**Evidence of Diagnostic Value of Ferritin in Patients with COVID-19**

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# Ferritin levels in severe vs. non-severe groups

## **Supplementary Table 1.** Studies included in severe vs. non-severe comparison

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Country** | **Study design** | **Severe** | | | **Non-severe** | | |
| **No.** | **Age** | **Sex, male** | **No.** | **Age** | **Sex, male** |
| Cai Q. et al. 2020 (1) | China | Retrospective study | 58 | 61.8 ± 2.9 | 39 (67.2%) | 240 | 42.5 ± 4.2 | 106 (44.2%) |
| Chen G. et al. 2020 (2) | China | Retrospective study | 11 | 61.1 ± 2.8 | 10 (90.9%) | 10 | 50.7 ± 3.8 | 7  (70.0%) |
| Chen R. et al. 2020 (3) | China | Retrospective study | 203 | 61 ± 13.7 | 131 (64.5%) | 345 | 67.3 ± 12.1 | 182 (52.8%) |
| Cugno M. et al. 2020 (4) | Italy | Retrospective study | 14 | NS | NS | 17 | NS | NS |
| Dahan S. et al. 2020 (5) | Israel | Cross-sectional study | 10 | NS | NS | 29 | NS | NS |
| Ghweil AA. et al. 2020 (6) | Egypt | Retrospective study | 30 | 62.6±10.1 | 20 (66.7%) | 36 | 55.5 ±10.1 | 28  (77.8%) |
| Guirao JJ. et al. 2020 (7) | Spain | Cohort study | 6 | 64.5 ± 2.3 | 5  (83.3%) | 44 | 63.4 ± 4.5 | 36  (81.8%) |
| Gunder R. et al. 2020 (8) | Turkey | Retrospective study | 50 | 62.2 ± 11.9 | 33 (66.0%) | 172 | 47.7 ±16.1 | 99  (57.6%) |
| Huang H. et al. 2020 (9) | China | Retrospective study | 21 | 61.4± 16.4 | 12 (57.1%) | 43 | 41.2 ±15.7 | 25  (58.1%) |
| Itelman E. et al. 2020 (10) | Izrael | Retrospective study | 26 | 61 ± 14 | 21 (80.8%) | 136 | 49.2 ±21.0 | 84  (61.8%) |
| Liu J. et al. 2020 (11) | China | Retrospective study | 13 | 59.7 ± 10.1 | 7  (53.8%) | 27 | 43.2 ±12.3 | 8  (29.6%) |
| Liu T. et al. 2020 (12) | China | Retrospective study | 69 | 56.3 ± 17 | 33 (47.8%) | 11 | 36.5 ± 9.3 | 1  (9.1%) |
| Popov GT. et al. 2020 (13) | Bulgaria | Retrospective study | 43 | 63.0 ± 12.8 | 33 (76.8%) | 95 | 48.3 ±15.7 | 54  (56.9%) |
| Qin C. et al. 2020 (14) | China | Retrospective study | 286 | 60.5 ± 3 | 155 (54.2%) | 166 | 52.3 ± 3.5 | 80  (48.2%) |
| Shah Y. et al. 2020 (15) | UK | Retrospective study | 10 | 60.5 ± 6.4 | 5  (50.0%) | 20 | 57.5 ± 3.5 | 12  (60.0%) |
| Sun Y. et al. 2020 (16) | China | Retrospective study | 19 | 59.4 ± 13.7 | NS | 44 | 42.3 ±20.6 | NS |
| Wang F. et al. 2020 (17) | China | Retrospective study | 35 | 61.3 ± 12.2 | NS | 30 | 52.2 ±12.4 | NS |
| Xu X. et al. 2020 (18) | China | Retrospective study | 41 | 63.2 ± 14.5 | 15 (31.9%) | 47 | 52.5 ±14.6 | 21  (44.7%) |
| Xu Y. et al. 2020 (19) | China | Retrospective multi-center case series | 25 | 67.8 ± 6.1 | 13  (52.0%) | 44 | 48.5 ± 6.9 | 22  (50.0%) |
| Zeng Z. et al. 2020 (20) | China | Retrospective study | 224 | 62.7 ± 4.8 | 121  (54.0%) | 93 | 58.1 ± 3.8 | 41  (44.1%) |

Legend: NS = Not specifield;

References:

1. Cai Q, Huang D, Ou P, et al. COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. Allergy. 2020 Jul;75(7):1742-1752. doi: 10.1111/all.14309.
2. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020; 130(5):2620-2629. doi: 10.1172/JCI137244.
3. Chen R, Sang L, Jiang M, et al. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. J Allergy Clin Immunol. 2020 Jul;146(1):89-100. doi: 10.1016/j.jaci.2020.05.003.
4. Cugno M, Meroni PL, Gualtierotti R, et al. Complement activation in patients with COVID-19: A novel therapeutic target. J Allergy Clin Immunol. 2020 Jul;146(1):215-217. doi: 10.1016/j.jaci.2020.05.006.
5. Dahan S, Segal G, Katz I, et al. Ferritin as a Marker of Severity in COVID-19 Patients: A Fatal Correlation. Isr Med Assoc J. 2020; 8(22):429-434.
6. Ghweil AA, Hassan MH, Khodeary A, et al. Characteristics, Outcomes and Indicators of Severity for COVID-19 Among Sample of ESNA Quarantine Hospital's Patients, Egypt: A Retrospective Study. Infect Drug Resist. 2020 Jul 17;13:2375-2383. doi: 10.2147/IDR.S263489.
7. Guirao JJ, Cabrera CM, Jiménez N, Rincón L, Urra JM. High serum IL-6 values increase the risk of mortality and the severity of pneumonia in patients diagnosed with COVID-19. Mol Immunol. 2020; 128:64-68. doi: 10.1016/j.molimm.2020.10.006.
8. Guner R, Hasanoğlu I, Kayaaslan B, et al. COVID-19 experience of the major pandemic response center in the capital: Results of the pandemic's first month in Turkey. Turk J Med Sci. 2020 Jul 19. doi: 10.3906/sag-2006-164.
9. Huang H, Song B, Xu Z, et al. Predictors of coronavirus disease 2019 severity: A retrospective study of 64 cases . Jpn J Infect Dis. 2020 Aug 1. doi: 10.7883/yoken.JJID.2020.298.
10. Itelman E, Wasserstrum Y, Segev A, et al. Clinical Characterization of 162 COVID-19 patients in Israel: Preliminary Report from a Large Tertiary Center. Isr Med Assoc J. 2020 May;22(5):271-274.
11. Liu J, Li S, Liu J, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine. 2020; 55:102763. doi: 10.1016/j.ebiom.2020.102763.
12. Liu T, Zhang J, Yang Y, et al. The potential role of IL-6 in monitoring severe case of coronavirus disease 2019. medRxiv 2020. doi: 10.1101/2020.03.01.20029769v2.
13. Popov GT, Baymakova M, Vaseva V, Kundurzhiev T, Mutafchiyski V. Clinical Characteristics of Hospitalized Patients with COVID-19 in Sofia, Bulgaria. Vector Borne Zoonotic Dis. 2020 Oct 14. doi: 10.1089/vbz.2020.2679.
14. Qin C, Zhou L, Hu Z, et al. Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020 Jul 28;71(15):762-768. doi: 10.1093/cid/ciaa248.
15. Shah A, Frost JN, Aaron L, et al. Systemic hypoferremia and severity of hypoxemic respiratory failure in COVID-19. Crit Care. 2020; 24(1):320. doi: 10.1186/s13054-020-03051-w.
16. Sun Y, Dong Y, Wang L, et al. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience. J Autoimmun. 2020 Aug;112:102473. doi: 10.1016/j.jaut.2020.102473.
17. Wang F, Hou H, Luo Y, et al. The laboratory tests and host immunity of COVID-19 patients with different severity of illness. JCI Insight. 2020 May 21;5(10):e137799. doi: 10.1172/jci.insight.137799.
18. Xu X, Yu MQ, Shen Q, et al. Analysis of inflammatory parameters and disease severity for 88 hospitalized COVID-19 patients in Wuhan, China. Int J Med Sci. 2020 Jul 25;17(13):2052-2062. doi: 10.7150/ijms.47935.
19. Xu Y, Li Y, Zeng Q, et al. Clinical Characteristics of SARS-CoV-2 Pneumonia Compared to Controls in Chinese Han Population. medRxiv 2020. doi: 10.1101/2020.03.08.20031658v1.
20. Zeng Z, Yu H, Chen H, et al. Longitudinal changes of inflammatory parameters and their correlation with disease severity and outcomes in patients with COVID-19 from Wuhan, China. Crit Care. 2020; 24(1):525. doi: 10.1186/s13054-020-03255-0.

# Ferritin levels in ICU vs. non-ICU groups

Obraz zawierający stół

Opis wygenerowany automatycznie

**Supplementary Figure 1.** Forest plot of ferritin levels in ICU vs. non-ICU group. The center of each square represents the weighted mean difference for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results.

## **Supplementary Table 2.** Studies included in ICU vs. non-ICU comparison

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Country** | **Study design** | **ICU group** | | | **Non-ICU group** | | |
| **No.** | **Age** | **Sex, male** | **No.** | **Age** | **Sex, male** |
| Aloisio E. et al. 2020 (1) | Italy | Retrospective study | 47 | 63.8 ± 3.7 | 41 (87.2%) | 380 | 67 ± 4.5 | 252 (66.3%) |
| El Aidaoui K. et al. 2020 (2) | Marroco | Retrospective observational study | 45 | 64.8 ± 4.9 | 35 (77.9%) | 89 | 42.3 ± 7.8 | 38  (42.7%) |
| Guirao JJ. Et al. 2020 (3) | Spain | Cohort study | 8 | 62.1 ± 2.8 | 7  (87.5%) | 42 | 63.8 ± 1.8 | 34  (80.9%) |
| Liu Sp et al. 2020 (4) | China | Retrospective study | 41 | 63 ± 15 | 28 (71.8%) | 214 | 61 ± 11.3 | 108 (50.9%) |
| Maeda T. et al. 2020 (5) | USA | Retrospective study | 57 | 67 ± 5.2 | 31 (54.4%) | 167 | 64.5 ± 4.3 | 96  (57.5%) |

References:

1. Aloisio A, Chibireva M, Serafini L, et al. A comprehensive appraisal of laboratory biochemistry tests as major predictors of COVID-19 severity. Arch Pathol Lab Med. 2020 Jul 10. doi: 10.5858/arpa.2020-0389-SA.
2. El Aidaoui K, Haoudar A, Khalis M, et al. Predictors of Severity in Covid-19 Patients in Casablanca, Morocco. Cureus. 2020; 12(9):e10716. doi: 10.7759/cureus.10716.
3. Guirao JJ, Cabrera CM, Jiménez N, Rincón L, Urra JM. High serum IL-6 values increase the risk of mortality and the severity of pneumonia in patients diagnosed with COVID-19. Mol Immunol. 2020; 128:64-68. doi: 10.1016/j.molimm.2020.10.006.
4. Liu SP, Zhang Q, Wang W, et al. Hyperglycemia is a strong predictor of poor prognosis in COVID-19. Diabetes Res Clin Pract. 2020; 167:108338. doi: 10.1016/j.diabres.2020.108338.
5. Maeda T, Obata R, Do DR, Kuno T. The association of interleukin-6 value, interleukin inhibitors, and outcomes of patients with COVID-19 in New York City. J Med Virol. 2020 Jul 28. doi: 10.1002/jmv.26365.

# Ferritin levels in death vs. survival groups

Obraz zawierający stół

Opis wygenerowany automatycznie

**Supplementary Figure 2.** Forest plot of ferritin levels in death vs. survival group. The center of each square represents the weighted mean difference for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results.

## **Supplementary Table 3.** Studies included in death vs. survival comparison

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Country** | **Study design** | **Death group** | | | **Survival group** | | |
| **No.** | **Age** | **Sex, male** | **No.** | **Age** | **Sex, male** |
| Aloisio E. et al. 2020 (1) | Italy | Retrospective study | 89 | 73.3 ± 2.2 | 70 (78.7%) | 338 | 58.3 ± 3.5 | 223 (65.9%) |
| Asghar MS. et al. 2020 | Pakistan | Retrospective observational multicenter study | 101 | 61.0 ± 11.6 | 66 (65.3%) | 263 | 49.3 ±16.1 | 66 (25.1%) |
| Bonetti G. et al. 2020 | Italy | Cohort study | 70 | 76.1 ± 5.7 | 45 (64.3%) | 74 | 62.5 ± 3.3 | 51 (68.9%) |
| Chen R. et al. 2020 | China | Retrospective study | 103 | 66.9 ± 12.1 | 69 (67.0%) | 445 | 53.5 ±13.9 | 244 (54.8%) |
| Covino M. et al. 2020 | Italy | Single-center retrospective observational study | 23 | 84.8 ± 0.8 | 12 (52.2%) | 46 | 84.5 ± 2.3 | 25 (54.3%) |
| Garcia PDW. et al. 2020 | Multi-country | Prospective observational cohort study | 97 | 70.5 ± 2.7 | 69 (71.1%) | 301 | 62 ± 2.7 | 231 (76.7%) |
| Guirao JJ. et al. 2020 | Spain | Cohort study | 14 | 69.0 ± 3.1 | 11 (78.6%) | 36 | 61.4 ± 1.7 | 30 (83.3%) |
| Laguna-Goya R. et al. 2020 | Spain | Prospective cohort study | 36 | 64.8 ± 4.3 | 25 (69.4%) | 465 | 51.5 ± 2.3 | 292 (62.9%) |
| Li Q. et al. 2020 | China | Retrospective study | 26 | 67.3 ± 3.8 | 20 (76.9%) | 296 | 49.3 ± 4.5 | 147 (49.8%) |
| Lohse et al. 2020 | France | Retrospective study | 10 | 80 ± 10.1 | NS | 24 | 73.1 ±11.1 | NS |
| Ronderos Botero DM. et al. 2020 | USA | Retrospective study | 25 | 62.4±12.7 | 20 (80.0%) | 132 | 50.6±17.1 | 89 (67.4%) |
| Ruan Q. et al. 2020 | China | Retrospective study | 68 | 57.5 ± 19.0 | 49 (72.1%) | 82 | 56.2 ±10.7 | 53 (64.6%) |
| Zhou F. et al. 2020 | China | Retrospective multicenter cohort study | 54 | 69.3 ± 3.8 | 38 (70.4%) | 137 | 51.8 ± 2.2 | 81 (59.1%) |

References:

1. Aloisio A, Chibireva M, Serafini L, et al. A comprehensive appraisal of laboratory biochemistry tests as major predictors of COVID-19 severity. Arch Pathol Lab Med. 2020 Jul 10. doi: 10.5858/arpa.2020-0389-SA.
2. Asghar MS, Kazmi SJH, Khan NA, et al. Poor Prognostic Biochemical Markers Predicting Fatalities Caused by COVID-19: A Retrospective Observational Study From a Developing Country. Cureus. 2020 Aug 5;12(8):e9575. doi: 10.7759/cureus.9575.
3. Bonetti G, Manelli F, Patroni A, et al. Laboratory predictors of death from coronavirus disease 2019 (COVID-19) in the area of Valcamonica, Italy. Clin Chem Lab Med. 2020 Jun 25;58(7):1100-1105. doi: 10.1515/cclm-2020-0459.
4. Chen R, Sang L, Jiang M, et al. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. J Allergy Clin Immunol. 2020 Jul;146(1):89-100. doi: 10.1016/j.jaci.2020.05.003.
5. Covino M, De Matteis G, Santoro M, et al. Clinical characteristics and prognostic factors in COVID-19 patients aged ≥80 years. Geriatr Gerontol Int. 2020 Jul;20(7):704-708. doi: 10.1111/ggi.13960.
6. Garcia PDW, Fumeaux T, Guerci P, et al. Prognostic factors associated with mortality risk and disease progression in 639 critically ill patients with COVID-19 in Europe: Initial report of the international RISC-19-ICU prospective observational cohort. EClinicalMedicine. 2020 Aug;25:100449. doi: 10.1016/j.eclinm.2020.100449.
7. Guirao JJ, Cabrera CM, Jiménez N, Rincón L, Urra JM. High serum IL-6 values increase the risk of mortality and the severity of pneumonia in patients diagnosed with COVID-19. Mol Immunol. 2020; 128:64-68. doi: 10.1016/j.molimm.2020.10.006.
8. Laguna-Goya R, Utrero-Rico A, Talayero P, et al. IL-6-based mortality risk model for hospitalized patients with COVID-19. J Allergy Clin Immunol. 2020; 146(4):799-807.e9. doi: 10.1016/j.jaci.2020.07.009.
9. Li Q, Zhang J, Ling Y, et al. A simple algorithm helps early identification of SARS-CoV-2 infection patients with severe progression tendency. Infection. 2020; 48(4):577-584. doi: 10.1007/s15010-020-01446-z.
10. Lohse A, Klopfenstein T, Balblanc JC, et al. Predictive factors of mortality in patients treated with tocilizumab for acute respiratory distress syndrome related to coronavirus disease 2019 (COVID-19). Microbes Infect. 2020; 22(9):500-503. doi: 10.1016/j.micinf.2020.06.005.
11. Ronderos Botero DM, Omar AMS, Sun HK, et al. COVID-19 in the Healthy Patient Population: Demographic and Clinical Phenotypic Characterization and Predictors of In-Hospital Outcomes. Arterioscler Thromb Vasc Biol. 2020; 40(11):2764-2775. doi: 10.1161/ATVBAHA.120.314845.
12. Ruan Q, Yang K, Wang W, Jiang L, Song J. Correction to: Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020; 46(6):1294-1297. doi: 10.1007/s00134-020-06028-z.
13. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395(10229):1054-1062. doi: 10.1016/S0140-6736(20)30566-3.