Can laboratory evaluation differentiate between coronavirus disease-2019, influenza, and respiratory syncytial virus infections? A retrospective cohort study

Ariel Ben Shimol[1,2], Shani Dahan[1,2], Nachshol Alon[1,2], Shelly Soffer[1,2], Keren Hod[5], Tal Brosh-Nissimov[6], Yehuda Shoenfeld[7], Amir Dagan[3,4]

[1]Internal Medicine B, Assuta Medical Center, Ashdod, Israel

[2]Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheba, Israel

[3]Department of Rheumatology, Wolfson Medical Center, Holon, Israel

[4]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

[5]Department of Academy and Research, Assuta Medical Centers, Tel Aviv, Israel

[6]Infectious Diseases Unit, Assuta Ashdod Hospital, Ashdod, Israel

[7]Sheba Medical Center, The Zabludowicz Center for Autoimmune Diseases, Ramat Gan, Israel

Aim To identify clinical and laboratory parameters that can assist in the differential diagnosis of coronavirus disease 2019 (COVID-19), influenza, and respiratory syncytial virus (RSV) infections.

Methods In this retrospective cohort study, we obtained basic demographics and laboratory data from all 685 hospitalized patients confirmed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza virus, or RSV from 2018 to 2020. A multiple logistic regression was employed to investigate the relationship between COVID-19 and laboratory parameters.

Results SARS-CoV-2 patients were significantly younger than RSV ($P=0.001$) and influenza virus ($P=0.022$) patients. SARS-CoV-2 patients also displayed a significant male predominance over influenza virus patients ($P=0.047$). They also had significantly lower white blood cell count (median 6.3×10^6 cells/μ) compared with influenza virus ($P<0.001$) and RSV ($P=0.001$) patients. Differences were also observed in other laboratory values but were insignificant in a multivariate analysis.

Conclusions Male sex, younger age, and low white blood cell count can assist in the diagnosis of COVID-19 over other viral infections. However, the differences between the groups were not substantial enough and would probably not suffice to distinguish between the viral illnesses in the emergency department.

Correspondence to:
Amir Dagan
Department of Rheumatology
Wolfson Medical Center
Ha-Lokhamim St 62
Holon 5822012, Israel
Dr.a.dagan@gmail.com

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an RNA virus causing coronavirus disease 2019 (COVID-19). First identified in the Chinese province of Hubei in late 2019, COVID-19 was declared a global pandemic by the World Health Organization in March 2020 (1).

As of July 2021, there were more than 180 million confirmed COVID-19 cases and more than four million patients who died due to the disease complications (2). Moreover, the disease caused a substantial economic and social burden (3), and affected health care quality (4-7).

The diagnosis of COVID-19 is currently determined primarily by molecular methods and antigen tests (8,9). Radiographic diagnosis is possible as well (10,11). This practice often consumes valuable time and expensive equipment (12). There is a growing need to accelerate the diagnostic process by enabling point-of care diagnosis in various ambulatory settings, while keeping it accurate to ensure the necessary precautionary measures (13).

The clinical presentation of SARS-CoV-2 infection resembles that of other respiratory viruses, with predominant symptoms of fever, cough, fatigue, and dyspnea (14-17). Hematological abnormalities, including leukopenia, lymphopenia, and thrombocytopenia, are common among COVID-19 patients, as well as elevated levels of C-reactive protein (CRP), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and ferritin (14,15,18-21). Some of these inflammatory markers correlated with disease severity and mortality (22,23).

The influenza season of 2021 in the Northern hemisphere was relatively weak in contrast with predictions. Low to zero rates of influenza were detected in several countries. This was attributed to social distancing, masks wearing, and a reduced number of air travelers (24). Despite a growing number of vaccinated individuals (25), the emergence of new SARS-CoV-2 variants suggest that COVID-19 is here to stay. Seasonal viruses such as influenza virus and respiratory syncytial virus (RSV) could rebound in the following winter, with the loosening of restrictions.

Differentiating between COVID-19 and other respiratory viral illnesses on clinical grounds alone can be very challenging. These viral infections share similarities in the transmission route and symptoms (26-28). Several small studies attempted to delineate the differences in the clinical presentation of SARS-CoV-2 and influenza infections (29-31). In this study, we aimed to identify demographic and laboratory parameters that can assist in the early differentiation between SARS-CoV-2, influenza, and RSV infections in the emergency department.

METHODS

Study design

This retrospective cohort study was conducted in Samson Assuta-Ashdod Hospital, Israel. Ethical approval was given by the institutional Ethics Committee, which waived the informed consent.

Inclusion and exclusion criteria

The study enrolled all adult patients hospitalized in Samson Assuta-Ashdod hospital confirmed with a positive real-time polymerase chain reaction (RT-PCR) test to have SARS-CoV-2, influenza, or RSV during the period 2018-2020. Pediatric patients and two patients with dual-positive RT-PCR tests for RSV and influenza were excluded.

Data collection

The following data were retrieved for each patient: age, sex, basic medical background, and laboratory analyses values documented at admission. Laboratory tests included white blood cells count (WBC), absolute lymphocyte count, platelet count, serum lactate dehydrogenase levels (DH), alanine aminotransferase (ALT), serum creatinine, C-reactive protein (CRP), albumin, and ferritin concentrations. Information regarding hospital length of stay was obtained.

Statistical analysis

The normality of distribution was assessed with one-sample Kolmogorov-Smirnov test. Continuous data are presented as mean ± standard deviation (SD) or median (interquartile range), and categorical variables as the number of patients (percentage). For two-group comparisons, the Fisher exact test or chi square test were used for categorical variables, and the Mann-Whitney test or t test for continuous variables. For three-group comparisons the Fisher exact test or the chi square test were used for categorical variables, and the Kruskal-Wallis test for continuous variables.

Multiple logistic regressions were used to assess the relationship between SARS-CoV-2 and the laboratory parameters found in the univariate analyses to be significantly associated with SARS-CoV-2 infection (ie, WBC, ferritin, ALT), with

Ben Shimol et al: Can laboratory evaluation differentiate between COVID-19, influenza, and RSV infections?

CMJ

547

age and sex adjustment. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated. The significance level was set at $P < 0.05$ (two tailed). Statistical analyses were performed with SPSS, version 26 (IBM Corp., Armonk, NY, USA).

RESULTS

Study population

The final analyses included 685 patients, classified into three groups: the RSV group with 79 patients; the influenza group with 393 patients; and the SARS-CoV-2 group with 213 patients (Table 1)

The study groups did not significantly differ in comorbidities ($P = 0.523$). Hospital length of stay was longer in the SARS-CoV-2 group ($P < 0.001$).

In the univariate analyses, compared with the influenza and RSV group, SARS-CoV-2 patients had significantly lower WBC count ($P < 0.001$ and $P < 0.001$, respectively) (Figure 1) and significantly higher ALT ($P = 0.017$ and $P = 0.003$, respectively) and ferritin ($P = 0.017$ and $P = 0.045$, respectively).

The RSV group had higher platelet count ($P = 0.007$) than SARS-CoV-2 patients. SARS-CoV-2 patients had higher LDH

($P = 0.035$) and serum albumin levels ($P = 0.007$) than the influenza group.

Based on the univariate analysis, a logistic regression model was built (Table 2). The model included the variables significant in both comparisons in the univariate analysis: age, sex, WBC, ALT, and serum ferritin. SARS-CoV-2 patients
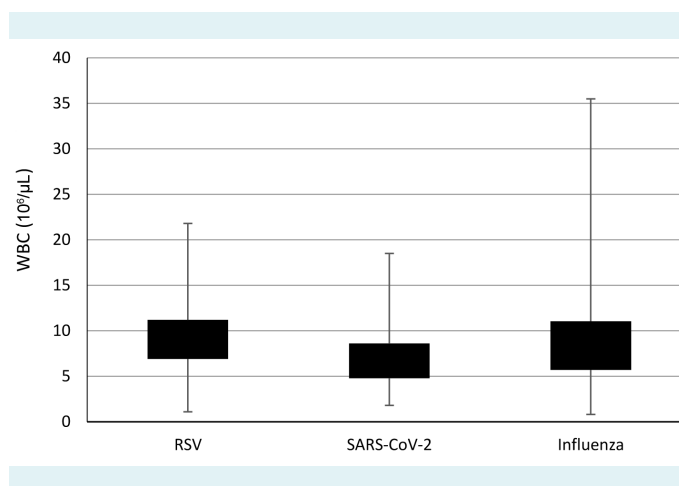

FIGURE 1. White blood cells (WBC, 10^6 cells/μL) levels in the study groups. RSV – respiratory syncytial virus; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2.

TABLE 1. Demographics and laboratory analyses in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza virus, and respiratory syncytial virus (RSV)

Characteristics	Patients with			P		
	SARS-CoV-2 (n = 213)	RSV (n = 79)	Influenza (n = 393)	SARS-CoV-2 vs RSV	SARS-CoV-2 vs influenza	three-group comparisons
Age (y), median (interquartile range [IQR])	62.16 (44-77.5)	76.24 (70-86)	68.14 (57-83)	<0.001	<0.001	<0.001
Sex, n (%)				0.025	0.014	0.017
male	121 (56.8)	33 (41.8)	181 (46.1)			
female	92 (43.2)	46 (58.2)	212 (53.9)			
Comorbidities n (%)*	133 (62.4)	54 (68.4)	242 (61.6)	0.411	0.861	0.523
Laboratory analyses, median (IQR)						
white blood cells (10^6/μL)	6.3 (4.8-8.6)	8.6 (6.9-11.2)	8 (5.7-11)	<0.001	<0.001	<0.001
absolute lymphocyte count (10^6/μL)	1.1 (0.8-1.5)	1.0 (0.7-1.6)	0.9 (0.6-1.4)	0.371	<0.001	0.001
platelet count (10^3/μL)	202 (163-247)	220 (181-287)	199 (158-254)	0.007	0.664	0.009
lactate dehydrogenase, (U/L)	438 (333-591)	402 (344-494)	409 (329-507)	0.199	0.035	0.098
creatinine (mg/dL)	0.9 (0.8-1.1)	1 (0.8-1.3)	0.9 (0.7-1.3)	0.163	0.224	0.328
alanine aminotransferase (U/L)	21 (14-35)	16.5 (12-23.25)	18 (13-28.75)	0.003	0.017	0.006
C-reactive protein (mg/L)	41 (10.9-100)	36 (17.8-86.6)	44.4 (19.7-85)	0.907	0.241	0.386
albumin (g/dL)	3.7 (3.4-4.1)	3.7 (3.5-4)	3.65 (3.3-4)	0.693	0.007	0.020
ferritin (μg/L)	329 (158-663)	210 (99-515)	245 (127-448)	0.045	0.017	0.024
Hospitalization length of stay (days) median (IQR)	4.9 (2.6-9.6)	4.2 (3.1-8.8)	3.5 (2.2-6.4)	0.752	0.001	<0.001

*Comorbidities include a prior diagnosis of at least one condition: diabetes mellitus, obesity, current malignancy, dementia, immunocompromised state (including organ transplant recipients, acquired immune deficiency syndrome, chronic use of corticosteroids of at least 20 mg prednisone per day or equivalent).

were significantly more frequently male (P=0.047), were younger (P=0.022), and had lower WBC count (P<0.001) than influenza patients. They also were significantly younger (P=0.001) and had a lower WBC count than RSV patients (P=0.001). SARS-CoV-2 were younger (P<0.001) and had longer length of stay (P<0.001) and lower WBC (<0.001) and platelet count (P=0.002), and higher absolute lymphocyte count (P=0.001), albumin (P=0.020), ALT (P=0.006), and ferritin (P=0.024) than other two groups. Serum LDH and serum creatinine were not significantly different (P=0.098 and P=0.328, respectively).

DISCUSSION

According to our study, in hospitalized patients with viral respiratory infections, SARS-CoV-2 infection was associated with male sex, younger age, lengthier hospitalization, and lower WBC counts in comparison with RSV and influenza infections.

Influenza virus and RSV are respiratory infections associated with significant morbidity and mortality during the winter season (32-34). The recent COVID-19 pandemic made the differentiation between respiratory viruses even harder. Moreover, different treatment approaches, the need for isolation precautions, and epidemiologic investigations require a rapid diagnosis of SARS-CoV-2 over other respiratory viruses.

In our study, the SARS-CoV-2 group was younger than the influenza and RSV group. This may be explained by two reasons. First, while all three diseases infect all age groups, a substantial share of young adults with COVID-19 present with severe symptoms (14,35). Second, lockdowns, collaps-

ing health care services, disinformation, and higher anxiety and symptoms awareness probably encourage even people with mild symptoms to seek medical advice (36).

In addition, the SARS-CoV-2 group consisted mostly of men, while influenza and RSV groups exhibited female predominance. This supports the results of former studies, which reported a high male:female ratio among COVID-19 patients (14,37). Furthermore, male sex was a risk factor for severe disease and mortality in COVID-19 patients. Thus, one would expect a higher hospitalization rate for men (38-40). This might explain the higher proportion of male inpatients in our study.

In accordance with other studies, we found lower WBC count in SARS-CoV-2 patients compared with influenza and RSV (18). Other studies observed lymphocytopenia as a characteristic finding in COVID-19 patients (15,41). The younger age of our SARS-CoV-2 group even strengthens this claim, as WBC count tends to decline with age (42). Though absolute lymphocyte count was relatively low in our SARS-CoV-2 group, it was even lower in the RSV and influenza groups. Therefore, low lymphocyte count should not be considered specific in distinguishing COVID-19 from other viral infections. In this regard, the low WBC count in COVID-19 patients could not be explained solely by a low lymphocyte count. We assume that other components of WBC were also responsible for the total low count. Tanni et al (43) found significantly lower eosinophils levels in SARS-CoV-2 patients compared with influenza patients. Another study linked COVID-19 with lower monocyte counts (31). The immune dysregulation caused by COVID-19, as described by Ehrenfeld et al (44), could be another possible explanation for a lower WBC count in COVID-19.

TABLE 2. Logistic regression analysis comparing 1) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza virus and 2) SARS-CoV-2 and respiratory syncytial virus (RSV)

	P value	Odds ratio	95% confidence interval
SARS-CoV-2 group (n=213) vs influenza group (n=393)			
age (y)	0.022	1.013	1.002-1.024
male sex	0.047	1.550	1.006-2.389
ferritin (µg/L)	0.557	1.000	1.000-1.000
alanine aminotransferase (U/L)	0.812	1.000	0.997-1.004
white blood cells (million/µL)	<0.001	1.152	1.085-1.224
SARS-CoV-2 group (n=213) vs RSV group (n=79)			
age (y)	0.001	0.963	0.942-0.985
male sex	0.133	0.567	0.270-1.189
ferritin (µg/L)	0.712	1.000	0.999-1.000
alanine aminotransferase (U/L)	0.891	1.001	0.987-1.015
white blood cells (million/µL)	<0.001	0.842	0.759-0.935

Ben Shimol et al: Can laboratory evaluation differentiate between COVID-19, influenza, and RSV infections?

CMJ

549

Interestingly, although former studies found serum ferritin to be an important marker, as well as a prognostic factor in COVID-19, our study found no significant differences in ferritin levels or CRP, another inflammatory marker (22). This finding suggests ferritin to be a factor in other viral infections as well, as observed previously (45).

The hospital length of stay was longer for our SARS-CoV-2 patients compared with influenza and RSV patients. This finding, which indicates greater severity of COVID-19 compared with the other studied diseases, becomes even more noteworthy when one considers that SARS-CoV-2 patients were younger than patients hospitalized for the other viruses.

Several limitations could generate substantial bias in our data analysis. First, we collected data only from hospitalized patients; outpatients and home care patients were not included. This could affect the generalizability of the study, given that most COVID-19 patients have mild disease and many are asymptomatic (46,47). Second, the laboratory data were collected only at admission. These point values, however, could vary during the natural history of the disease. Third, though we included all inpatients with a diagnosis of either SARS-CoV-2, influenza, or RSV, the results of our study should be validated by a prospective study. Last, the demographics and clinical profile in this study do not reflect the general population. The participants were old and most of them had comorbidities. In addition, as mentioned in the first limitation, all of the participants suffered from moderate-severe disease. Whether our results can be extended to younger patients without comorbidities and with mild disease is currently unknown.

Although in our study SARS-CoV-2 infection was associated with male sex, younger age, lengthier hospitalization, and lower WBC counts in comparison with RSV and influenza, the differences between the groups were not substantial enough and would not suffice to distinguish between the illnesses in the emergency department. Molecular and other microbiologic diagnostic techniques, when available, still provide a more accurate and reliable diagnosis of COVID-19.

References

1 Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020;91:157-60. Medline:32191675

2 WHO Coronavirus Disease (COVID-19) Dashboard. Available from: https://covid19.who.int/. Available from: July 8, 2021.

3 Ashraf BN. Economic impact of government interventions during the COVID-19 pandemic: International evidence from financial markets. J Behav Exp Finance. 2020;27:100371. Medline:32835011 doi:10.1016/j.jbef.2020.100371

4 Saqib MAN, Siddiqui S, Qasim M, Jamil MA, Rafique I, Awan UA, et al. Effect of COVID-19 lockdown on patients with chronic diseases. Diabetes Metab Syndr. 2020;14:1621-3. Medline:32889403 doi:10.1016/j.dsx.2020.08.028

5 Søreide K, Hallet J, Matthews JB, Schnitzbauer AA, Line PD, Lai PBS, et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. Br J Surg. 2020;107:1250-61. Medline:32350857 doi:10.1002/bjs.11670

6 Tam CCF, Cheung KS, Lam S, Wong A, Yung A, Sze M, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment-elevation myocardial infarction care in hong Kong, China. Circ Cardiovasc Qual Outcomes. 2020;13:e006631. Medline:32182131 doi:10.1161/CIRCOUTCOMES.120.006631

7 Chong MY, Wang WC, Hsieh WC, Lee CY, Chiu NM, Yeh WC, et al. Psychological impact of severe acute respiratory syndrome on health workers in a tertiary hospital. Br J Psychiatry. 2004;185:127-33. Medline:15286063 doi:10.1192/bjp.185.2.127

8 Overview of Testing for SARS-CoV-2 | CDC. Specimen collection. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html. Accessed: October 6, 2021.

9 Shen M, Zhou Y, Ye J, Abdullah AL-maskri AA, Kang Y, Zeng S, et al. Recent advances and perspectives of nucleic acid detection for coronavirus. J Pharm Anal. 2020;10:97-101. Medline:32292623 doi:10.1016/j.jpha.2020.02.010

10 Brun AL, Gence-Breney A, Trichereau J, Ballester MC, Vasse M, Chabi ML, et al. COVID-19 pneumonia: high diagnostic accuracy of chest CT in patients with intermediate clinical probability. Eur Radiol. 2021;31:1969-77. Medline:33011877 doi:10.1007/s00330-020-07346-y

11 Li Y, Xia L. Coronavirus disease 2019 (COVID-19): Role of chest CT in diagnosis and management. AJR Am J Roentgenol. 2020;214:1280-6. Medline:32130038 doi:10.2214/AJR.20.22954

12 Overview of Testing for SARS-CoV-2 (COVID-19) | CDC. National

Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. 2020.

13   Ryabkova VA, Churilov LP, Shoenfeld Y. Influenza infection, SARS, MERS and COVID-19: Cytokine storm – The common denominator and the lessons to be learned. Clin Immunol. 2021;223:108652. Medline:33333256 doi:10.1016/j.clim.2020.108652

14   Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-20. Medline:32109013 doi:10.1056/NEJMoa2002032

15   Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323:1061-9. Medline:32031570 doi:10.1001/jama.2020.1585

16   Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506. Medline:31986264 doi:10.1016/S0140-6736(20)30183-5

17   Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis. 2020;34:101623. Medline:32179124 doi:10.1016/j.tmaid.2020.101623

18   Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. Lancet Haematol. 2020;7:e671-8. Medline:32659214 doi:10.1016/S2352-3026(20)30217-9

19   Perricone C, Bartoloni E, Bursi R, Cafaro G, Guidelli GM, Shoenfeld Y, et al. COVID-19 as part of the hyperferritinemic syndromes: the role of iron depletion therapy. Immunol Res. 2020;68:213-24. Medline:32681497 doi:10.1007/s12026-020-09145-5

20   Colafrancesco S, Alessandri C, Conti F, Priori R. COVID-19 gone bad: A new character in the spectrum of the hyperferritinemic syndrome? Autoimmun Rev. 2020;19:102573. Medline:32387470 doi:10.1016/j.autrev.2020.102573

21   Ruscitti P, Berardicurti O, Di Benedetto P, Cipriani P, Iagnocco A, Shoenfeld Y, et al. Severe COVID-19, another piece in the puzzle of the hyperferritinemic syndrome. an immunomodulatory perspective to alleviate the storm. Front Immunol. 2020;11:1130. Medline:32574264 doi:10.3389/fimmu.2020.01130

22   Dahan S, Segal G, Katz I, Hellou T, Tietel M, Bryk G, et al. Ferritin as a marker of severity in COVID-19 patients: A fatal correlation. Isr Med Assoc J. 2020;22:429-34. Medline:33236582

23   Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180:934. Medline:32167524 doi:10.1001/jamainternmed.2020.0994

24   Jones N. How COVID-19 is changing the cold and flu season. Nature. 2020;588:388-90. Medline:33324005 doi:10.1038/d41586-020-03519-3

25   Hannah R, Macdonald B, Giattino C, Roser M. Coronavirus (COVID-19) vaccinations - statistics and research - our world in data. 2021. Available from: https://ourworldindata.org/covid-vaccinations. Accessed: July 8, 2021.

26   Memoli MJ, Athota R, Reed S, Czajkowski L, Bristol T, Proudfoot K, et al. The natural history of influenza infection in the severely immunocompromised vs nonimmunocompromised hosts. Clin Infect Dis. 2014;58:214-24. Medline:24186906 doi:10.1093/cid/cit725

27   Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. Lancet Infect Dis. 2007;7:257-65. Medline:17376383 doi:10.1016/S1473-3099(07)70029-4

28   Hall CB, Long CE, Schnabel KC. Respiratory syncytial virus infections in previously healthy working adults. Clin Infect Dis. 2001;33:792-6. Medline:11512084 doi:10.1086/322657

29   Zayet S, Kadiane-Oussou NJ, Lepiller Q, Zahra H, Royer PY, Toko L, et al. Clinical features of COVID-19 and influenza: a comparative study on Nord Franche-Comte cluster. Microbes Infect. 2020;22:481-8. Medline:32561409 doi:10.1016/j.micinf.2020.05.016

30   Lin Y-H, Luo W, Wu D-H, Lu F, Hu S-X, Yao X-Y, et al. Comparison of clinical, laboratory, and radiological characteristics between SARS-CoV-2 infection and community-acquired pneumonia caused by influenza virus. Medicine (Baltimore). 2020;99:e23064. Medline:33126398 doi:10.1097/MD.0000000000023064

31   Chen J, Pan Y, Li G, Xu W, Zhang L, Yuan S, et al. Distinguishing between COVID-19 and influenza during the early stages by measurement of peripheral blood parameters. J Med Virol. 2020;93:1029-37. Medline:32749709 doi:10.1002/jmv.26384

32   Johnstone J, Majumdar SR, Fox JD, Marrie TJ. Viral infection in adults hospitalized with community-acquired pneumonia: Prevalence, pathogens, and presentation. Chest. 2008;134:1141-8. Medline:18689592 doi:10.1378/chest.08-0888

33   Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet. 2018;391:1285-300. Medline:29248255 doi:10.1016/S0140-6736(17)33293-2

34   Cohen R, Babushkin F, Geller K, Finn T. Characteristics of hospitalized adult patients with laboratory documented Influenza A, B and respiratory syncytial virus – A single center retrospective observational study. Lin B, editor. PLoS One. 2019;14(3):e0214517.

35   Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507-13. Medline:32007143 doi:10.1016/S0140-6736(20)30211-7

36   Goodwin R, Wiwattanapantuwong J, Tuicomepee A, Suttiwan P, Watakakosol R. Anxiety and public responses to covid-19: Early data from Thailand. J Psychiatr Res. 2020;129:118-21.

Ben Shimol et al: Can laboratory evaluation differentiate between COVID-19, influenza, and RSV infections?

551

CMJ

Medline:32912591 doi:10.1016/j.jpsychires.2020.06.026

37 Bwire GM. Coronavirus: Why men are more vulnerable to Covid-19 than women? SN Compr Clin Med. 2020;4:1-3. Medline:32838138 doi:10.1007/s42399-020-00341-w

38 Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender differences in patients with COVID-19: focus on severity and mortality. Front Public Health. 2020;8:152. Medline:32411652 doi:10.3389/fpubh.2020.00152

39 Pérez-López FR, Tajada M, Savirón-Cornudella R, Sánchez-Prieto M, Chedraui P, Terán E. Coronavirus disease 2019 and gender-related mortality in European countries: A meta-analysis. Maturitas. 2020;141:59-62. Medline:33036704 doi:10.1016/j.maturitas.2020.06.017

40 The sex, gender and COVID-19 project | Global Health 50/50. Available from: https://globalhealth5050.org/the-sex-gender-and-covid-19-project/. Accessed: July 8, 2021.

41 Liu X, Zhang R, He G. Hematological findings in coronavirus disease 2019: indications of progression of disease. Ann Hematol. 2020;99:1421-8. Medline:32495027 doi:10.1007/s00277-020-04103-5

42 Nah EH, Kim S, Cho S, Cho HI. Complete blood count reference intervals and patterns of changes across pediatric, adult, and geriatric ages in Korea. Ann Lab Med. 2018;38:503-11. Medline:30027692 doi:10.3343/alm.2018.38.6.503

43 Tanni F, Akker E, Zaman MM, Figueroa N, Tharian B, Hupart KH. Eosinopenia and covid-19. J Am Osteopath Assoc. 2020;120:504-8. Medline:32672799

44 Ehrenfeld M, Tincani A, Andreoli L, Cattalini M, Greenbaum A, Kanduc D, et al. Covid-19 and autoimmunity. Autoimmun Rev. 2020;19:102597. Medline:32535093 doi:10.1016/j.autrev.2020.102597

45 Lalueza A, Ayuso B, Arrieta E, Trujillo H, Folgueira D, Cueto C, et al. Elevation of serum ferritin levels for predicting a poor outcome in hospitalized patients with influenza infection. Clin Microbiol Infect. 2020;26:1557.e9-15. Medline:32120038 doi:10.1016/j.cmi.2020.02.018

46 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323:1239-42. Medline:32091533 doi:10.1001/jama.2020.2648

47 He J, Guo Y, Mao R, Zhang J. Proportion of asymptomatic coronavirus disease 2019: A systematic review and meta-analysis. J Med Virol. 2021;93:820-30. Medline:32691881 doi:10.1002/jmv.26326