

TESIS

AKURASI D-DIMER SEBAGAI PREDIKTOR KEMATIAN PASIEN COVID-19 DI RSUD SITI FATIMAH PROVINSI SUMATERA SELATAN



OLEH :

**NAMA : DEWIE SURANTI
NIM : 10012682226007**

**PROGRAM STUDI ILMU KESEHATAN MASYARAKAT (S2)
FAKULTAS KESEHATAN MASYARAKAT
UNIVERSITAS SRIWIJAYA
2024**

TESIS

AKURASI D-DIMER SEBAGAI PREDIKTOR KEMATIAN PASIEN COVID-19 DI RSUD SITI FATIMAH PROVINSI SUMATERA SELATAN

Diajukan untuk Memenuhi Salah Satu Syarat Memperoleh Gelar (S2)
Magister Kesehatan Masyarakat pada Fakultas Kesehatan Masyarakat
Universitas Sriwijaya



OLEH :

NAMA : DEWIE SURANTI
NIM : 10012682226007

**PROGRAM STUDI ILMU KESEHATAN MASYARAKAT (S2)
FAKULTAS KESEHATAN MASYARAKAT
UNIVERSITAS SRIWIJAYA
2024**

HALAMAN PENGESAHAN

AKURASI D-DIMER SEBAGAI PREDIKTOR KEMATIAN PASIEN COVID-19 DI RSUD SITI FATIMAH PROVINSI SUMATERA SELATAN

TESIS

Diajukan untuk Memenuhi Salah Satu Syarat Memperoleh Gelar (S2)
Magister Kesehatan Masyarakat pada Fakultas Kesehatan Masyarakat
Universitas Sriwijaya

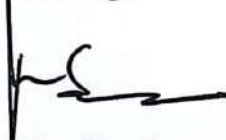
OLEH

NAMA : DEWIE SURANTI

NIM : 10012682226007

Palembang, Juli 2024

Pembimbing I



Prof. Dr. Rico Januar Sitorus, SKM., M.Kes. (Epid)
NIP. 198101212003121002

Pembimbing II



Dr. Iche Andriyani Liberty, SKM, M.Kes.
NIP. 199002072015104201

Mengetahui,

Dekan Fakultas Kesehatan Masyarakat
Universitas Sriwijaya



Dr. Misnawati, S.K.M., M.K.M.
NIP. 195606092002122001

HALAMAN PERSETUJUAN

Karya tulis ilmiah berupa Tesis dengan judul “Akurasi D-dimer sebagai Prediktor Kematian Pasien COVID-19 di RSUD Siti Fatimah Provinsi Sumatera Selatan” telah dipertahankan di hadapan Panitia Sidang Ujian Tesis Program Studi Magister (S2) Ilmu Kesehatan Masyarakat Fakultas Kesehatan Masyarakat Universitas Sriwijaya pada tanggal 03 Juli 2024 dan telah diperbaiki, diperiksa serta disetujui sesuai dengan masukan Panitia Sidang Ujian Tesis Program Studi Magister (S2) Ilmu Kesehatan Masyarakat Fakultas Kesehatan Masyarakat Universitas Sriwijaya.

Palembang, 03 Juli 2024

Tim Penguji Karya Tulis Ilmiah berupa Tesis

Ketua :

1. Najmah, S.K.M., M.P.H., Ph.D
NIP 198307242006042003

()

Anggota :

2. Prof. Dr. Rico Januar Sitorus, S.K.M., M.Kes (Epid)
NIP 198101212003121002
3. Dr. Iche Andriyani Liberty, S.K.M., M.Kes
NIP 199002072015104201
4. Prof. Dr. dr. H.M. Zulkarnain, M.Med., Sc., PKK
NIP 196109031989031002
5. Prof. Dr.rer.med. H. Hamzah Hasyim, S.K.M., M.K.M. ()
NIP 197312262002121001

()
()
()
()



Mengetahui,
Dekan Fakultas Kesehatan Masyarakat


Dr. Misnaniarti, S.K.M., M.K.M.
NIP. 1976060920021201

Koordinator Program Studi
S2 Ilmu Kesehatan Masyarakat


Prof. Dr. Rostika Flora, S.Kep., M.Kes
NIP. 197109271994032004

HALAMAN PERNYATAAN INTEGRITAS

Yang bertanda tangan di bawah ini :

Nama : Dewie Suranti

NIM : 10012682226007

Judul Tesis : Akurasi D-dimer sebagai Prediktor Kematian Pasien COVID-19
di RSUD Siti Fatimah Provinsi Sumatera Selatan

Menyatakan bahwa Laporan Tesis saya merupakan hasil karya sendiri didampingi tim pembimbing dan bukan hasil penjiplakan/plagiat. Apabila ditemukan unsur penjiplakan/*plagiat* dalam Tesis ini, maka saya bersedia menerima sanksi akademik dari Universitas Sriwijaya sesuai aturan yang berlaku.

Demikian, pernyataan ini saya buat dalam keadaan sadar dan tanpa ada paksaan dari siapapun.



Palembang, 03 Juli 2024

Dewie Suranti
NIM. 10012682226007

HALAMAN PERNYATAAN PERSETUJUAN PUBLIKASI

Yang bertanda tangan di bawah ini :

Nama : Dewie Suranti

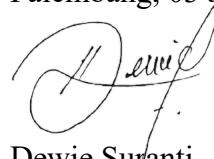
NIM : 10012682226007

Judul Tesis : Akurasi D-dimer sebagai Prediktor Kematian Pasien COVID-19
di RSUD Siti Fatimah Provinsi Sumatera Selatan

Memberikan izin kepada Pembimbing dan Universitas Sriwijaya untuk mempublikasikan hasil penelitian saya untuk kepentingan akademik apabila dalam waktu 1 (satu) tahun tidak mempublikasikan karya penelitian saya. Dalam kasus ini saya setuju menempatkan Pembimbing sebagai penulis korespondensi (*Corresponding author*).

Demikian, pernyataan ini saya buat dalam keadaan sadar dan tanpa ada paksaan dari siapapun.

Palembang, 03 Juli 2024



Dewie Suranti
NIM. 10012682226007

EPIDEMIOLOGY AND BIOSTATISTICS
MAGISTER PROGRAM OF PUBLIC HEALTH SCIENCE
FACULTY OF PUBLIC HEALTH
SRIWIJAYA UNIVERSITY
Scientific papers in the form of thesis
July 03, 2024

Dewie Suranti ; Supervised by Rico Januar Sitorus and Iche Andriyani Liberty

Accuracy D-dimer as A Predictor of Death in COVID-19 Patient at RSUD Siti Fatimah, South Sumatra
xxiii + 198 pages, 10 picture, 67 table, 5 attachment

ABSTRACT

Background: *The COVID-19 pandemic, which has spread worldwide and resulted in fatalities, has had a significant impact. Globally, as of March 7, 2023, there have been 759,408,703 confirmed cases of COVID-19, including 6,866,434 deaths, reported to the WHO. Indonesia ranked first in the highest number of COVID-19 cases in ASEAN in 2021, with a total of 4,253,598 cases. According to the Indonesia Health Profile for 2021, the COVID-19 Case Fatality Rate (CFR) in Indonesia was 3.4%, with South Sumatra being the fifth-ranked province. The increase in D-dimer levels and poor laboratory test results serve as markers of worsening patient condition, which is also supported by age and comorbidities. The objective of this study was to determine the accuracy of D-dimer as a predictor of mortality in COVID-19 patients at RSUD Siti Fatimah.*

Method: *This study employed a retrospective cohort design using secondary data from COVID-19 patients with medical records treated at RSUD Siti Fatimah, South Sumatra Province, from January to December 2021. The sampling technique involved total sampling, comprising 928 patients.*

Results: *The majority of patients (83.94%) survived, and 59.16% had D-dimer levels below 500 ng/mL. The average D-dimer levels were higher in patients who died compared to those who survived (p -value <0.001), and there was a significant association between D-dimer levels and COVID-19 patient outcomes. The group of patients with D-dimer levels ≥ 500 ng/mL had a 3 times higher risk of death compared to the group of patients with D-dimer levels < 500 ng/mL, considering variables such as age, comorbid hypertension, diabetes mellitus, cardiovascular disease, tuberculosis, chronic obstructive pulmonary disease, symptoms, vaccination, oxygen saturation, leukocyte, and monocyte. The AUC (area under the curve) value was 0.969, with a sensitivity of 89% and a specificity of 96%.*

Conclusion: *D-dimer serves as a predictor of mortality in COVID-19 patients at RSUD Siti Fatimah, South Sumatra Province.*

Keywords: *COVID-19, D-dimer, mortality*

References: *200 (1995-2024)*

EPIDEMIOLOGI DAN BIostatistik
PROGRAM STUDI MAGISTER (S2) ILMU KESEHATAN MASYARAKAT
FAKULTAS KESEHATAN MASYARAKAT
UNIVERSITAS SRIWIJAYA

Karya tulis ilmiah berupa Tesis,

03 Juli 2024

Dewie Suranti ; Dibimbing oleh Rico Januar Sitorus dan Iche Andriyani Liberty

Akurasi D-dimer sebagai Prediktor Kematian Pasien COVID-19 di RSUD Siti Fatimah Provinsi Sumatera Selatan

xxiii + 198 halaman, 10 gambar, 67 tabel, 5 lampiran

ABSTRAK

Latar belakang : Pandemi COVID-19 yang sudah menyebar ke seluruh dunia bahkan menyebabkan kematian. Secara global, terhitung sampai tanggal 7 Maret 2023, terdapat 759.408.703 kasus COVID-19 yang dikonfirmasi, termasuk 6.866.434 kematian, yang dilaporkan ke WHO. Indonesia menempati peringkat pertama dengan kasus COVID-19 terbanyak di ASEAN pada tahun 2021 yaitu sebanyak 4.253.598 kasus. Berdasarkan Profil Kesehatan Indonesia tahun 2021 angka kematian (*Case Fatality Rate / CFR*) COVID-19 di Indonesia sebesar 3,4% dan Sumatera Selatan merupakan provinsi peringkat ke-5. Peningkatan kadar D-dimer dan hasil pemeriksaan laboratorium yang buruk menjadi penanda perburukan kondisi pasien yang juga didukung oleh faktor usia dan komorbiditas. Tujuan penelitian ini untuk mengetahui akurasi D-dimer sebagai prediktor kematian pasien COVID-19 di RSUD Siti Fatimah.

Metode : Penelitian menggunakan desain kohort retrospektif menggunakan data sekunder berupa pasien COVID-19 yang memiliki rekam medik dan dirawat di RSUD Siti Fatimah Provinsi Sumatera Selatan dari Januari-Desember 2021. Teknik pengambilan sampel menggunakan *total sampling* berjumlah 928 pasien.

Hasil : Sebagian besar pasien (83,94%) berhasil bertahan hidup, kemudian 59,16% memiliki kadar D-dimer di bawah 500 ng/mL. Rata-rata kadar D-dimer lebih tinggi pada pasien yang meninggal dibandingkan pasien yang masih hidup (*p-value* < 0,001) dan terdapat hubungan bermakna antara kadar D-dimer dengan luaran pasien COVID-19. Kelompok pasien dengan kadar D-dimer ≥ 500 ng/mL mempunyai risiko kematian 3 kali untuk mengalami kematian dibandingkan kelompok pasien dengan kadar D-dimer < 500 ng/mL dengan mempertimbangkan variabel usia, komorbid hipertensi, diabetes melitus, *cardiovascular disease*, tuberkulosis, penyakit paru obstruktif kronis, gejala, vaksinasi, saturasi oksigen, leukosit dan monosit. Nilai AUC (*area under the curve*) 0,969, sensitivitas 89% dan spesifisitas 96%.

Kesimpulan : D-dimer berperan sebagai prediktor kematian pasien COVID-19 di RSUD Siti Fatimah Provinsi Sumatera Selatan.

Kata Kunci : COVID-19, D-dimer, kematian

Kepustakaan : 200 (1995-2024)

KATA PENGANTAR

Assalamu'alaikum Warahmatullah Wabarakatuh.

Puji dan syukur penulis haturkan kepada Allah SWT yang telah melimpahkan taufik dan hidayah-Nya sehingga tesis dengan judul **“Akurasi D-dimer sebagai Prediktor Kematian Pasien COVID-19 di RSUD Siti Fatimah Provinsi Sumatera Selatan”** ini dapat terselesaikan. Shalawat beserta salam tak lupa penulis lantunkan untuk junjungan Nabi Muhammad SAW.

Pada kesempatan ini, saya ingin mengucapkan terima kasih yang sebesar-besarnya kepada semua pihak yang telah membantu dan mendukung saya dalam menyelesaikan penelitian ini terutama kepada:

1. Prof. Dr. Taufiq Marwa, S.E., M.Si. selaku Rektor Universitas Sriwijaya.
2. Dr. Misnaniarti, S.K.M., M.K.M. selaku Dekan Fakultas Kesehatan Masyarakat Universitas Sriwijaya.
3. Prof. Dr. Rostika Flora, S.Kep., M.Kes. selaku Koordinator Program Studi Magister Ilmu Kesehatan Masyarakat Fakultas Kesehatan Masyarakat Universitas Sriwijaya.
4. Prof. Dr. Rico Januar Sitoris, S.K.M., M.Kes (Epid) selaku dosen pembimbing I yang telah memberikan masukan, arahan, bimbingan, dan ketersediaan waktunya dalam membantu saya menyusun penulisan proposal tesis ini.
5. Dr. Iche Andriyani Liberty, S.K.M., M.Kes., selaku dosen pembimbing II yang telah memberikan masukan, arahan, bimbingan, dan ketersediaan waktunya dalam membantu saya menyusun penulisan proposal tesis ini.
6. Ibu Najmah, SKM., MPH., Ph.D., Bapak Prof. Dr. dr. H.M. Zulkarnain, M.Med.,Sc., PKK., dan Bapak Prof. Dr.rer.med. H. Hamzah Hasyim, SKM., MKM., sebagai tim penguji yang telah memberikan waktu dan kesempatan untuk membimbing serta menguji tesis ini. Bimbingan, masukan, dan saran yang diberikan sangat berharga bagi perkembangan penelitian saya.
7. Prof. Dr. dr. Fachmi Idris, M.Kes. selaku atasan saya yang telah memberikan rekomendasi, doa, dukungan, serta kesempatan untuk saya dapat bekerja sambil melanjutkan pendidikan S2 ini.

8. Prof. Dr. dr. RM. Suryadi Tjekyan, DTM&H., M.P.H. yang telah memberikan rekomendasi serta doa dan dukungan yang membangun. Diikuti dengan *supporter* Ketua Bagian, Staf Dosen, dan Staf Admin Bagian IKM-IKK FK Unsri yang tak henti-hentinya menyemangati dan memberikan doa terbaik.
9. Kedua orang tua dan saudara tercinta yang telah memberikan *support* baik moral maupun material. Terima kasih telah menjadi “rumah” yang sesungguhnya bagi saya.
10. Seluruh rekan-rekan sejawat Program Studi Magister Ilmu Kesehatan Masyarakat Universitas Sriwijaya yang telah berbagi ide, masukan, dan diskusi yang sangat berharga.

Penulis menyadari bahwa dalam penyusunan naskah tesis ini masih jauh dari kesempurnaan. Untuk itu, kritik dan saran yang bersifat membangun sangat diharapkan demi terwujudnya naskah tesis yang berkualitas. Semoga tesis ini dapat memberikan informasi dan manfaat bagi semua pihak.

Akhir kata, saya ucapkan terima kasih.

Wassalamu’alaikum Warahmatullahi Wabarakatuh.

Palembang, 03 Juli 2024

Penulis

RIWAYAT HIDUP

Penulis dilahirkan pada tanggal 30 April 1998 di Kota Palembang. Putri ketiga dari Bapak Satiman dan Ibu Rubiyati, dan memiliki 2 saudara kandung lainnya.

Penulis menyelesaikan pendidikan dasar di SD Tamansiswa Cabang Pendawa Palembang pada tahun 2009. Melanjutkan pendidikan menengah pertama di SMP Negeri 50 Palembang sampai tahun 2012, kemudian pendidikan menengah atas di SMA Negeri 18 Palembang hingga tahun 2015. Penulis juga menyelesaikan pendidikan di Universitas Sriwijaya jurusan Ilmu Kesehatan Masyarakat peminatan Epidemiologi dan Biostatistik dan tamat tahun 2019.

Penulis pernah bekerja sebagai Sekretaris Divisi ERIA (Emergensi Rawat Intensif Anak) di RSUP Dr. Mohammad Hoesin Palembang dari tahun 2019 sampai 2020. Selanjutnya, penulis pernah bekerja sebagai Tenaga Kontrak Promosi Kesehatan di Puskesmas Mekar Sari, Kecamatan Rantau Alai, Kabupaten Ogan Ilir dalam rentang tahun 2020 sampai 2021. Kemudian dari awal tahun 2022 sampai saat ini, penulis bekerja sebagai *Personal Assistant* Prof. Dr. dr. Fachmi Idris, M.Kes di Bagian IKM-IKK Fakultas Kedokteran Universitas Sriwijaya.

Pada pertengahan tahun 2022 penulis tercatat sebagai mahasiswa pada program studi Magister Ilmu Kesehatan Masyarakat Fakultas Kesehatan Masyarakat Universitas Sriwijaya Palembang, Bidang Kajian Umum (BKU) Epidemiologi dan Biostatistik.

DAFTAR ISI

	Halaman
HALAMAN SAMPUL LUAR	i
HALAMAN JUDUL	ii
HALAMAN PENGESAHAN.....	iii
HALAMAN PERSETUJUAN	iv
HALAMAN PERNYATAAN INTEGRITAS.....	v
HALAMAN PERNYATAAN PERSETUJUAN PUBLIKASI.....	vi
ABSTRACT	vii
ABSTRAK	viii
KATA PENGANTAR.....	ix
RIWAYAT HIDUP	xi
DAFTAR ISI.....	xii
DAFTAR TABEL	xvi
DAFTAR GAMBAR.....	xix
DAFTAR LAMPIRAN	xx
DAFTAR SINGKATAN	xxi
BAB I PENDAHULUAN.....	1
1.1. Latar Belakang	1
1.2. Rumusan Masalah.....	3
1.3. Tujuan Penelitian	4
1.3.1. Tujuan Umum.....	4
1.3.2. Tujuan Khusus	4
1.4. Manfaat Penelitian	6
1.4.1. Manfaat Teoritis.....	6
1.4.2. Manfaat Praktis	6
BAB II TINJAUAN PUSTAKA.....	7
2.1. COVID-19.....	7
2.1.1. Epidemiologi.....	8
2.1.2. Etiopatogenesis	9
2.1.3. Diagnosis	12
2.1.4. Pemeriksaan Laboratorium	14
2.1.5. Parameter Laboratorium dan Prognosis Pasien COVID-19	17
2.2. D-dimer	19

2.2.1.	Definisi D-dimer	19
2.2.2.	Struktur dan Pembentukan D-dimer	20
2.2.3.	Metode Pemeriksaan D-dimer	22
2.3.	D-dimer dan COVID-19	23
2.4.	Kerangka Teori	28
2.5.	Kerangka Konsep	29
2.6.	Hipotesis	29
BAB III METODE PENELITIAN		32
3.1.	Jenis Penelitian	32
3.2.	Lokasi dan Waktu Penelitian	32
3.2.1.	Lokasi Penelitian	32
3.2.2.	Waktu Penelitian	33
3.3.	Populasi dan Sampel	33
3.3.1.	Populasi	33
3.3.2.	Sampel Penelitian	33
3.4.	Perhitungan Besar Sampel Minimal	33
3.5.	Teknik Pengambilan Sampel	34
3.6.	Kriteria Inklusi dan Eksklusi	34
3.6.1.	Kriteria Inklusi	34
3.6.2.	Kriteria Eksklusi	35
3.7.	Variabel Penelitian	35
3.7.1.	Variabel Bebas	35
3.7.2.	Variabel Terikat	35
3.8.	Definisi Operasional	36
3.9.	Cara Pengumpulan Data	42
3.10.	Cara Pengolahan Data	42
3.11.	Analisis Data	42
3.11.1.	Analisis Deskriptif	42
3.11.2.	Analisis Inferensial	43
3.12.	Etika Penelitian	44
3.13.	Alur Penelitian	45
BAB IV HASIL DAN PEMBAHASAN		46
4.1.	Gambaran Umum Lokasi Penelitian	46
4.2.	Hasil	47

4.2.1.	Gambaran kadar D-dimer, demografik, komorbid, gejala, vaksinasi, waktu <i>onset</i> , pemeriksaan vital, pemeriksaan hematologi, dan luaran pasien COVID-19	47
4.2.2.	Hubungan Kadar D-dimer dengan Luaran Pasien COVID-19 .	50
4.2.3.	Hubungan Usia dengan Luaran Pasien COVID-19.....	51
4.2.4.	Hubungan Jenis Kelamin dengan Luaran Pasien COVID-19...	53
4.2.5.	Hubungan Indeks Massa Tubuh (IMT) dengan Luaran Pasien COVID-19	53
4.2.6.	Hubungan Komorbid Hipertensi dengan Luaran Pasien COVID-19	54
4.2.7.	Hubungan Komorbid Diabetes Melitus (DM) dengan Luaran Pasien COVID-19	55
4.2.8.	Hubungan Komorbid <i>Cardiovascular Disease</i> (CVD) dengan Luaran Pasien COVID-19.....	56
4.2.9.	Hubungan Komorbid Autoimun dengan Luaran Pasien COVID-19	57
4.2.10.	Hubungan Komorbid Ginjal dengan Luaran Pasien COVID-19	58
4.2.11.	Hubungan Komorbid <i>Tuberculosis</i> (TBC) dengan Luaran Pasien COVID-19	59
4.2.12.	Hubungan Komorbid Penyakit Paru Obstruktif Kronis (PPOK) dengan Luaran Pasien COVID-19	59
4.2.13.	Hubungan Gejala dengan Luaran Pasien COVID-19	60
4.2.14.	Hubungan Vaksinasi dengan Luaran Pasien COVID-19.....	61
4.2.15.	Hubungan Waktu <i>Onset</i> dengan Luaran Pasien COVID-19	62
4.2.16.	Hubungan <i>Mean Arterial Pressure</i> (MAP) dengan Luaran Pasien COVID-19	64
4.2.17.	Hubungan Denyut Nadi dengan Luaran Pasien COVID-19.....	65
4.2.18.	Hubungan Saturasi Oksigen dengan Luaran Pasien COVID-19	66
4.2.19.	Hubungan Laju Pernapasan dengan Luaran Pasien COVID-19	67
4.2.20.	Hubungan Suhu Tubuh dengan Luaran Pasien COVID-19.....	69
4.2.21.	Hubungan Hemoglobin dengan Luaran Pasien COVID-19	70
4.2.22.	Hubungan Hematokrit dengan Luaran Pasien COVID-19	72
4.2.23.	Hubungan Leukosit dengan Luaran Pasien COVID-19	73
4.2.24.	Hubungan Trombosit dengan Luaran Pasien COVID-19.....	74
4.2.25.	Hubungan Eritrosit dengan Luaran Pasien COVID-19	75
4.2.26.	Hubungan Basofil dengan Luaran Pasien COVID-19.....	76

4.2.27.	Hubungan Eosinofil dengan Luaran Pasien COVID-19.....	78
4.2.28.	Hubungan Limfosit dengan Luaran Pasien COVID-19.....	79
4.2.29.	Hubungan Monosit dengan Luaran Pasien COVID-19.....	80
4.2.30.	Hubungan Neutrofil Segmen dengan Luaran Pasien COVID-19	82
4.2.31.	Peran dan akurasi kadar D-dimer sebagai prognostik <i>survival</i> pada pasien COVID-19.....	83
4.2.32.	Pemodelan dan Penilaian Kualitas Model Prognostik Pasien COVID-19 Berdasarkan Identifikasi Faktor Risiko	85
4.2.33.	Pengujian <i>Confounding</i>	94
4.2.34.	Pengujian Interaksi	96
4.2.35.	Pengembangan Sistem Skoring Model.....	96
4.2.36.	Kekuatan Uji.....	99
4.3.	Pembahasan.....	100
4.3.1.	Karakteristik Pasien COVID-19	100
4.3.2.	Pengembangan Skor Prognostik berdasarkan Faktor Risiko yang Diidentifikasi.....	101
4.3.3.	Faktor Prediktor Kematian Pasien COVID-19	105
4.4.	Keterbatasan Penelitian.....	117
BAB V KESIMPULAN DAN SARAN		118
5.1.	Kesimpulan	118
5.2.	Saran	119
DAFTAR PUSTAKA		120
LAMPIRAN.....		144

DAFTAR TABEL

	Halaman
Tabel 3.1 Definisi Operasional	36
Tabel 4.1 Gambaran kadar D-dimer, demografik, komorbid, gejala, vaksinasi, waktu <i>onset</i> , pemeriksaan vital, pemeriksaan hematologi, dan luaran pasien COVID-19.....	47
Tabel 4.2 Perbedaan kadar D-dimer berdasarkan luaran pasien COVID-19... ..	50
Tabel 4.3 Hubungan kadar D-dimer dengan luaran pasien COVID-19.....	51
Tabel 4.4 Perbedaan usia berdasarkan luaran pasien COVID-19	52
Tabel 4.5 Hubungan usia dengan luaran pasien COVID-19	52
Tabel 4.6 Hubungan jenis kelamin dengan luaran pasien COVID-19.....	53
Tabel 4.7 Perbedaan IMT berdasarkan luaran pasien COVID-19	54
Tabel 4.8 Hubungan IMT dengan luaran pasien COVID-19.....	54
Tabel 4.9 Hubungan komorbid hipertensi dengan luaran pasien COVID-19..	55
Tabel 4.10 Hubungan komorbid DM dengan luaran pasien COVID-19	56
Tabel 4.11 Hubungan komorbid CVD dengan luaran pasien COVID-19	56
Tabel 4.12 Hubungan komorbid autoimun dengan luaran pasien COVID-19.	57
Tabel 4.13 Hubungan komorbid ginjal dengan luaran pasien COVID-19.....	58
Tabel 4.14 Hubungan komorbid TBC dengan luaran pasien COVID-19	59
Tabel 4.15 Hubungan komorbid PPOK dengan luaran pasien COVID-19	60
Tabel 4.16 Hubungan gejala dengan luaran pasien COVID-19.....	61
Tabel 4.17 Hubungan vaksinasi dengan luaran pasien COVID-19	62
Tabel 4.18 Perbedaan waktu <i>onset</i> berdasarkan luaran pasien COVID-19	63
Tabel 4.19 Hubungan waktu <i>onset</i> dengan luaran pasien COVID-19.....	63
Tabel 4.20 Perbedaan MAP berdasarkan luaran pasien COVID-19.....	64
Tabel 4.21 Hubungan MAP dengan luaran pasien COVID-19.....	64
Tabel 4.22 Perbedaan denyut nadi berdasarkan luaran pasien COVID-19.....	65
Tabel 4.23 Hubungan denyut nadi dengan luaran pasien COVID-19	66
Tabel 4.24 Perbedaan saturasi oksigen berdasarkan luaran pasien COVID-1966	
Tabel 4.25 Hubungan saturasi oksigen dengan luaran pasien COVID-19.....	67
Tabel 4.26 Perbedaan laju pernapasan berdasarkan luaran pasien COVID-19	68

Tabel 4.27 Hubungan laju pernapasan dengan luaran pasien COVID-19	68
Tabel 4.28 Perbedaan suhu tubuh berdasarkan luaran pasien COVID-19.....	69
Tabel 4.29 Hubungan suhu tubuh dengan luaran pasien COVID-19.....	70
Tabel 4.30 Perbedaan hemoglobin berdasarkan luaran pasien COVID-19	71
Tabel 4.31 Hubungan hemoglobin dengan luaran pasien COVID-19	71
Tabel 4.32 Perbedaan hematokrit berdasarkan luaran pasien COVID-19	72
Tabel 4.33 Hubungan hematokrit dengan luaran pasien COVID-19.....	72
Tabel 4.34 Perbedaan leukosit berdasarkan luaran pasien COVID-19.....	73
Tabel 4.35 Hubungan leukosit dengan luaran pasien COVID-19.....	74
Tabel 4.36 Perbedaan trombosit berdasarkan luaran pasien COVID-19	74
Tabel 4.37 Hubungan trombosit dengan luaran pasien COVID-19.....	75
Tabel 4.38 Perbedaan eritrosit berdasarkan luaran pasien COVID-19	76
Tabel 4.39 Hubungan eritrosit dengan luaran pasien COVID-19	76
Tabel 4.40 Perbedaan basofil berdasarkan luaran pasien COVID-19.....	77
Tabel 4.41 Hubungan basofil dengan luaran pasien COVID-19	77
Tabel 4.42 Perbedaan eosinofil berdasarkan luaran pasien COVID-19	78
Tabel 4.43 Hubungan eosinofil dengan luaran pasien COVID-19	78
Tabel 4.44 Perbedaan limfosit berdasarkan luaran pasien COVID-19	79
Tabel 4.45 Hubungan limfosit dengan luaran pasien COVID-19.....	80
Tabel 4.46 Perbedaan monosit berdasarkan luaran pasien COVID-19.....	81
Tabel 4.47 Hubungan monosit dengan luaran pasien COVID-19	81
Tabel 4.48 Perbedaan neutrofil segmen berdasarkan luaran pasien COVID-19	82
Tabel 4.49 Hubungan neutrofil segmen dengan luaran pasien COVID-19	82
Tabel 4.50 Peran dan akurasi D-dimer sebagai prognostik <i>survival</i> pasien COVID-19.....	83
Tabel 4.51 Hasil Seleksi Bivariat.....	85
Tabel 4.52 Hasil uji multivariat tahap awal model 1	87
Tabel 4.53 Hasil uji multivariat tahap akhir model 1.....	88
Tabel 4.54 Penilaian Kualitas Model 1	88
Tabel 4.55 Hasil uji multivariat tahap awal model 2	90
Tabel 4.56 Hasil uji multivariat tahap akhir model 2.....	90

Tabel 4.57 Penilaian Kualitas Model 2	91
Tabel 4.58 Hasil uji multivariat tahap awal model 3	92
Tabel 4.59 Hasil uji multivariat tahap akhir model 3.....	92
Tabel 4.60 Penilaian Kualitas Model 3	93
Tabel 4.61 Uji <i>confounding</i> jenis kelamin pada model 1.....	95
Tabel 4.62 Uji <i>confounding</i> IMT pada model 1.....	95
Tabel 4.63 Uji <i>confounding</i> waktu <i>onset</i> pada model 1.....	95
Tabel 4.64 Interaksi usia dan waktu <i>onset</i> pada model 1.....	96
Tabel 4.65 Skor untuk setiap prediktor dari model 1.....	97
Tabel 4.66 Model 2 berdasarkan usia	97

DAFTAR GAMBAR

	Halaman
Gambar 2.1 Struktur SARS-CoV-2	7
Gambar 2.2 Deteksi antigen rekombinan spesifik SARS-CoV-2	17
Gambar 2.3 Proses pembentukan D-dimer	21
Gambar 2.4 Uji Diagnostik untuk Kuantifikasi D-dimer.....	23
Gambar 2.5 Teori Trias Virchow	25
Gambar 2.6 Kerangka Teori.....	28
Gambar 2.7 Kerangka Konsep	29
Gambar 3.1 Alur Penelitian.....	45
Gambar 4.1 Kurva <i>survival</i> COVID-19 berdasarkan kadar D-dimer	84
Gambar 4.2 Contoh kartu skoring pasien COVID-19.....	98

DAFTAR LAMPIRAN

	Halaman
Lampiran 1. Nilai Rujukan Hasil Pemeriksaan Laboratorium.....	142
Lampiran 2. Sertifikat Etik.....	145
Lampiran 3. Hasil Analisis Statistik	146
Lampiran 4. Syntax Stata	186
Lampiran 5. Matriks Perbaikan Ujian Tesis	199

DAFTAR SINGKATAN

ACE	: <i>Angiotensin Converting Enzym</i>
ACEI	: <i>Angiotensin Converting Enzym Inhibitor</i>
ADAMTS13	: <i>A Disintegrin and Metalloprotease with Thrombospondin Type 1 Repeats-13</i>
ALC	: <i>Absolute Lymphocyte Count</i>
ALT	: <i>Alanin Aminotransferase</i>
ARB	: <i>Angiotensin Receptors Blockers</i>
ARDS	: <i>Acute Respiratory Distress Syndrome</i>
ASEAN	: <i>Association of Southeast Asian Nations</i>
AST	: <i>Aspartate Aminotransferase</i>
AT	: <i>Antitrombin</i>
AUC	: <i>Area Under Curve</i>
CDC	: <i>Centers of Disease Control</i>
CEP	: <i>Composite End-Point</i>
CFR	: <i>Case Fatality Rate</i>
COVID-19	: <i>Corona Virus Disease 19</i>
CRP	: <i>C-Reactive Protein</i>
CSSE	: <i>Center for Systems Science and Engineering</i>
Ct value	: <i>Cycle Threshold Value</i>
CVD	: <i>Cardiovascular Disease</i>
DIC	: <i>Disseminated Intravascular Coagulation</i>
DM	: <i>Diabetes Melitus</i>
DVT	: <i>Deep Vein Thrombosis</i>
ELFA	: <i>Enzym Linked Immunofluorescent Assay</i>
ELISA	: <i>Enzym Linked Immunosorbent Assay</i>
HR	: <i>Hazard Ratio</i>
hs-CRP	: <i>high-sensitivity C-reactive protein</i>
HWF	: <i>Hierarchically Well Formulated</i>
IBV	: <i>Infectious Bronchitis Virus</i>
ICTV	: <i>The Internasional Committee on Taxonomy of Viruses</i>

ICU	: <i>Intensive Care Unit</i>
IFN	: <i>Interferon</i>
IgA	: <i>Imunoglobulin A</i>
IgG	: <i>Imunoglobulin G</i>
IgM	: <i>Imunoglobulin M</i>
IL	: <i>Interleukin</i>
IMT	: <i>Indeks Massa Tubuh</i>
ISARIC	: <i>Internasional Severe Acute Respiratory and Emerging Infection Consortium</i>
ISPA	: <i>Infeksi Saluran Pernapasan Akut</i>
LDH	: <i>Lactate Dehydrogenase</i>
MAP	: <i>Mean Arterial Pressure</i>
MERS-CoV	: <i>Middle East Respiratory Syndrome Coronavirus</i>
MHV	: <i>Mouse Hepatitis Virus</i>
MLR	: <i>Monocyte-Lymphocyte Rasio</i>
NAAT	: <i>Nucleic Acid Amplification Test</i>
NLR	: <i>Neutrophil-Lymphocyte Ratio</i>
NO	: <i>Nitric Oxide</i>
PE	: <i>Pulmonary Embolism</i>
PHEOC	: <i>Public Health Emergency Operation Center</i>
PLR	: <i>Platelet-Lymphocyte Rasio</i>
PT	: <i>Prothrombin Time</i>
RNA	: <i>Ribonucleic Acid</i>
ROC	: <i>Receiver Operating Characteristic</i>
RSUD	: <i>Rumah Sakit Umum Daerah</i>
rRT-PCR	: <i>Real-time Reverse-Transcriptase Polymerase Chain Reaction</i>
RT-PCR	: <i>Real Time Polymerase Chain Reaction</i>
SARS-CoV-2	: <i>Severe Acute Respiratory Syndrome Coronavirus 2</i>
SK	: <i>Surat Keputusan</i>
ssRNA	: <i>Positive-sense Single-Stranded RNA</i>
ssRNA-	: <i>Negative-sense Single-Stranded RNA</i>
TLR-4	: <i>Toll Like Receptor 4</i>

TMPRSS2	: <i>Transmembrane protease serine 2</i>
TNF- α	: <i>Tumor Necrosis Factor Alpha</i>
VTE	: <i>Venous Thromboembolism</i>
vWF	: <i>von Willebrand Factor</i>
WHO	: <i>World Health Organization</i>

BAB I

PENDAHULUAN

1.1. Latar Belakang

Corona Virus Disease 19 atau yang disebut dengan COVID-19 adalah penyakit infeksi yang disebabkan oleh corona virus yang diberi nama SARS-CoV karena homologi genomnya (P. Zhou *et al.*, 2020). Coronavirus adalah virus RNA untai tunggal (+ssRNA) yang besar dan positif dari famili Coronaviridae. Coronavirus dapat menginfeksi berbagai vertebrata, termasuk kelelawar, burung, trenggiling, ular, tikus, dan manusia (Andersen *et al.*, 2020; Asselah *et al.*, 2021). Penyebaran virus COVID-19 dimulai dari peristiwa penularan zoonosis yang terjadi melalui Pasar Grosir Makanan Laut Huanan yang memperdagangkan hewan liar hidup dan kemudian berkembang menjadi penularan antar manusia (Li *et al.*, 2020; Chen *et al.*, 2020). Sejak Desember 2019, wabah penyakit COVID-19 ditemukan pertama kali di Kota Wuhan Provinsi Hube China dan menyebar ke seluruh dunia. Pada tanggal 11 Maret 2020, WHO mendeklarasikan COVID-19 sebagai pandemi (Gómez-Mesa *et al.*, 2021). Pandemi COVID-19 yang sudah menyebar ke seluruh dunia bahkan menyebabkan kematian. Secara global, terhitung sampai tanggal 7 Maret 2023, terdapat 759.408.703 kasus COVID-19 yang dikonfirmasi, termasuk 6.866.434 kematian, yang dilaporkan ke WHO. Kemudian, terhitung sampai tanggal 6 Maret 2023, total 13.229.471.213 dosis vaksin telah diberikan (WHO, 2023).

Di Indonesia, terhitung sampai tanggal 12 Maret 2023 terdapat 6.739.067 kasus terkonfirmasi COVID-19 yang terbagi menjadi 6.574.788 (97,6%) kasus sembuh, 160.948 (2,4%) kasus meninggal, dan sebanyak 3.331 masih kasus aktif (PHEOC Kemkes RI, 2023). Indonesia menempati peringkat pertama dengan kasus COVID-19 terbanyak di ASEAN pada tahun 2021 yaitu sebanyak 4.253.598 kasus (Kementerian Kesehatan RI, 2021). Menurut laporan mingguan penanganan COVID-19 terhitung tanggal 18 Oktober 2021, pada periode bulan Juli 2021 diketahui adanya lonjakan kasus COVID-19 dan kematian yang cukup tinggi. Hal ini ada kaitannya dengan mobilitas penduduk. Hampir di semua provinsi, mobilitas penduduk pada bulan Mei 2021 rata-rata lebih tinggi dibandingkan dengan bulan-

bulan sebelumnya, yang mana pada bulan tersebut terdapat hari libur panjang, sehingga terjadi lonjakan kasus COVID-19 pada bulan Juli 2021 (Kemenkes RI, 2021).

Berdasarkan Profil Kesehatan Indonesia tahun 2021 angka kematian (*Case Fatality Rate / CFR*) COVID-19 di Indonesia sebesar 3,4%. Sumatera Selatan merupakan provinsi peringkat ke-5 dengan CFR lebih besar dibandingkan angka nasional yaitu sebesar 5,1% setelah Lampung (7,8%), Jawa Timur (7,4%), Jawa Tengah (6,2%), dan Aceh (5,4%) (Kementerian Kesehatan RI, 2022). Kematian terkait COVID-19 sebagian besar terkait dengan hiperkoagulabilitas dan peningkatan risiko kejadian tromboemboli vena (VTE), yang mengarah ke peradangan trombosis dalam kondisi parah (Zhan et al., 2021). Komplikasi dan koagulopati arteri dan vena trombotik termasuk *Disseminated Intravascular Coagulation (DIC)* telah menjadi penyebab utama morbiditas dan mortalitas terutama pada pasien dengan kondisi komorbiditas, rawat inap berkepanjangan, masuk *Intensive Care Unit (ICU)*, dan ventilasi mekanik. Peradangan yang berlebihan, aktivasi trombosit, disfungsi endotel, dan stasis memainkan peran penting dalam perkembangan komplikasi trombotik (Gungor et al., 2021).

Sebuah studi telah melaporkan bahwa COVID-19 dikaitkan dengan kelainan hemostatik dan peningkatan kadar D-dimer yang berhubungan dengan kematian pasien (Tang et al., 2020; Zhang et al., 2020). D-dimer adalah produk degradasi fibrin dan mencerminkan aktivasi jalur trombotik dan fibrinolitik (Henry and Lippi, 2020; Thachil, Tang, et al., 2020; Xiong, Liang and Wei, 2020; Zhang et al., 2020). Diantara parameter klinis dan biokimia yang terkait dengan prognosis yang buruk, peningkatan kadar D-dimer menjadi prediksi untuk sindrom gangguan pernapasan akut (ISPA), kebutuhan untuk masuk ke unit perawatan intensif (ICU) atau kematian (Tang et al., 2020; Wu and McGoogan, 2020; Hassan et al., 2022). D-dimer dapat digunakan sebagai biomarker prognostik untuk mendiagnosis keadaan trombotik, termasuk emboli paru, trombosis arteri, dan DIC (Olson, 2015). Peningkatan D-dimer dilaporkan pada 35-40% pasien dengan COVID-19, terutama pada orang tua dan orang yang memiliki penyakit penyerta (Tang et al., 2020). D-dimer dianggap normal apabila nilainya kurang dari 0,5 µg/mL. D-dimer telah diidentifikasi sebagai indikator potensial untuk prognosis pada pasien COVID-19

(Bounds and Kok, 2023). Selain peningkatan kadar D-dimer, hasil pemeriksaan laboratorium yang buruk dapat menjadi penanda perburukan kondisi pasien yang juga didukung oleh faktor usia dan komorbiditas. Kondisi tersebut dapat mempengaruhi tingkat CEP (*Composite End-Point*) pada pasien COVID-19. CEP didefinisikan sebagai kondisi pasien yang membutuhkan akses unit perawatan intensif (ICU), ventilasi invasif, bahkan sampai pada kematian pasien COVID-19 (Driggin *et al.*, 2020).

Saat ini penelitian mengenai D-dimer sebagai prediktor kematian pasien COVID-19 di Provinsi Sumatera Selatan masih terbatas. Berdasarkan penjelasan latar belakang di atas, penelitian ini dilakukan untuk mengetahui akurasi D-dimer sebagai prediktor kematian pasien COVID-19 di RSUD Siti Fatimah. RSUD Siti Fatimah adalah salah satu rumah sakit rujukan pasien COVID-19 di Provinsi Sumatera Selatan berdasarkan SK Gubernur Sumsel Nomor 201/KTPS/DINKES/2020 yang diterbitkan pada 23 Maret 2020.

1.2. Rumusan Masalah

Sejak Desember 2019, wabah penyakit COVID-19 menyebar bahkan menyebabkan kematian ke seluruh dunia. Terhitung sampai tanggal 7 Maret 2023, terdapat 6.866.434 kasus kematian akibat COVID-19 yang dilaporkan ke WHO. Di Indonesia, terhitung sampai tanggal 12 Maret 2023 terdapat 6.739.067 kasus terkonfirmasi COVID-19 yang terbagi menjadi 6.574.788 (97,6%) kasus sembuh dan 160.948 (2,4%) kasus meninggal. Indonesia menempati peringkat pertama dengan kasus COVID-19 terbanyak di ASEAN pada tahun 2021 yaitu sebanyak 4.253.598 kasus. Menurut laporan mingguan penanganan COVID-19 pada bulan Juli 2021 diketahui adanya lonjakan kasus COVID-19 dan kematian yang cukup tinggi yang diduga ada kaitannya dengan mobilitas penduduk. Berdasarkan Profil Kesehatan Indonesia tahun 2021 angka kematian (*Case Fatality Rate / CFR*) COVID-19 di Indonesia sebesar 3,4%. Sumatera Selatan merupakan provinsi peringkat ke-5 dengan CFR lebih besar dibandingkan angka nasional yaitu sebesar 5,1%. Sehubungan dengan merebaknya pandemi COVID-19, D-dimer telah diidentifikasi sebagai indikator potensial untuk prognosis pada pasien COVID-19 disertai dengan kondisi pemeriksaan laboratorium yang buruk dan dipengaruhi

faktor lain seperti usia dan komorbid. Oleh karena itu penelitian ini dilakukan untuk mengetahui akurasi D-dimer sebagai prediktor kematian pasien COVID-19 di RSUD Siti Fatimah.

1.3. Tujuan Penelitian

1.3.1. Tujuan Umum

Mengetahui akurasi D-dimer sebagai prediktor kematian pasien COVID-19 di RSUD Siti Fatimah.

1.3.2. Tujuan Khusus

Tujuan khusus penelitian ini adalah:

1. Mengidentifikasi gambaran kadar D-dimer, demografik (usia, jenis kelamin, IMT), komorbid, gejala, vaksinasi, waktu *onset*, pemeriksaan vital (*mean arterial pressure*/MAP, denyut nadi, saturasi oksigen, laju pernapasan, suhu tubuh), pemeriksaan hematologi (hemoglobin, hematokrit, leukosit, trombosit, eritrosit, basofil, eosinofil, limfosit, monosit, neutrofil segmen), dan luaran pasien COVID-19 di RSUD Siti Fatimah.
2. Menganalisis hubungan D-dimer dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
3. Menganalisis hubungan usia dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
4. Menganalisis hubungan jenis kelamin dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
5. Menganalisis hubungan indeks massa tubuh (IMT) dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
6. Menganalisis hubungan komorbid hipertensi dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
7. Menganalisis hubungan komorbid diabetes melitus dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
8. Menganalisis hubungan komorbid *cardiovascular disease* (CVD) dengan luaran pasien COVID-19 di RSUD Siti Fatimah.

9. Menganalisis hubungan komorbid autoimun dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
10. Menganalisis hubungan komorbid ginjal dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
11. Menganalisis hubungan komorbid *tuberculosis* (TBC) dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
12. Menganalisis hubungan komorbid penyakit paru obstruktif kronis (PPOK) dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
13. Menganalisis hubungan gejala dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
14. Menganalisis hubungan vaksinasi dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
15. Menganalisis hubungan waktu *onset* dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
16. Menganalisis hubungan *mean arterial pressure* (MAP) dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
17. Menganalisis hubungan denyut nadi dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
18. Menganalisis hubungan saturasi oksigen dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
19. Menganalisis hubungan laju pernapasan dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
20. Menganalisis hubungan suhu tubuh dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
21. Menganalisis hubungan hemoglobin dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
22. Menganalisis hubungan hematokrit dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
23. Menganalisis hubungan leukosit dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
24. Menganalisis hubungan trombosit dengan luaran pasien COVID-19 di RSUD Siti Fatimah.

25. Menganalisis hubungan eritrosit dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
26. Menganalisis hubungan basofil dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
27. Menganalisis hubungan eosinofil dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
28. Menganalisis hubungan limfosit dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
29. Menganalisis hubungan monosit dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
30. Menganalisis hubungan neutrofil segmen dengan luaran pasien COVID-19 di RSUD Siti Fatimah.
31. Menganalisis peran D-dimer dan mengetahui akurasi D-dimer sebagai prognostik *survival* pada pasien COVID-19 di RSUD Siti Fatimah.
32. Mengembangkan skor prognostik untuk pasien COVID-19 berdasarkan penemuan faktor-faktor risiko yang diidentifikasi dengan mempertimbangkan variabel kandidat *confounding*.

1.4. Manfaat Penelitian

1.4.1. Manfaat Teoritis

Penelitian ini diharapkan dapat bermanfaat untuk memberikan dasar ilmiah dalam melengkapi landasan teoritis dan pemahaman patogenesis tentang peran D-dimer pada pasien COVID-19, khususnya mengenai hubungannya dengan prognostik *survival*-nya. Serta mengenai hubungan antara gambaran demografik, klinis dan hasil laboratorium terhadap *survival* pasien COVID-19.

1.4.2. Manfaat Praktis

Penelitian ini diharapkan dapat menjadi salah satu pendukung perlunya mengukur kadar D-dimer pada saat masuk rumah sakit sebagai prediktor kematian pasien COVID-19. Selanjutnya, diharapkan agar penelitian ini dapat membuka peluang untuk melakukan penelitian lebih lanjut mengenai peran D-dimer dan mediator lain pada COVID-19.

DAFTAR PUSTAKA

- Abayomi, A. *et al.* (2021) 'Presenting Symptoms and Predictors of Poor Outcomes Among 2,184 Patients with COVID-19 in Lagos State, Nigeria', *International Journal of Infectious Diseases*, 102, pp. 226–232. Available at: <https://doi.org/10.1016/j.ijid.2020.10.024>.
- Abdulkhaleq, L.A. *et al.* (2018) 'The crucial roles of inflammatory mediators in inflammation: A review', *Veterinary World*, 11(5), pp. 627–635. Available at: <https://doi.org/10.14202/vetworld.2018.627-635>.
- Acter, T. *et al.* (2020) 'Evolution of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as coronavirus disease 2019 (COVID-19) pandemic: A global health emergency', *Science of The Total Environment*, 730, p. 138996. Available at: <https://doi.org/10.1016/j.scitotenv.2020.138996>.
- Adam, S.S., Key, N.S. and Greenberg, C.S. (2009) 'D-dimer antigen: current concepts and future prospects', *Blood*, 113(13), pp. 2878–2887. Available at: <https://doi.org/10.1182/blood-2008-06-165845>.
- Aggarwal, A.N. *et al.* (2021) 'Active pulmonary tuberculosis and coronavirus disease 2019: A systematic review and meta-analysis', *PLOS ONE*, 16(10), p. e0259006. Available at: <https://doi.org/10.1371/journal.pone.0259006>.
- Aggarwal, M., Dass, J. and Mahapatra, M. (2020) 'Hemostatic Abnormalities in COVID-19: An Update', *Indian Journal of Hematology and Blood Transfusion*, 36(4), pp. 616–626. Available at: <https://doi.org/10.1007/s12288-020-01328-2>.
- Ahmad, T. *et al.* (2020) 'COVID-19: The Emerging Immunopathological Determinants for Recovery or Death', *Frontiers in Microbiology*, 11. Available at: <https://doi.org/10.3389/fmicb.2020.588409>.
- Andersen, K.G. *et al.* (2020) 'The proximal origin of SARS-CoV-2', *Nature Medicine*, 26(4), pp. 450–452. Available at: <https://doi.org/10.1038/s41591-020-0820-9>.
- Andersson-Evelönn, E. *et al.* (2020) 'Combining epigenetic and clinicopathological variables improves specificity in prognostic prediction in clear cell renal cell

- carcinoma', *Journal of Translational Medicine*, 18(1), p. 435. Available at: <https://doi.org/10.1186/s12967-020-02608-1>.
- Angela, K.A.P. and Sumohadi, I.M.D. (2022) 'Hubungan D-dimer dengan tingkat keparahan infeksi COVID-19', *Intisari Sains Medis*, 13(2), pp. 393–398. Available at: <https://doi.org/10.15562/ism.v13i2.1412>.
- Asakura, H. and Ogawa, H. (2021) 'COVID-19-associated coagulopathy and disseminated intravascular coagulation', *International Journal of Hematology*, 113(1), pp. 45–57. Available at: <https://doi.org/10.1007/s12185-020-03029-y>.
- Asselah, T. *et al.* (2021) 'COVID-19: Discovery, diagnostics and drug development', *Journal of Hepatology*, 74(1), pp. 168–184. Available at: <https://doi.org/10.1016/j.jhep.2020.09.031>.
- Astuti, I. and Ysrafil (2020) 'Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): An overview of viral structure and host response', *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 14(4), pp. 407–412. Available at: <https://doi.org/10.1016/j.dsx.2020.04.020>.
- Bae, SungA *et al.* (2021) 'Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis', *Heart*, 107(5), pp. 373–380. Available at: <https://doi.org/10.1136/heartjnl-2020-317901>.
- Bae, Sohyun *et al.* (2021) 'New Scoring System for Predicting Mortality in Patients with COVID-19', *Yonsei Medical Journal*, 62(9), p. 806. Available at: <https://doi.org/10.3349/ymj.2021.62.9.806>.
- Bansal, H. and Mittal, R. (2020) 'COVID-19: A Global Health Emergency', *International Journal of Research and Analytical Review (IJRAR)*, 7(3), pp. 436–459. Available at: <https://doi.org/http://doi.one/10.1729/Journal.24043>.
- Berbudi, A. *et al.* (2020) 'Type 2 Diabetes and its Impact on the Immune System', *Current Diabetes Reviews*, 16(5), pp. 442–449. Available at: <https://doi.org/10.2174/1573399815666191024085838>.
- Böhm, M. *et al.* (2020) 'Coronavirus Disease 2019 (COVID-19) and its implications for cardiovascular care: expert document from the German Cardiac Society and the World Heart Federation', *Clinical Research in*

- Cardiology*, 109(12), pp. 1446–1459. Available at: <https://doi.org/10.1007/s00392-020-01656-3>.
- Boopathi, S., Poma, A.B. and Kolandaivel, P. (2020) ‘Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment’, *Journal of Biomolecular Structure and Dynamics*, pp. 1–10. Available at: <https://doi.org/10.1080/07391102.2020.1758788>.
- Bounds, E.J. and Kok, S.J. (2023) *D Dimer*. StatPearls Publishing LLC. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK431064/> (Accessed: 15 June 2023).
- Brinkman, J.E., Toro, F. and Sharma, S. (2023) *Physiology, Respiratory Drive*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available at: <https://pubmed.ncbi.nlm.nih.gov/29494021/> (Accessed: 29 May 2023).
- Brümmer, L.E. *et al.* (2021) ‘Accuracy of novel antigen rapid diagnostics for SARS-CoV-2: A living systematic review and meta-analysis.’, *PLoS medicine*, 18(8), p. e1003735. Available at: <https://doi.org/10.1371/journal.pmed.1003735>.
- Basic, N. *et al.* (2022) ‘Vaccination provides protection from respiratory deterioration and death among hospitalized COVID-19 patients: Differences between vector and mRNA vaccines’, *Journal of Medical Virology*, 94(6), pp. 2849–2854. Available at: <https://doi.org/10.1002/jmv.27666>.
- Cao, Y. *et al.* (2020) ‘Digital PCR as an Emerging Tool for Monitoring of Microbial Biodegradation.’, *Molecules (Basel, Switzerland)*, 25(3). Available at: <https://doi.org/10.3390/molecules25030706>.
- Cascella, M. *et al.* (2023) *Features, Evaluation, and Treatment of Coronavirus (COVID-19)*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK554776/> (Accessed: 29 July 2023).
- CDC (2023) *Test for Past Infection*. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/testing/serology-overview.html> (Accessed: 1 July 2023).

- Cegolon, L. *et al.* (2020) 'Hypothesis to explain the severe form of COVID-19 in Northern Italy', *BMJ Global Health*, 5(6), p. e002564. Available at: <https://doi.org/10.1136/bmjgh-2020-002564>.
- Chan, J.F.-W. *et al.* (2020) 'A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster', *The Lancet*, 395(10223), pp. 514–523. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30154-9](https://doi.org/10.1016/S0140-6736(20)30154-9).
- Channappanavar, R. and Perlman, S. (2017) 'Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology', *Seminars in Immunopathology*, 39(5), pp. 529–539. Available at: <https://doi.org/10.1007/s00281-017-0629-x>.
- Chen, G. *et al.* (2020) 'Clinical and immunological features of severe and moderate coronavirus disease 2019', *Journal of Clinical Investigation*, 130(5), pp. 2620–2629. Available at: <https://doi.org/10.1172/JCI137244>.
- Chen, L.-D. *et al.* (2020) 'Association between cytokine profiles and lung injury in COVID-19 pneumonia', *Respiratory Research*, 21(1), p. 201. Available at: <https://doi.org/10.1186/s12931-020-01465-2>.
- Chen, N. *et al.* (2020) 'Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study', *The Lancet*, 395(10223), pp. 507–513. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7).
- Chilamakuri, R. and Agarwal, S. (2021) 'COVID-19: Characteristics and Therapeutics', *Cells*, 10(2), p. 206. Available at: <https://doi.org/10.3390/cells10020206>.
- Cho, S.-Y. *et al.* (2021) 'Prognosis Score System to Predict Survival for COVID-19 Cases: a Korean Nationwide Cohort Study.', *Journal of medical Internet research*, 23(2), p. e26257. Available at: <https://doi.org/10.2196/26257>.
- Chung, I. and Lip, G.Y.H. (2003) 'Virchow's Triad Revisited: Blood Constituents', *Pathophysiology of Haemostasis and Thrombosis*, 33(5–6), pp. 449–454. Available at: <https://doi.org/10.1159/000083844>.

- Coccia, E.M. and Battistini, A. (2015) 'Early IFN type I response: Learning from microbial evasion strategies', *Seminars in Immunology*, 27(2), pp. 85–101. Available at: <https://doi.org/10.1016/j.smim.2015.03.005>.
- Cong, Y., Verlhac, P. and Reggiori, F. (2017) 'The Interaction between Nidovirales and Autophagy Components', *Viruses*, 9(7), p. 182. Available at: <https://doi.org/10.3390/v9070182>.
- Connors, J.M. (2017) 'Thrombophilia Testing and Venous Thrombosis', *New England Journal of Medicine*, 377(12), pp. 1177–1187. Available at: <https://doi.org/10.1056/NEJMra1700365>.
- Connors, J.M. and Levy, J.H. (2020) 'COVID-19 and its implications for thrombosis and anticoagulation.', *Blood*, 135(23), pp. 2033–2040. Available at: <https://doi.org/10.1182/blood.2020006000>.
- Cordero, A. *et al.* (2021) 'Mortality associated with cardiovascular disease in patients with COVID-19', *REC: CardioClinics*, 56(1), pp. 30–38. Available at: <https://doi.org/10.1016/j.rccl.2020.10.005>.
- Costela-Ruiz, V.J. *et al.* (2020) 'SARS-CoV-2 infection: The role of cytokines in COVID-19 disease', *Cytokine & Growth Factor Reviews*, 54, pp. 62–75. Available at: <https://doi.org/10.1016/j.cytogfr.2020.06.001>.
- CSSE (2023) *COVID-19 Maps*. Available at: <https://coronavirus.jhu.edu/map.html> (Accessed: 1 July 2023).
- Cui, J., Li, F. and Shi, Z.-L. (2019) 'Origin and evolution of pathogenic coronaviruses', *Nature Reviews Microbiology*, 17(3), pp. 181–192. Available at: <https://doi.org/10.1038/s41579-018-0118-9>.
- Devreese, K.M.J. (2021) 'COVID-19–related laboratory coagulation findings', *International Journal of Laboratory Hematology*, 43(S1), pp. 36–42. Available at: <https://doi.org/10.1111/ijlh.13547>.
- Djharuddin, I. *et al.* (2021) 'Comorbidities and mortality in COVID-19 patients', *Gaceta Sanitaria*, 35, pp. S530–S532. Available at: <https://doi.org/10.1016/j.gaceta.2021.10.085>.
- Driggin, E. *et al.* (2020) 'Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic.', *Journal of*

- the American College of Cardiology*, 75(18), pp. 2352–2371. Available at: <https://doi.org/10.1016/j.jacc.2020.03.031>.
- Du, Y. *et al.* (2021) ‘Hypertension is a clinically important risk factor for critical illness and mortality in COVID-19: A meta-analysis’, *Nutrition, Metabolism and Cardiovascular Diseases*, 31(3), pp. 745–755. Available at: <https://doi.org/10.1016/j.numecd.2020.12.009>.
- Effenberger, M. *et al.* (2021) ‘Systemic inflammation as fuel for acute liver injury in COVID-19’, *Digestive and Liver Disease*, 53(2), pp. 158–165. Available at: <https://doi.org/10.1016/j.dld.2020.08.004>.
- Eljilany, I. and Elzouki, A.-N. (2020) ‘D-Dimer, Fibrinogen, and IL-6 in COVID-19 Patients with Suspected Venous Thromboembolism: A Narrative Review’, *Vascular Health and Risk Management*, Volume 16, pp. 455–462. Available at: <https://doi.org/10.2147/VHRM.S280962>.
- Elo, I.T. *et al.* (2022) ‘Evaluation of Age Patterns of COVID-19 Mortality by Race and Ethnicity From March 2020 to October 2021 in the US’, *JAMA Network Open*, 5(5), p. e2212686. Available at: <https://doi.org/10.1001/jamanetworkopen.2022.12686>.
- Elziny, M.M. *et al.* (2021) ‘Case Report: Development of Miliary Pulmonary Tuberculosis in a Patient with Peritoneal Tuberculosis after COVID-19 Upper Respiratory Tract Infection’, *The American Journal of Tropical Medicine and Hygiene*, 104(5), pp. 1792–1795. Available at: <https://doi.org/10.4269/ajtmh.20-1156>.
- Fahey, E. and Doyle, S.L. (2019) ‘IL-1 Family Cytokine Regulation of Vascular Permeability and Angiogenesis’, *Frontiers in Immunology*, 10. Available at: <https://doi.org/10.3389/fimmu.2019.01426>.
- Favresse, J. *et al.* (2018) ‘D-dimer: Preanalytical, analytical, postanalytical variables, and clinical applications’, *Critical Reviews in Clinical Laboratory Sciences*, 55(8), pp. 548–577. Available at: <https://doi.org/10.1080/10408363.2018.1529734>.
- Felsenstein, S. *et al.* (2020) ‘COVID-19: Immunology and treatment options’, *Clinical Immunology*, 215, p. 108448. Available at: <https://doi.org/10.1016/j.clim.2020.108448>.

- Ferlita, S. *et al.* (2019) 'Type 2 Diabetes Mellitus and Altered Immune System Leading to Susceptibility to Pathogens, Especially Mycobacterium tuberculosis', *Journal of Clinical Medicine*, 8(12), p. 2219. Available at: <https://doi.org/10.3390/jcm8122219>.
- Ferrari, D. *et al.* (2020) 'Routine blood tests as a potential diagnostic tool for COVID-19', *Clinical Chemistry and Laboratory Medicine (CCLM)*, 58(7), pp. 1095–1099. Available at: <https://doi.org/10.1515/cclm-2020-0398>.
- Freeman, B. *et al.* (2020) 'Validation of a SARS-CoV-2 spike protein ELISA for use in contact investigations and serosurveillance.', *bioRxiv: the preprint server for biology* [Preprint]. Available at: <https://doi.org/10.1101/2020.04.24.057323>.
- Fu, J. *et al.* (2020) 'The clinical implication of dynamic neutrophil to lymphocyte ratio and D-dimer in COVID-19: A retrospective study in Suzhou China', *Thrombosis Research*, 192, pp. 3–8. Available at: <https://doi.org/10.1016/j.thromres.2020.05.006>.
- Gaffney, P.J. and Joe, F. (1979) 'The lysis of crosslinked human fibrin by plasmin yields initially a single molecular complex, D dimer-E', *Thrombosis Research*, 15(5–6), pp. 673–687. Available at: [https://doi.org/10.1016/0049-3848\(79\)90177-4](https://doi.org/10.1016/0049-3848(79)90177-4).
- Girardin, J.-L. *et al.* (2021) 'Contribution of pulmonary diseases to COVID-19 mortality in a diverse urban community of New York', *Chronic Respiratory Disease*, 18, p. 147997312098680. Available at: <https://doi.org/10.1177/1479973120986806>.
- Goldstein, J.R. and Lee, R.D. (2020) 'Demographic perspectives on the mortality of COVID-19 and other epidemics', *Proceedings of the National Academy of Sciences*, 117(36), pp. 22035–22041. Available at: <https://doi.org/10.1073/pnas.2006392117>.
- Gómez-Mesa, J.E. *et al.* (2021) 'Thrombosis and Coagulopathy in COVID-19', *Current Problems in Cardiology*, 46(3), p. 100742. Available at: <https://doi.org/10.1016/j.cpcardiol.2020.100742>.
- Gonzales, J.N., Lucas, R. and Verin, A.D. (2015) 'The Acute Respiratory Distress Syndrome: Mechanisms and Perspective Therapeutic Approaches.', *Austin*

- journal of vascular medicine*, 2(1), p. 1009. Available at: <https://pubmed.ncbi.nlm.nih.gov/26973981/> (Accessed: 29 April 2023).
- Guan, W., Ni, Z., *et al.* (2020) 'Clinical Characteristics of Coronavirus Disease 2019 in China', *New England Journal of Medicine*, 382(18), pp. 1708–1720. Available at: <https://doi.org/10.1056/NEJMoa2002032>.
- Guan, W., Liang, W., *et al.* (2020) 'Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis', *European Respiratory Journal*, 55(5), p. 2000547. Available at: <https://doi.org/10.1183/13993003.00547-2020>.
- Gungor, B. *et al.* (2021) 'Elevated D-dimer levels on admission are associated with severity and increased risk of mortality in COVID-19: A systematic review and meta-analysis', *The American Journal of Emergency Medicine*, 39, pp. 173–179. Available at: <https://doi.org/10.1016/j.ajem.2020.09.018>.
- Gupta, N. *et al.* (2020) 'A profile of a retrospective cohort of 22 patients with COVID-19 and active/treated tuberculosis', *European Respiratory Journal*, 56(5), p. 2003408. Available at: <https://doi.org/10.1183/13993003.03408-2020>.
- Hager, K. and Platt, D. (1995) 'Fibrin Degeneration Product Concentrations (D-Dimers) in the Course of Ageing', *Gerontology*, 41(3), pp. 159–165. Available at: <https://doi.org/10.1159/000213677>.
- Haji Aghajani, M. *et al.* (2022) 'Six-Month Follow-up of COVID-19 Patients: Mortality and Related Factors', *Archives of Iranian Medicine*, 25(8), pp. 557–563. Available at: <https://doi.org/10.34172/aim.2022.89>.
- Handayani, D. *et al.* (2020) 'Corona Virus Disease 2019', *Jurnal Respirologi Indonesia*, 40(2), pp. 119–129. Available at: <https://doi.org/10.36497/jri.v40i2.101>.
- Hanley, J.A. and McNeil, B.J. (1982) 'The meaning and use of the area under a receiver operating characteristic (ROC) curve.', *Radiology*, 143(1), pp. 29–36. Available at: <https://doi.org/10.1148/radiology.143.1.7063747>.
- Harlan, J. (2017) *Analisis Survival*. Depok: Gunadarma.
- Hassan, S. *et al.* (2022) 'The usefulness of D-dimer as a predictive marker for mortality in patients with COVID-19 hospitalized during the first wave in

- Italy', *PLOS ONE*, 17(7), p. e0264106. Available at: <https://doi.org/10.1371/journal.pone.0264106>.
- Hathcock, J.J. (2006) 'Flow effects on coagulation and thrombosis.', *Arteriosclerosis, thrombosis, and vascular biology*, 26(8), pp. 1729–37. Available at: <https://doi.org/10.1161/01.ATV.0000229658.76797.30>.
- Henry, B.M. and Lippi, G. (2020) 'Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection', *International Urology and Nephrology*, 52(6), pp. 1193–1194. Available at: <https://doi.org/10.1007/s11255-020-02451-9>.
- Henry, B.M. and Vikse, J. (2020) 'Clinical Characteristics of Covid-19 in China', *New England Journal of Medicine*, 382(19), pp. 1859–1862. Available at: <https://doi.org/10.1056/NEJMc2005203>.
- Hoeprich, P.D. and Doolittle, R.F. (1983) 'Dimeric half-molecules of human fibrinogen are joined through disulfide bonds in an antiparallel orientation', *Biochemistry*, 22(9), pp. 2049–2055. Available at: <https://doi.org/10.1021/bi00278a003>.
- Hoffmann, M. *et al.* (2020) 'SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor', *Cell*, 181(2), pp. 271–280.e8. Available at: <https://doi.org/10.1016/j.cell.2020.02.052>.
- Holshue, M.L. *et al.* (2020) 'First Case of 2019 Novel Coronavirus in the United States', *New England Journal of Medicine*, 382(10), pp. 929–936. Available at: <https://doi.org/10.1056/NEJMoa2001191>.
- Hosmer, D.W. and Lemeshow, S. (2000) *Applied Logistic Regression*. 2nd edn. New York: John Wiley & Sons, Inc.
- Hu, G. and Christman, J.W. (2019) 'Editorial: Alveolar Macrophages in Lung Inflammation and Resolution', *Frontiers in Immunology*, 10. Available at: <https://doi.org/10.3389/fimmu.2019.02275>.
- Huang, C. *et al.* (2020a) 'Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China', *The Lancet*, 395(10223), pp. 497–506. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).

- Huang, C. *et al.* (2020b) ‘Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China’, *The Lancet*, 395(10223), pp. 497–506. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
- Huang, I., Lim, M.A. and Pranata, R. (2020) ‘Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – A systematic review, meta-analysis, and meta-regression’, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 14(4), pp. 395–403. Available at: <https://doi.org/10.1016/j.dsx.2020.04.018>.
- Huespe, I.A. *et al.* (2023) ‘COVID-19 vaccines reduce mortality in hospitalized patients with oxygen requirements: Differences between vaccine subtypes. A multicontinental cohort study’, *Journal of Medical Virology*, 95(5). Available at: <https://doi.org/10.1002/jmv.28786>.
- Hueston, L. *et al.* (2020) ‘The Antibody Response to SARS-CoV-2 Infection’, *Open Forum Infectious Diseases*, 7(9). Available at: <https://doi.org/10.1093/ofid/ofaa387>.
- Ikram, A.S. and Pillay, S. (2022) ‘Admission vital signs as predictors of COVID-19 mortality: a retrospective cross-sectional study’, *BMC Emergency Medicine*, 22(1), p. 68. Available at: <https://doi.org/10.1186/s12873-022-00631-7>.
- Imanieh, M.H. *et al.* (2023) ‘A novel scoring system for early assessment of the risk of the COVID-19-associated mortality in hospitalized patients: COVID-19 BURDEN’, *European Journal of Medical Research*, 28(1), p. 4. Available at: <https://doi.org/10.1186/s40001-022-00908-4>.
- Innocenti, F. *et al.* (2021) ‘D-Dimer Tests in the Emergency Department: Current Insights.’, *Open access emergency medicine: OAEM*, 13, pp. 465–479. Available at: <https://doi.org/10.2147/OAEM.S238696>.
- Jafarzadeh, A. *et al.* (2021) ‘Protective Potentials of Type III Interferons in COVID-19 Patients: Lessons from Differential Properties of Type I- and III Interferons’, *Viral Immunology*, 34(5), pp. 307–320. Available at: <https://doi.org/10.1089/vim.2020.0076>.
- Jefferson, T. *et al.* (2021) *Analysis of the Transmission Dynamics of COVID-19: an Open evidence review*, *The Centre for Evidence-Based Medicine*. Available

- at: <https://www.cebm.net/evidence-synthesis/transmission-dynamics-of-covid-19/> (Accessed: 1 July 2023).
- Jo, S. *et al.* (2022) ‘Associations of symptom combinations with in-hospital mortality of coronavirus disease-2019 patients using South Korean National data’, *PLOS ONE*, 17(8), p. e0273654. Available at: <https://doi.org/10.1371/journal.pone.0273654>.
- Johnson, E.D., Schell, J.C. and Rodgers, G.M. (2019) ‘The D-dimer assay.’, *American journal of hematology*, 94(7), pp. 833–839. Available at: <https://doi.org/10.1002/ajh.25482>.
- Joly, B.S., Siguret, V. and Veyradier, A. (2020) ‘Understanding pathophysiology of hemostasis disorders in critically ill patients with COVID-19’, *Intensive Care Medicine*, 46(8), pp. 1603–1606. Available at: <https://doi.org/10.1007/s00134-020-06088-1>.
- Kania, M. *et al.* (2023) ‘Diabetes as a risk factor of death in hospitalized COVID-19 patients – an analysis of a National Hospitalization Database from Poland, 2020’, *Frontiers in Endocrinology*, 14. Available at: <https://doi.org/10.3389/fendo.2023.1161637>.
- Kelsey, J.L. *et al.* (1996) *Methods in Observational Epidemiology*. 2nd edn. New York: Oxford University Press.
- Kemenkes RI (2020) *Pedoman Pemeriksaan PCR SARS-CoV-2 Bagi Petugas Laboratorium*. Jakarta: Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan. Available at: <https://repository.badankebijakan.kemkes.go.id/id/eprint/3944/1/Pedoman%20Pemeriksaan%20PCR%20SARS-COV-2%20Bagi%20Petugas%20Laboratorium.pdf> (Accessed: 27 August 2023).
- Kemenkes RI (2021) *Ikhtisar Mingguan Covid-19 Edisi 13*. Jakarta. Available at: https://www.kemkes.go.id/downloads/resources/download/laporan-mingguan-covid/Laporan-Mingguan-Penanganan-Covid-19_18-Okt-2021.pdf (Accessed: 13 March 2023).
- Kementerian Kesehatan RI (2021) *Situasi Terkini Perkembangan Coronavirus Disease (Covid-19)*. Jakarta. Available at: <https://infeksiemerging.kemkes.go.id/document/situasi-terkini->

perkembangan-coronavirus-disease-covid-19-23-november-2021/view
(Accessed: 13 March 2023).

- Kementerian Kesehatan RI (2022) *Profil Kesehatan Indonesia 2021*. Jakarta: Kementerian Kesehatan Republik Indonesia.
- Kevadiya, B.D. *et al.* (2021) ‘Diagnostics for SARS-CoV-2 infections.’, *Nature materials*, 20(5), pp. 593–605. Available at: <https://doi.org/10.1038/s41563-020-00906-z>.
- Khayat, M., Fan, H. and Vali, Y. (2021) ‘COVID-19 promoting the development of active tuberculosis in a patient with latent tuberculosis infection: A case report’, *Respiratory Medicine Case Reports*, 32, p. 101344. Available at: <https://doi.org/10.1016/j.rmcr.2021.101344>.
- Kim, S.J. *et al.* (2017) ‘The clinical significance of D-dimer concentrations in patients with gestational hypertensive disorders according to the severity’, *Obstetrics & Gynecology Science*, 60(6), p. 542. Available at: <https://doi.org/10.5468/ogs.2017.60.6.542>.
- Knight, S.R., Ho, A., Pius, R., Buchan, I., Carson, G., Drake, T.M., Dunning, J., Fairfield, C.J., Gamble, C., Green, C.A., Gupta, R., Halpin, S., Hardwick, H.E., Holden, K.A., Horby, P.W., Jackson, C., Mclean, K.A., Merson, L., Nguyen-Van-Tam, J.S., Norman, L., Noursadeghi, M., Olliaro, P.L., Pritchard, M.G., Russell, C.D., Shaw, C.A., Sheikh, A., Solomon, T., Sudlow, C., Swann, O. V, Turtle, Lance CW, *et al.* (2020) ‘Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score.’, *BMJ (Clinical research ed.)*, 370, p. m3339. Available at: <https://doi.org/10.1136/bmj.m3339>.
- Knight, S.R., Ho, A., Pius, R., Buchan, I., Carson, G., Drake, T.M., Dunning, J., Fairfield, C.J., Gamble, C., Green, C.A., Gupta, R., Halpin, S., Hardwick, H.E., Holden, K.A., Horby, P.W., Jackson, C., Mclean, K.A., Merson, L., Nguyen-Van-Tam, J.S., Norman, L., Noursadeghi, M., Olliaro, P.L., Pritchard, M.G., Russell, C.D., Shaw, C.A., Sheikh, A., Solomon, T., Sudlow, C., Swann, O. V, Turtle, Lance CW, *et al.* (2020) ‘Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical

- Characterisation Protocol: development and validation of the 4C Mortality Score', *BMJ*, p. m3339. Available at: <https://doi.org/10.1136/bmj.m3339>.
- Knoll, R., Schultze, J.L. and Schulte-Schrepping, J. (2021) 'Monocytes and Macrophages in COVID-19', *Frontiers in Immunology*, 12. Available at: <https://doi.org/10.3389/fimmu.2021.720109>.
- Kuster, G.M. *et al.* (2020) 'SARS-CoV2: should inhibitors of the renin–angiotensin system be withdrawn in patients with COVID-19?', *European Heart Journal*, 41(19), pp. 1801–1803. Available at: <https://doi.org/10.1093/eurheartj/ehaa235>.
- Kusumawati, M. *et al.* (2023) 'The effect of diabetes mellitus on COVID-19 mortality among patients in a tertiary-level hospital in Bandung, Indonesia', *PLOS ONE*, 18(6), p. e0286797. Available at: <https://doi.org/10.1371/journal.pone.0286797>.
- LabCorp (2022) *Accelerated Emergency Use Authorization (EUA) Summary COVID-19 RT-PCR Test (Laboratory Corporation of America)*, *Labcorp's COVID-19 RT-PCR Test EUA Summary*. Available at: : <https://www.fda.gov/media/136151/download> (Accessed: 10 June 2023).
- Lagadinou, M. *et al.* (2020) 'Prognosis of COVID-19: Changes in laboratory parameters.', *Le infezioni in medicina*, 28(suppl 1), pp. 89–95. Available at: <https://pubmed.ncbi.nlm.nih.gov/32532944/> (Accessed: 29 April 2023).
- Lalkhen, A.G. and McCluskey, A. (2008) 'Clinical tests: sensitivity and specificity', *Continuing Education in Anaesthesia Critical Care & Pain*, 8(6), pp. 221–223. Available at: <https://doi.org/10.1093/bjaceaccp/mkn041>.
- Lemeshow, S. *et al.* (1990) *Adequacy of Sample Size in Health Studies*. Chichester: John Wiley & Sons Ltd.
- Leung, J.M. *et al.* (2020) 'ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19', *European Respiratory Journal*, 55(5), p. 2000688. Available at: <https://doi.org/10.1183/13993003.00688-2020>.
- Li, H., Liu, Z. and Ge, J. (2020) 'Scientific research progress of COVID-19/SARS-CoV-2 in the first five months', *Journal of Cellular and Molecular Medicine*, 24(12), pp. 6558–6570. Available at: <https://doi.org/10.1111/jcmm.15364>.

- Li, Q. *et al.* (2020) ‘Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia’, *New England Journal of Medicine*, 382(13), pp. 1199–1207. Available at: <https://doi.org/10.1056/NEJMoa2001316>.
- Liao, M. *et al.* (2020) ‘Single-cell landscape of bronchoalveolar immune cells in patients with COVID-19’, *Nature Medicine*, 26(6), pp. 842–844. Available at: <https://doi.org/10.1038/s41591-020-0901-9>.
- Lin, L. *et al.* (2020) ‘Hypothesis for potential pathogenesis of SARS-CoV-2 infection—a review of immune changes in patients with viral pneumonia’, *Emerging Microbes & Infections*, 9(1), pp. 727–732. Available at: <https://doi.org/10.1080/22221751.2020.1746199>.
- Linkins, L.-A. and Takach Lapner, S. (2017) ‘Review of D-dimer testing: Good, Bad, and Ugly’, *International Journal of Laboratory Hematology*, 39, pp. 98–103. Available at: <https://doi.org/10.1111/ijlh.12665>.
- Linkins, L-A and Takach Lapner, S. (2017) ‘Review of D-dimer testing: Good, Bad, and Ugly.’, *International journal of laboratory hematology*, 39 Suppl 1, pp. 98–103. Available at: <https://doi.org/10.1111/ijlh.12665>.
- Lippi, G. *et al.* (2014) ‘Causes of elevated D-dimer in patients admitted to a large urban emergency department’, *European Journal of Internal Medicine*, 25(1), pp. 45–48. Available at: <https://doi.org/10.1016/j.ejim.2013.07.012>.
- Lippi, G. and Plebani, M. (2020) ‘The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks’, *Clinical Chemistry and Laboratory Medicine (CCLM)*, 58(7), pp. 1063–1069. Available at: <https://doi.org/10.1515/cclm-2020-0240>.
- Liu, J. *et al.* (2020) ‘Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERS-CoV, and 2019-nCoV’, *Journal of Medical Virology*, 92(5), pp. 491–494. Available at: <https://doi.org/10.1002/jmv.25709>.
- Liu, Y. *et al.* (2021) ‘A systematic review and meta-analysis of incidence, prognosis, and laboratory indicators of venous thromboembolism in hospitalized patients with coronavirus disease 2019.’, *Journal of vascular*

- surgery. Venous and lymphatic disorders*, 9(5), pp. 1099-1111.e6. Available at: <https://doi.org/10.1016/j.jvsv.2021.01.012>.
- Longstaff, C. and Kolev, K. (2015) 'Basic mechanisms and regulation of fibrinolysis', *Journal of Thrombosis and Haemostasis*, 13, pp. S98–S105. Available at: <https://doi.org/10.1111/jth.12935>.
- Machhi, J. *et al.* (2020) 'The Natural History, Pathobiology, and Clinical Manifestations of SARS-CoV-2 Infections', *Journal of Neuroimmune Pharmacology*, 15(3), pp. 359–386. Available at: <https://doi.org/10.1007/s11481-020-09944-5>.
- Mackenzie, J.S. and Smith, D.W. (2020) 'COVID-19: a novel zoonotic disease caused by a coronavirus from China: what we know and what we don't', *Microbiology Australia*, 41(1), p. 45. Available at: <https://doi.org/10.1071/MA20013>.
- Madjid, M. *et al.* (2020) 'Potential Effects of Coronaviruses on the Cardiovascular System', *JAMA Cardiology*, 5(7), p. 831. Available at: <https://doi.org/10.1001/jamacardio.2020.1286>.
- Mandrekar, J.N. (2010) 'Receiver Operating Characteristic Curve in Diagnostic Test Assessment', *Journal of Thoracic Oncology*, 5(9), pp. 1315–1316. Available at: <https://doi.org/10.1097/JTO.0b013e3181ec173d>.
- Mann, E.R. *et al.* (2020) 'Longitudinal immune profiling reveals key myeloid signatures associated with COVID-19', *Science Immunology*, 5(51). Available at: <https://doi.org/10.1126/sciimmunol.abd6197>.
- Marshall, J.M. (1998) 'Chemoreceptors and cardiovascular control in acute and chronic systemic hypoxia', *Brazilian Journal of Medical and Biological Research*, 31(7), pp. 863–888. Available at: <https://doi.org/10.1590/S0100-879X1998000700002>.
- Martins-Filho, P.R., Tavares, C.S.S. and Santos, V.S. (2020) 'Factors associated with mortality in patients with COVID-19. A quantitative evidence synthesis of clinical and laboratory data', *European Journal of Internal Medicine*, 76, pp. 97–99. Available at: <https://doi.org/10.1016/j.ejim.2020.04.043>.
- Matsuno, A.K. *et al.* (2019) 'Human coronavirus alone or in co-infection with rhinovirus C is a risk factor for severe respiratory disease and admission to

- the pediatric intensive care unit: A one-year study in Southeast Brazil', *PLOS ONE*, 14(6), p. e0217744. Available at: <https://doi.org/10.1371/journal.pone.0217744>.
- MedCalc Software (2023) *MedCalc easy-to-use statistical software*, medcalc.org. Available at: <https://www.medcalc.org/manual/> (Accessed: 18 October 2023).
- Meza, D. *et al.* (2021) 'Mortality from COVID-19 in Patients with COPD: A US Study in the N3C Data Enclave', *International Journal of Chronic Obstructive Pulmonary Disease*, Volume 16, pp. 2323–2326. Available at: <https://doi.org/10.2147/COPD.S318000>.
- Michel, L., Rassaf, T. and Totzeck, M. (2018) 'Biomarkers for the detection of apparent and subclinical cancer therapy-related cardiotoxicity', *Journal of Thoracic Disease*, 10(S35), pp. S4282–S4295. Available at: <https://doi.org/10.21037/jtd.2018.08.15>.
- Molani, S. *et al.* (2022) 'Risk factors for severe COVID-19 differ by age for hospitalized adults', *Scientific Reports*, 12(1), p. 6568. Available at: <https://doi.org/10.1038/s41598-022-10344-3>.
- Moon, S.-S. *et al.* (2020) 'Clinical Characteristics and Mortality Predictors of COVID-19 Patients Hospitalized at Nationally-Designated Treatment Hospitals', *Journal of Korean Medical Science*, 35(36). Available at: <https://doi.org/10.3346/jkms.2020.35.e328>.
- Moore, B.B. and Kunkel, S.L. (2019) 'Attracting Attention: Discovery of IL-8/CXCL8 and the Birth of the Chemokine Field', *The Journal of Immunology*, 202(1), pp. 3–4. Available at: <https://doi.org/10.4049/jimmunol.1801485>.
- Mosesson, M.W. *et al.* (1995) 'The Covalent Structure of Factor XIIIa Crosslinked Fibrinogen Fibrils', *Journal of Structural Biology*, 115(1), pp. 88–101. Available at: <https://doi.org/10.1006/jsbi.1995.1033>.
- Mousquer, G.T., Peres, A. and Fiegenbaum, M. (2021) 'Pathology of TB/COVID-19 Co-Infection: The phantom menace', *Tuberculosis*, 126, p. 102020. Available at: <https://doi.org/10.1016/j.tube.2020.102020>.

- Mui, L.W., Lau, J.F. and Lee, H.K. (2021) ‘Thromboembolic complications of COVID-19.’, *Emergency radiology*, 28(2), pp. 423–429. Available at: <https://doi.org/10.1007/s10140-020-01868-0>.
- Muniangi-Muhitu, H. *et al.* (2020) ‘Covid-19 and Diabetes: A Complex Bidirectional Relationship’, *Frontiers in Endocrinology*, 11. Available at: <https://doi.org/10.3389/fendo.2020.582936>.
- Nachtigall, I. *et al.* (2020) ‘Clinical course and factors associated with outcomes among 1904 patients hospitalized with COVID-19 in Germany: an observational study’, *Clinical Microbiology and Infection*, 26(12), pp. 1663–1669. Available at: <https://doi.org/10.1016/j.cmi.2020.08.011>.
- Najmah (2017) *Statistika Kesehatan : Aplikasi STATA & SPSS*. Edited by P.P. Lestari. Jakarta: Salemba Empat.
- Navayi, M. *et al.* (2021) ‘Over 60 years of age as an independent prognostic factor of in-hospital mortality among COVID-19 patients: a cohort study in an Iranian high-incidence area’, *Public Health*, 200, pp. 33–38. Available at: <https://doi.org/10.1016/j.puhe.2021.09.007>.
- Nikolich-Žugich, J. (2018) ‘The twilight of immunity: emerging concepts in aging of the immune system’, *Nature Immunology*, 19(1), pp. 10–19. Available at: <https://doi.org/10.1038/s41590-017-0006-x>.
- Nucetelli, M. *et al.* (2020) ‘SARS-CoV-2 infection serology: a useful tool to overcome lockdown?’, *Cell Death Discovery*, 6(1), p. 38. Available at: <https://doi.org/10.1038/s41420-020-0275-2>.
- Olson, J.D. (2015) ‘D-dimer: An Overview of Hemostasis and Fibrinolysis, Assays, and Clinical Applications’, in, pp. 1–46. Available at: <https://doi.org/10.1016/bs.acc.2014.12.001>.
- Parikh, R. *et al.* (2008) ‘Understanding and using sensitivity, specificity and predictive values’, *Indian Journal of Ophthalmology*, 56(1), p. 45. Available at: <https://doi.org/10.4103/0301-4738.37595>.
- Park, J. *et al.* (2023) ‘Elevated circulating monocytes and monocyte activation in COVID-19 convalescent individuals’, *Frontiers in Immunology*, 14. Available at: <https://doi.org/10.3389/fimmu.2023.1151780>.

- Parolina, L. *et al.* (2022) 'Clinical characteristics of COVID-19 in patients with tuberculosis and factors associated with the disease severity', *International Journal of Infectious Diseases*, 124, pp. S82–S89. Available at: <https://doi.org/10.1016/j.ijid.2022.04.041>.
- Payus, A.O. *et al.* (2019) 'Pulmonary Embolism Masquerading as Severe Pneumonia: A Case Report', *Open Access Macedonian Journal of Medical Sciences*, 7(3), pp. 396–399. Available at: <https://doi.org/10.3889/oamjms.2019.114>.
- Peng, J. *et al.* (2020) 'Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): A multicenter, cross-sectional study', *Journal of Clinical Laboratory Analysis*, 34(10). Available at: <https://doi.org/10.1002/jcla.23475>.
- Petrone, L. *et al.* (2021) 'Coinfection of tuberculosis and COVID-19 limits the ability to in vitro respond to SARS-CoV-2', *International Journal of Infectious Diseases*, 113, pp. S82–S87. Available at: <https://doi.org/10.1016/j.ijid.2021.02.090>.
- PHEOC Kemkes RI (2023) *Covid-19*. Jakarta. Available at: <https://infeksiemerging.kemkes.go.id/dashboard/covid-19> (Accessed: 13 March 2023).
- Poudel, A. *et al.* (2021) 'D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19', *PLOS ONE*, 16(8), p. e0256744. Available at: <https://doi.org/10.1371/journal.pone.0256744>.
- Pranata, R., Lim, M.A., *et al.* (2020) 'Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression', *Journal of the Renin-Angiotensin-Aldosterone System*, 21(2), p. 147032032092689. Available at: <https://doi.org/10.1177/1470320320926899>.
- Pranata, R., Huang, I., *et al.* (2020) 'Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19—systematic review, meta-analysis, and meta-regression', *Journal of Stroke and Cerebrovascular*

- Diseases*, 29(8), p. 104949. Available at: <https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104949>.
- Qi, J. *et al.* (2020) 'The ratio of shock index to pulse oxygen saturation predicting mortality of emergency trauma patients', *PLOS ONE*, 15(7), p. e0236094. Available at: <https://doi.org/10.1371/journal.pone.0236094>.
- Raharjo, A.M., Sari, E.D. and Mufida, D.C. (2021) 'Correlation Between Leukocyte Differential Counts with The Severity and Outcome of Coronavirus Disease 2019 (COVID-19) Patients In Jember', *Jurnal Respirologi Indonesia*, 41(3), pp. 187–195. Available at: <https://doi.org/10.36497/jri.v41i3.186>.
- Rahman, S. *et al.* (2021) 'Epidemiology, pathogenesis, clinical presentations, diagnosis and treatment of COVID-19: a review of current evidence', *Expert Review of Clinical Pharmacology*, 14(5), pp. 601–621. Available at: <https://doi.org/10.1080/17512433.2021.1902303>.
- Rimmer, A. (2020) 'Covid-19: doctors in final trimester of pregnancy should avoid direct patient contact', *BMJ*, p. m1173. Available at: <https://doi.org/10.1136/bmj.m1173>.
- Ritacco, V. and Kantor, I.N. (2020) 'Tuberculosis and COVID-19: a dangerous relationship.', *Medicina*, 80 Suppl 6, pp. 117–118.
- Rizo-Télez, S.A. *et al.* (2020) 'The Neutrophil-to-Monocyte Ratio and Lymphocyte-to-Neutrophil Ratio at Admission Predict In-Hospital Mortality in Mexican Patients with Severe SARS-CoV-2 Infection (Covid-19)', *Microorganisms*, 8(10), p. 1560. Available at: <https://doi.org/10.3390/microorganisms8101560>.
- Robb, C.T. *et al.* (2020) 'Non-steroidal anti-inflammatory drugs, prostaglandins, and COVID-19', *British Journal of Pharmacology*, 177(21), pp. 4899–4920. Available at: <https://doi.org/10.1111/bph.15206>.
- RSUD Siti Fatimah (2018) *Profil RSUD Siti Fatimah Provinsi Sumatera Selatan, RSUD Siti Fatimah*. Available at: <http://rsud.sumselprov.go.id/#> (Accessed: 7 January 2024).
- Ruan, Q. *et al.* (2020) 'Correction to: Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China',

- Intensive Care Medicine*, 46(6), pp. 1294–1297. Available at: <https://doi.org/10.1007/s00134-020-06028-z>.
- Ryu, S.H. *et al.* (2019) ‘Diagnostic Significance of Fibrin Degradation Products and D-Dimer in Patients With Breast Cancer-Related Lymphedema’, *Annals of Rehabilitation Medicine*, 43(1), pp. 81–86. Available at: <https://doi.org/10.5535/arm.2019.43.1.81>.
- Sadie, S. *et al.* (2021) ‘The Impact of Age, Sex, and Race on the Association of Risk Factors and Mortality in COVID-19 Patients’, *Journal of Infectious Diseases and Epidemiology*, 7(6). Available at: <https://doi.org/10.23937/2474-3658/1510215>.
- dos Santos, W.G. (2020) ‘Natural history of COVID-19 and current knowledge on treatment therapeutic options’, *Biomedicine & Pharmacotherapy*, 129, p. 110493. Available at: <https://doi.org/10.1016/j.biopha.2020.110493>.
- Sastry, S., Cuomo, F. and Muthusamy, J. (2022) ‘COVID-19 and thrombosis: The role of hemodynamics’, *Thrombosis Research*, 212, pp. 51–57. Available at: <https://doi.org/10.1016/j.thromres.2022.02.016>.
- Setti, L. *et al.* (2020) ‘Airborne Transmission Route of COVID-19: Why 2 Meters/6 Feet of Inter-Personal Distance Could Not Be Enough’, *International Journal of Environmental Research and Public Health*, 17(8), p. 2932. Available at: <https://doi.org/10.3390/ijerph17082932>.
- Shang, Y. *et al.* (2020) ‘Scoring systems for predicting mortality for severe patients with COVID-19.’, *EClinicalMedicine*, 24, p. 100426. Available at: <https://doi.org/10.1016/j.eclinm.2020.100426>.
- Soares, R. de C.M., Mattos, L.R. and Raposo, L.M. (2020) ‘Risk Factors for Hospitalization and Mortality due to COVID-19 in Espírito Santo State, Brazil’, *The American Journal of Tropical Medicine and Hygiene*, 103(3), pp. 1184–1190. Available at: <https://doi.org/10.4269/ajtmh.20-0483>.
- Soni, M. *et al.* (2020) ‘D-dimer level is a useful predictor for mortality in patients with COVID-19: Analysis of 483 cases’, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 14(6), pp. 2245–2249. Available at: <https://doi.org/10.1016/j.dsx.2020.11.007>.

- Soraya, G.V. and Ulhaq, Z.S. (2020) 'Crucial laboratory parameters in COVID-19 diagnosis and prognosis: An updated meta-analysis.', *Medicina clinica (English ed.)*, 155(4), pp. 143–151. Available at: <https://doi.org/10.1016/j.medcle.2020.05.004>.
- Stein, R.A. and Young, L.M. (2020) 'From ACE2 to COVID-19: A multiorgan endothelial disease.', *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*, 100, pp. 425–430. Available at: <https://doi.org/10.1016/j.ijid.2020.08.083>.
- Tang, N. *et al.* (2020) 'Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia', *Journal of Thrombosis and Haemostasis*, 18(4), pp. 844–847. Available at: <https://doi.org/10.1111/jth.14768>.
- Tanni, F. *et al.* (2020) 'Eosinopenia and COVID-19', *Journal of Osteopathic Medicine*, 120(8), pp. 504–508. Available at: <https://doi.org/10.7556/jaoa.2020.091>.
- Thachil, J., Cushman, M., *et al.* (2020) 'A proposal for staging COVID-19 coagulopathy', *Research and Practice in Thrombosis and Haemostasis*, 4(5), pp. 731–736. Available at: <https://doi.org/10.1002/rth2.12372>.
- Thachil, J., Tang, N., *et al.* (2020) 'ISTH interim guidance on recognition and management of coagulopathy in COVID-19', *Journal of Thrombosis and Haemostasis*, 18(5), pp. 1023–1026. Available at: <https://doi.org/10.1111/jth.14810>.
- Trevethan, R. (2017) 'Sensitivity, Specificity, and Predictive Values: Foundations, Plabilities, and Pitfalls in Research and Practice', *Frontiers in Public Health*, 5. Available at: <https://doi.org/10.3389/fpubh.2017.00307>.
- Trigo, J. *et al.* (2020) 'Factors associated with the presence of headache in hospitalized COVID-19 patients and impact on prognosis: a retrospective cohort study', *The Journal of Headache and Pain*, 21(1), p. 94. Available at: <https://doi.org/10.1186/s10194-020-01165-8>.
- Udugama, B. *et al.* (2020) 'Diagnosing COVID-19: The Disease and Tools for Detection', *ACS Nano*, 14(4), pp. 3822–3835. Available at: <https://doi.org/10.1021/acsnano.0c02624>.

- Varga, Z. *et al.* (2020) ‘Endothelial cell infection and endotheliitis in COVID-19’, *The Lancet*, 395(10234), pp. 1417–1418. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30937-5](https://doi.org/10.1016/S0140-6736(20)30937-5).
- Wang, Z. *et al.* (2020) ‘Clinical Features of COVID-19 Patients with Different Outcomes in Wuhan: A Retrospective Observational Study’, *BioMed Research International*, 2020, pp. 1–10. Available at: <https://doi.org/10.1155/2020/2138387>.
- Weitz, J.I., Fredenburgh, J.C. and Eikelboom, J.W. (2017) ‘A Test in Context: D-Dimer’, *Journal of the American College of Cardiology*, 70(19), pp. 2411–2420. Available at: <https://doi.org/10.1016/j.jacc.2017.09.024>.
- WHO (2021) *Antigen-detection in the diagnosis of SARS-CoV-2 infection: interim guidance*. Available at: <https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays> (Accessed: 23 June 2023).
- WHO (2023) *WHO Coronavirus (COVID-19) Dashboard*. Available at: <https://covid19.who.int> (Accessed: 13 March 2023).
- Wu, Y. *et al.* (2020) ‘Clinical Characteristics and Immune Injury Mechanisms in 71 Patients with COVID-19’, *mSphere*, 5(4). Available at: <https://doi.org/10.1128/mSphere.00362-20>.
- Wu, Z. and McGoogan, J.M. (2020) ‘Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China’, *JAMA*, 323(13), p. 1239. Available at: <https://doi.org/10.1001/jama.2020.2648>.
- Xie, M. and Chen, Q. (2020) ‘Insight into 2019 novel coronavirus — An updated interim review and lessons from SARS-CoV and MERS-CoV’, *International Journal of Infectious Diseases*, 94, pp. 119–124. Available at: <https://doi.org/10.1016/j.ijid.2020.03.071>.
- Xiong, M., Liang, X. and Wei, Y. (2020) ‘Changes in blood coagulation in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis’, *British Journal of Haematology*, 189(6), pp. 1050–1052. Available at: <https://doi.org/10.1111/bjh.16725>.

- Yang, H. and Lu, S. (2020) 'COVID-19 and tuberculosis', *Journal of Translational Internal Medicine*, 8(2), pp. 59–65. Available at: <https://doi.org/10.2478/jtim-2020-0010>.
- Yao, Y. *et al.* (2020a) 'D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study', *Journal of Intensive Care*, 8(1), p. 49. Available at: <https://doi.org/10.1186/s40560-020-00466-z>.
- Yao, Y. *et al.* (2020b) 'D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study', *Journal of Intensive Care*, 8(1), p. 49. Available at: <https://doi.org/10.1186/s40560-020-00466-z>.
- Yi, Y. *et al.* (2020) 'COVID-19: what has been learned and to be learned about the novel coronavirus disease', *International Journal of Biological Sciences*, 16(10), pp. 1753–1766. Available at: <https://doi.org/10.7150/ijbs.45134>.
- Zeng, J.-H. *et al.* (2020) 'First case of COVID-19 complicated with fulminant myocarditis: a case report and insights', *Infection*, 48(5), pp. 773–777. Available at: <https://doi.org/10.1007/s15010-020-01424-5>.
- Zhan, H. *et al.* (2021) 'Diagnostic Value of D-Dimer in COVID-19: A Meta-Analysis and Meta-Regression', *Clinical and Applied Thrombosis/Hemostasis*, 27, p. 107602962110109. Available at: <https://doi.org/10.1177/10760296211010976>.
- Zhang, L. *et al.* (2020) 'D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19', *Journal of Thrombosis and Haemostasis*, 18(6), pp. 1324–1329. Available at: <https://doi.org/10.1111/jth.14859>.
- Zhao, K. *et al.* (2020) 'Clinical features in 52 patients with COVID-19 who have increased leukocyte count: a retrospective analysis', *European Journal of Clinical Microbiology & Infectious Diseases*, 39(12), pp. 2279–2287. Available at: <https://doi.org/10.1007/s10096-020-03976-8>.
- Zhao, M. *et al.* (2020) 'Comparison of clinical characteristics and outcomes of patients with coronavirus disease 2019 at different ages', *Aging*, 12(11), pp. 10070–10086. Available at: <https://doi.org/10.18632/aging.103298>.
- Zheng, Z. *et al.* (2020) 'Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis', *Journal of Infection*, 81(2), pp. e16–e25. Available at: <https://doi.org/10.1016/j.jinf.2020.04.021>.

Zhou, F. *et al.* (2020) ‘Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study’, *The Lancet*, 395(10229), pp. 1054–1062. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3).

Zhou, P. *et al.* (2020) ‘A pneumonia outbreak associated with a new coronavirus of probable bat origin’, *Nature*, 579(7798), pp. 270–273. Available at: <https://doi.org/10.1038/s41586-020-2012-7>.