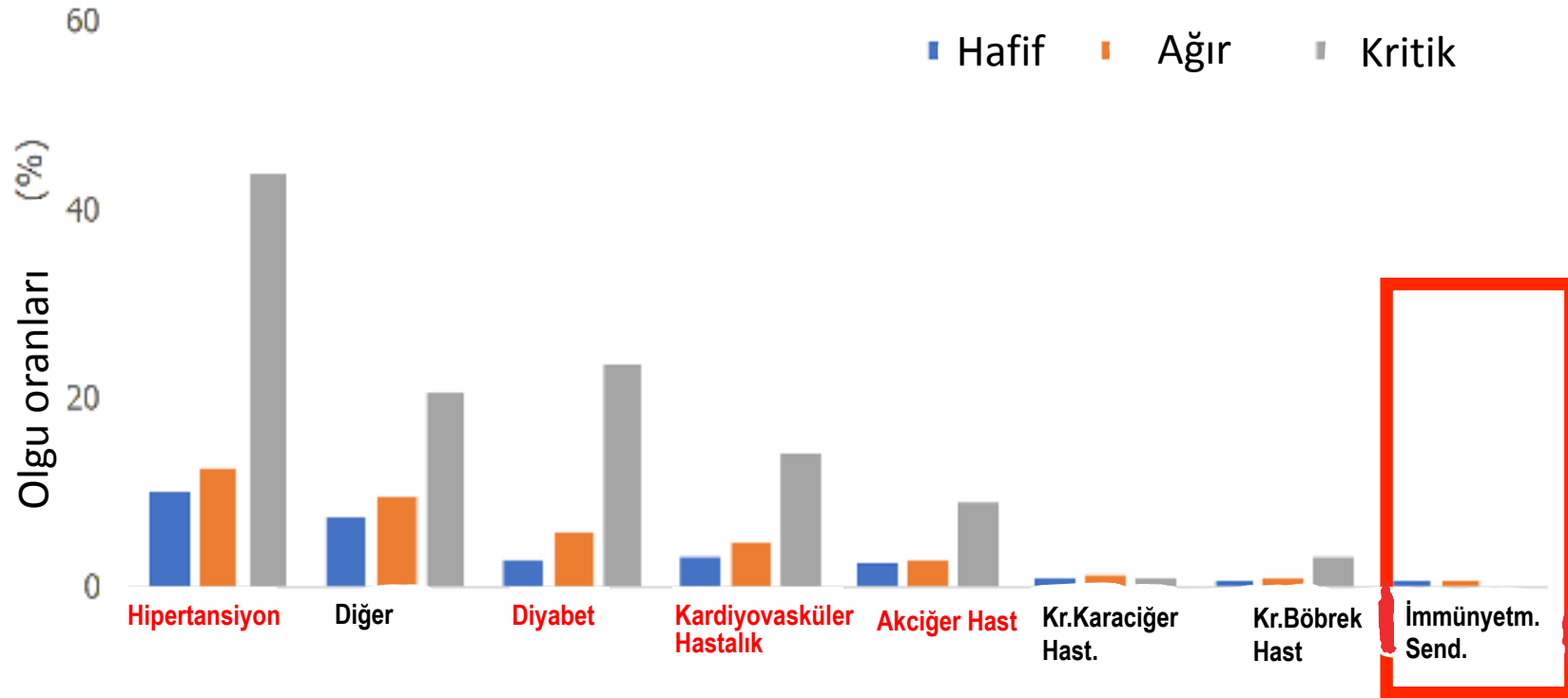
Tam olarak bilinmemektedir.

Artmış risk?

Seyri daha mı kötü?

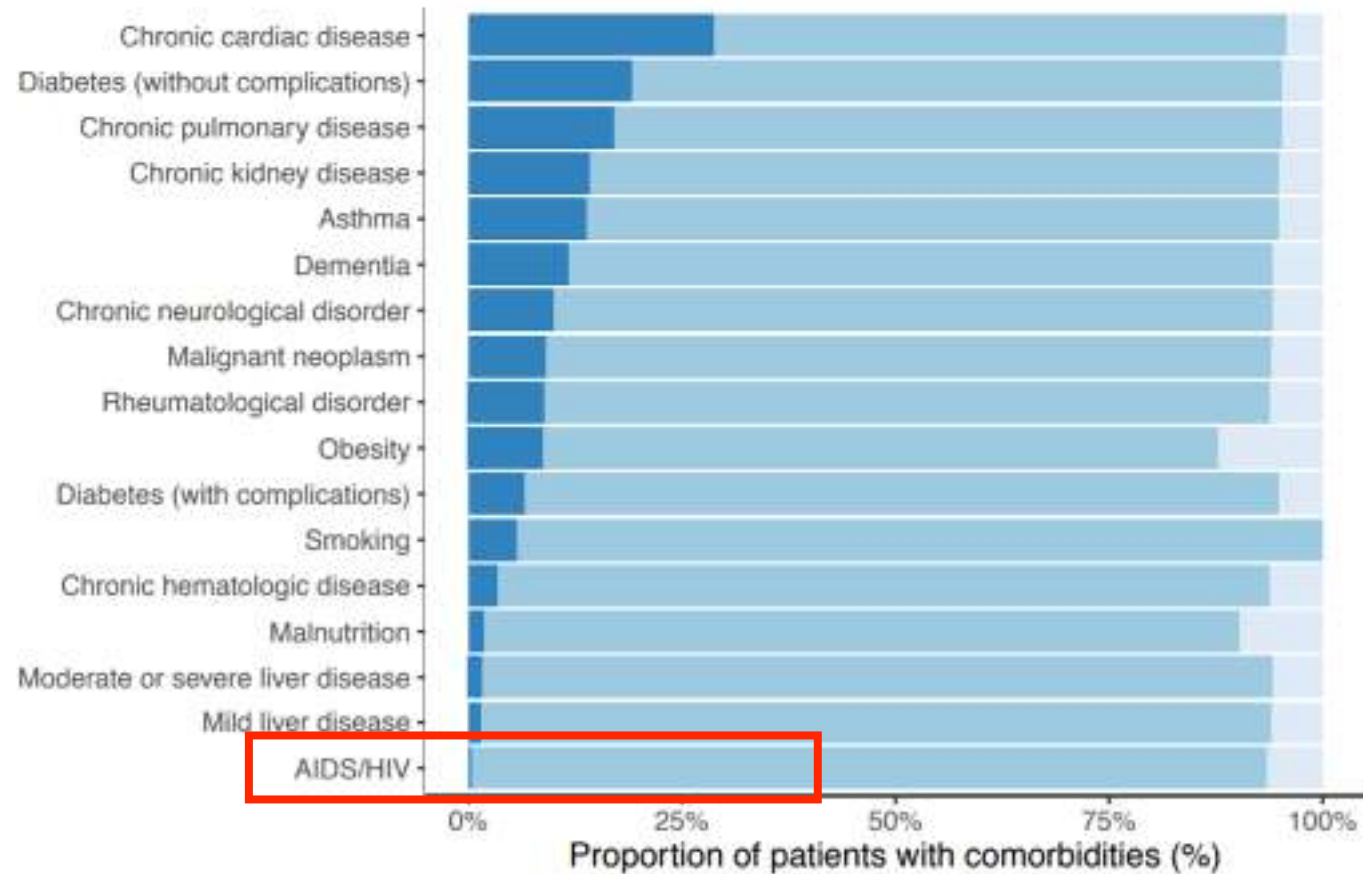
Tedavi altında olan VL baskılanmış, CD4 ü yüksek kişilerde diđer kişilere benzer. MERS ve SARS bu kişilerde farklı seyretmemiştir.

COVID 19'da Ko-morbid Hastalıklar (Çin verileri)



19230 Kesinleşmiş Olgu

COVID 19'da Ko-morbid Hastalıklar (Birleşik Krallık verileri)



Docherty, Annemarie B., et al. "Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol." *medRxiv* (2020).

Co-infection of SARS-CoV-2 and HIV in a Patient in Wuhan City, China

Bildirilen ilk vaka

- Feng Zhu¹, Yang Cao², Shuyun Xu³, Min Zhou³

28 OCA 2020 **ŞUB 2020** **ŞUB 2020** **ŞUB 2020**

<p>61 y, Erkek Ateş (37,5 C) kuru öksürük</p> <p><u>Risk Faktörleri</u></p> <ul style="list-style-type: none">• Tip 2 DM• Sigara <p><u>Laboratuvar</u></p> <ul style="list-style-type: none">• Hafif Lenfopeni• BT <p>Bilateral buzlu cam opasiteleri</p>	<p><u>1 ŞUB 2020</u> Nefes Darlığı geliyor</p> <p><u>3 ŞUB 2020</u> SARS-CoV-2 (RT-PCR) Pozitif Anti-HIV: pozitif Cd4:%4.75 Ly:560/mm3 BT: Bilateral buzlu cam opasiteleri artıyor</p>	<p>SaO2: %80 (Oda havasında) SaO2: %91 (5 lt/dk)</p> <p><u>Tedavi</u></p> <ul style="list-style-type: none">• Lpr/r 2x2• Moxi 400 mg/gün• γ-globulin• Methilpredn.	<p><u>9 ŞUB 2020</u> Belirgin klinik ve radyolojik iyileşme</p> <p>SaO2: %95 (2 lt/dk)</p> <p><u>15 ŞUB 2020</u> • İki RT-PCR: Negatif</p> <p><u>17 ŞUB 2020</u> Taburcu</p>
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HIV ile yaşayan hastalarda COVID-19 : Klinik vaka serisi

- 5 Hastalık seri

*Jose L Blanco, Juan Ambrosioni,
Felipe Garcia, Esteban Martínez,
Alex Soriano, Josep Mallolas,
*Jose M Miro, on behalf the COVID-19
in HIV Investigators†*

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Demographics and baseline HIV status					
Age (years)	40	49	29	40	31
Gender	Transgender	Male	Male	Male	Transgender
HIV-risk factor and exposure	MSM, gym worker	Bisexual man, health-care worker	MSM, sexual worker participant in ChemSex session 6 days before	MSM, dinner 5 days before with another person who was COVID-19 positive	MSM, sexual worker
Comorbidities*	None	Hypothyroidism	None	Asthma	None
HIV status					
Year of HIV diagnosis	2007	2003	2013	2003	2020
Last CD4 cell count (cells per μ L)	616	445	604	1140	13
Last CD4:CD8 ratio	0.8	0.46	1.1	1.2	0.1
HIV viral load at or before admission (copies per mL)	<50	<50	<50	<50	45500
ART-regimen before admission	Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat	Abacavir, lamivudine, and dolutegravir	Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat	Abacavir, lamivudine; and dolutegravir	No ART: current diagnosis is late presenter

Klinik Bulgular

Clinical findings on admission

Duration of symptoms, days	2	5	2	3	7
Diagnosis	Upper respiratory tract infection	Lower respiratory tract infection	Upper respiratory tract infection	Lower respiratory tract infection	Lower respiratory tract infection
Symptoms and vital signs					
Temperature	Fever (38.7°C)	Fever (39°C)	Fever (39.5°C)	Fever (39.5°C)	Fever (38.5°C)
Symptoms	Cough, malaise, headache	Cough	Cough, malaise, headache, dyspnoea	Cough, malaise, headache, dyspnoea	Cough, dyspnoea
Blood pressure (mm Hg)	140/90	110/70	129/69	115/76	127/56
Respiratory rate (breaths per min)	14	28	16	24	20
Heart rate (beats per min)	90	94	78	103	121
Chest x-ray findings	Normal	Bilateral ground-glass opacities	Normal	Right basal interstitial infiltrate	Right basal pneumonia with pleural effusion
O ₂ saturation in ambient air	SpO ₂ 100%	SpO ₂ <90%	SpO ₂ 97%	SpO ₂ 94%	SpO ₂ <90%
PaO ₂ /FiO ₂ ratio	ND	182	ND	ND	230
Laboratory results					
White blood cell count (cells per 10 ⁹ /L)	7840	29 160	6730	6140	14 670
Lymphocyte (cells per 10 ⁹ /L)	2700	1170 (4%)	1500	1600	900

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
(Continued from previous page)					
Platelets (cells per 10 ⁹ /L)	345 000	135 000	124 000	186 000	309 000
LDH (U/L)	ND	316	256	465	1149
C-reactive protein (mg/dL)	ND	30	0.72	0.43	40
D-dimer (ng/mL)	ND	>10 000	400	300	ND
Ferritin (ng/mL)	ND	1020	ND	1044	866
Procalcitonin (ng/mL)	ND	ND	<0.03	ND	ND
Severity of the infection at admission	Mild	Severe	Mild	Moderate	Severe

Treatment and outcomes

ART†	ART at admission maintained	Tenofovir disoproxil fumarate, and emtricitabine plus lopinavir-boosted ritonavir (on going)	Tenofovir disoproxil fumarate, and emtricitabine plus lopinavir-boosted ritonavir (for 3 days)	Tenofovir disoproxil fumarate, and emtricitabine plus lopinavir-boosted ritonavir (for 14 days)	Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat (on going)
Other antiviral treatments	No	Interferon beta-1b (for 7 days), hydroxychloroquine (for 7 days)	Hydroxychloroquine (for 5 days)	Hydroxychloroquine (for 5 days)	Interferon beta-1b (for 4 days), hydroxychloroquine (for 5 days)
Other antibiotics	No	Meropenem (for 16 days), linezolid (for 14 days)	Azithromycin (for 5 days)	Azithromycin (for 5 days), cefixime (for 5 days)	Azithromycin (for 5 days), ceftaroline fosamil (for 7 days), co-trimoxazole (for 21 days, followed by secondary prophylaxis)
Admitted to an intensive care unit	No	Yes	No	No	Yes
Invasive or non-invasive mechanical ventilation	No	Invasive	No	No	Non-invasive
Corticosteroids or tocilizumab	No	Tocilizumab, 400 mg one single dose (on day 10)	No	Inhaled corticosteroids	Corticosteroids
Length of hospital stay (days)	1	21	3	4	12
Length of home hospitalisation (days)‡	13	10	..
Outcomes	Cured	Still at hospital	Cured	Cured	Cured
Additional comments	..	Extracorporeal membrane oxygenation since day 13 (on going)	Concomitant <i>Pneumocystis jiroveci</i> and bacterial pneumonia treatment



HIV/SARS-CoV-2 co-infected patients in Istanbul, Turkey

Journal:	<i>Journal of Medical Virology</i>
Manuscript ID	JMV-20-8681.R1
Wiley - Manuscript type:	Letter to the Editor
Date Submitted by the Author:	26-Apr-2020
Complete List of Authors:	Altuntas Aydin, Ozlem; University of Health Sciences Bakirkoy Dr Sadi Konuk Training and Research Hospital Kumbasar Karaosmanoglu, Hayat; University of Health Sciences Bakirkoy Dr Sadi Konuk Training and Research Hospital Kart Yasar, Kadriye; University of Health Sciences Bakirkoy Dr Sadi Konuk Training and Research Hospital
Keywords:	SARS coronavirus < Virus classification, Coronavirus < Virus classification, Human immunodeficiency virus < Virus classification

COVIDProtocols v2.0

Search protocols

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Bakırköy Sađeđ Koruyucu EAH

Deneyimi

Yaş	Cins	HIV Tarihi (yıl)	ART	COVID tedavisi	Sonuç
34	E	10	Kesmiş	Plaquenil	Taburcu
44	E	12	TDF/FTC+DTG	Plaquenil	Ex
35	E	2	Genvoya	Plaquenil	Taburcu
36	E	4	Genvoya	Plaquenil	Taburcu

COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients

Age (years)	Sex	Years since HIV diagnosis	Antiretroviral treatment (ART)	Years of ART	CD4 T-cell count per mm ³	CD4/CD8 ratio	CD4 T-cell nadir (count per mm ³)	HIV-RNA (copies/mL)	COVID-19 clinical classification	Outcome	
1	44	M	14	DTG/ABC/3TC	13	754	0.83	165	<50	Mild	Recovered
2	33	F	7	RPV/TAF/FTC	6	619	0.9	347	<50	Mild	Recovered
3	38	M	5	BIC/TAF/FTC	2	1189	1.53	541	<50	Mild	Recovered
4	53	M	11	NVP/ABC/3TC	12	810	0.53	295	<50	Mild	Recovered
5	60	M	7	DTG/TDF/FTC	5.5	892	1.00	362	<50	Mild	Recovered
6	51	M	20	DTG/3TC	10	402	0.4	329	<50	Mild	Recovered
7	63	M	17	DTG/ABC/3TC	5.5	1087	0.9	439	<50	Mild	Recovered
8	65	M	13	BIC/TAF/FTC	9	122	0.93	440	<50	Mild	Recovered
9	82	M	28	DRV/COBI/TAF/FTC	28	179	0.4	151	900	Critical	ICU, NIV, death
10	53	M	10	DRV/COBI/TAF/FTC	0.5	285	0.25	204	842	Critical	ICU, IV, discharged, recovered
11	33	M	10	DRV/COBI/TAF/FTC	10	751	1.89	325	<50	Mild	Recovered
12	31	M	5	EVG/COBI/TAF/FTC	5	1000	1.15	810	<50	Mild	Recovered
13	37	M	10	EVG/COBI/TAF/FTC	8	946	1.13	530	<50	Mild	Recovered
14	37	F	5	DOR/TDF/FTC	5	402	0.5	na	<50	Severe	Hospital, discharged, recovered
15	36	M	4	DTG/ABC/3TC	4	718	1.2	na	<50	Critical	ICU, IV, discharged from ICU, Hospital
16	68	M	14	DRV/COBI/TAF/FTC	14	499	0.9	340	<50	Severe	Hospital, discharged, recovered
17	42	M	11	RPV/TDF/FTC	na	613	1.3	430	<50	Critical	ICU, discharged, recovered
18	35	M	3	DTG/3TC	na	538	1.0	439	<50	Mild	Recovered
19	55	M	10	RPV/TAF/FTC	10	780	1.89	370	<50	Mild	Recovered
20	55	M	21	BIC/TAF/FTC	21	69	0.05	8	<50	Critical	ICU, IV, death
21	58	M	18	DTG	14	573	0.8	314	<50	Mild	Recovered
22	30	M	6	DTG/ABC/3TC	6	608	1.00	608	<50	Mild	Recovered
23	26	M	na	BIC/TAF/FTC	na	na	na	na	Mild	Recovered	
24	59	M	15	DOR/TDF/FTC	15	718	1.75	230	<50	Critical	ICU, IV, death
25	31	M	7	BIC/TAF/FTC	5	667	1.09	380	<50	Mild	Recovered
26	63	M	20	NVP/TAF/FTC	20	693	4.94	111	<50	Mild	Recovered
27	53	M	6	EVG/COBI/TAF/FTC	6	717	0.95	457	<50	Mild	Recovered
28	54	M	15	BIC/TAF/FTC	15	457	0.68	126	<50	Mild	Hospital, discharged, recovered
29	70	M	13	NVP/TAF/FTC	13	336	0.38	250	<50	Mild	Hospital, discharged, recovered

Komorbiditeler: 20/33 (%60)
Ölüm oranı: 3/32 (%9)
Olguların %76'sı hafif geçiriyor

Exitus

9.Hasta: 82 yaş
20.Hasta: CD4 sayısı 69/mm³
24.Hasta: HT,KOAH,DM tip2



COVID-19 ile İnsan İmmün Yetmezlik Virüsü Olan Hastaların Klinik Özellikleri ve Sonuçları

Clinical features and outcomes of HIV patients with coronavirus disease 2019

Agostino Riva, Andrea Giacomelli, Annalisa Ridolfo, Chiara Atzori, Cristina Gervasoni, Dario Cattaneo, Davide Minisci, Letizia Oreni, Paola Meraviglia

- 47 hasta- vaka serisi
- Tüm olgular ART almakta
- Ortalama yaş: 51
- 28/47 SARS-Cov-2 (RT-PCR): pozitif (%60)
- Komorbiditeler: %64'ü en az bir komorbidite
- Fatalite hızı: 2/47 (**%4,3**)
 - 1.olgu: Obez
 - 2.olgu: KVH+ Kanser
- Aynı hastanede HIV negatif, COVID 19 olguların fatalite hızı: **%17**

HIV infection and risk of COVID-19 mortality

A meta-analysis

[Yonghai Dong](#), MD,^a [Zhongjian Li](#), MD,^a [Sheng Ding](#), MD,^a [Shulong Liu](#), MD,^b [Zhiyuan Tang](#), MD,^c [Lina Jia](#), MD,^d [Jiahong Liu](#), MD,^{a,*} and [Yun Liu](#), MD^e

Monitoring Editor: Vipul Kumar Singh.

Dahil edilme kriterleri

1. Doğrulanmış COVID-19 olgular
2. 2 grup: HIV (+)/(-)
3. COVID-19'a bağlı ölüm sonuçları mevcut
4. Her iki grup örneklem büyüklüğü>100
5. RKÇ, Kohort , vaka-kontrol

Dışlama kriterleri

- Derlemeler, olgu sunumları, mektuplar

Sonuçlar

1. 632 yayın → 10 dahil edilmiş
2. 41.113 COVID-19/HIV+
18.081.257 COVID-19/HIV-

Genel sonuçlar

- COVID-19/HIV+ fatalite hızı %3.44
- COVID-19/HIV- fatalite hızı %0.42

❑ Beş çalışma – COVID 19 /HIV koenf –ölüm riski yüksek

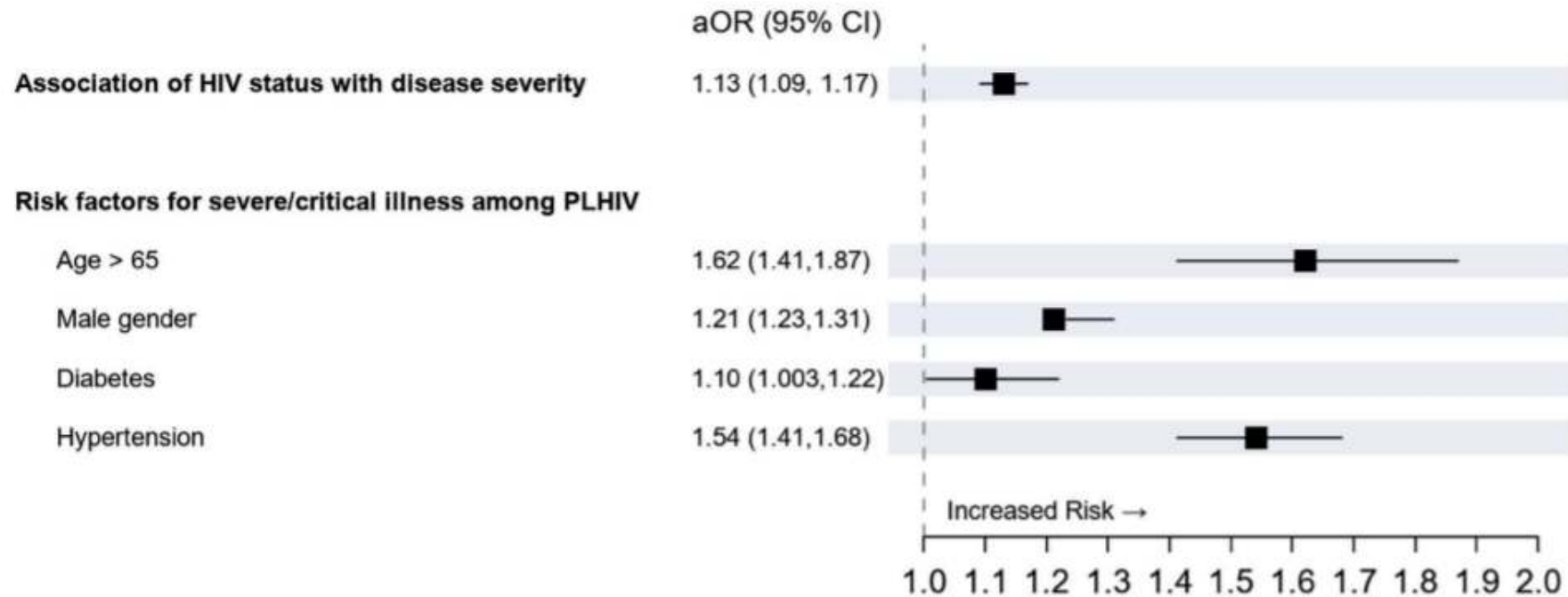
❑ Beş çalışma – COVID 19 /HIV koenf –ölüm riski açısından ilişki yok

COVID-19/HIV+
Koenfeksiyonund
a Alt Grup Analizi
(Ölüm riski)

Ülke	Odds Oranı
ABD	1.520
Güney Afrika	1.122
Birleşik Krallık	0.878

Dong, Yonghai, et al. *Medicine* 100.26 (2021).

Hastaneye yatış sırasında HIV enfeksiyonu ve ciddi veya kritik COVID-19 hastalığı riski (DSÖ- Temmuz 2021)



The upper part of the figure shows HIV infection as a significant independent risk factor for severe or critical presentation of COVID-19, after adjusting for age, sex, burden of underlying conditions (adjusted odds ratio (aOR)). The lower part of the figure shows the adjusted odds ratio for each risk factor for severe or critical presentation of COVID-19 among PLHIV, after controlling for the other risk factors.

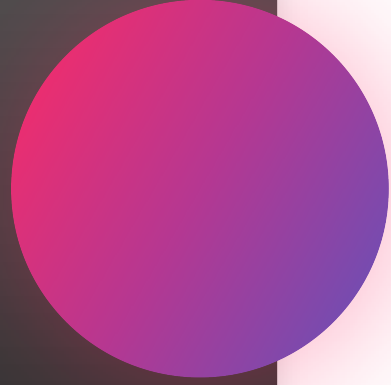
Sonuç

- Normal CD4 hücre sayısı ve baskılanmış viral yük ile tedavi gören HIV pozitif kişilerin ciddi COVID 19 riski kesin değildir
- Geleneksel risk faktörleri daha ön plana çıkmaktadır
 - KVH
 - Hipertansiyon
 - Diyabet
 - Obezite
 - KOAH
 - Sigara (Sigarayı bırakma teşvik edilmeli)

Pnömonokok ve influenza aşıları güncel tutulmalıdır

CD4<200/mm³: Fırsatçı enfeksiyon profilaksiler unutulmamalı

HIV ve COVID-19'un ölüm riski arasındaki ilişkinin gelecekte hala güncellenmesi gerekmektedir



Teşekkürle r

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