affect bacteremia duration and concluded that optimal management of SAB should target bacterial clearance to avoid the incremental increase in mortality with each day of persistence of positive blood cultures.

Over the last decade, there has been tremendous success in decreasing the rate of methicillin-resistant *S. aureus* (MRSA) bacteremia in the United States [2]. However, the case fatality rate of the disease has remained relatively stable and varies from 15% to 50% in individual studies [3]. Vancomycin has consistently been shown to be inferior to antistaphylococcal β-lactams for treatment of methicillin-sensitive *S. aureus* bacteremia [3]. However, in cases of MRSA bacteremia, vancomycin remains the mainstay of therapy and alternative antimicrobials have not been proven to be superior [4]. Unexpected but consistent evidence of synergy of the combination of β-lactams with vancomycin have been reported in vitro, supported also by the observations in animal models of MRSA bacteremia [5]. In clinical practice, cases series have been published regarding the successful use of combination therapy as salvage in clearing blood cultures in cases of persistent bacteremia [6]. Recently, in a multicenter randomized controlled trial evaluating the use of combination of β-lactams with vancomycin or daptomycin among 356 randomized patients, the combination therapy arm significantly shortened the duration of MRSA bacteremia [7]. However, it did not prove to have a difference in the primary composite outcome that also included mortality, microbiologic failure, or relapse. Importantly there was a significant increase in the acute kidney injury rate observed in the combination therapy, an observation that substantiates previous retrospective studies that observed a similar trend [8].

Regardless of the cause, persistent bacteremia is considered a surrogate for complicated SAB, as the likelihood for metastatic infection increases with the persistence of bacteremia. The metastatic complications have been shown to lead to poorer outcomes [9]. Even in the absence of metastatic complications, there is retrospective evidence that persistent bacteremia may be an independent predictor of mortality [10]. However, randomized studies have not associated an earlier clearance of bacteremia with a mortality benefit to date [7].

As antimicrobial strategies that achieve earlier clearance of blood cultures become available, caution should be used when the early clearance of blood cultures is considered the be-all and end-all outcome.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

Ioannis M. Zacharioudakis and Fainareti N. Zervou

Division of Infectious Diseases and Immunology, Department of Medicine, New York University School of Medicine, New York, New York, USA

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Correspondence: I. M. Zacharioudakis, New York University Langone School of Medicine, 550 First Ave, 14th Floor, New York, NY 10016 (ioannis.zacharioudakis@nyulangone.org).

Clinical Infectious Diseases® 2021;72(1):179–80

DOI: 10.1093/cid/ciaa439

Inverse Association Between Chronic Hepatitis B Infection and Coronavirus Disease 2019 (COVID-19): Immune Exhaustion or Coincidence?

To the Editor—We read with great interest the report by Zhao et al, regarding a case of delayed immune response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a patient with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) coinfection [1]. The authors stipulate that previous HIV and HCV infection could confer immune dysfunction providing a differential immune response during coronavirus disease 2019 (COVID-19) development.

This report, as most initial reports, originated in China, which has an intermediate-high prevalence of chronic hepatitis B (HBV) infection [2]. We evaluated all peer-reviewed articles, written in the English language, reporting cases of COVID-19 infection and specifically defining rates of HBV infection and hospital admission, since 1 December 2019 until 25 March 2020 and found a surprisingly low prevalence of chronic HBV in COVID-19 cases admitted to the hospital. Indeed, Of the 2054 cases that were reported with this information, only 28 patients (1.36%) were reported positive for HBV.

Table 1. Rates of Hepatitis B Infection Among Patients With Coronavirus Disease 2019 and the General Population by Region and Age Group

Study	Region Studied	No. of Patients	Age Group of COVID-19 Patients, y, median (IQR)	No. of Patients With HBV	Hepatitis B Rate, %		
					COVID-19 Patients	Region	Similar Age Group in Region
Zhao et al [6]	Anhui, China	19	48 (27–56)	1	5.26	7.44	7.5–9[a]
Guan et al [7]	China	1099	47 (35–58)	23	2.1	6.89	~5.5–7[a]
Chen et al [8]	Wuhan, China	99	55.5 (36–64)	0	0	6.89[b]	~5.5–7[b]
Xu et al [9][c]	Wuhan, China	62	41 (32–52)	2	3.22	6.89[b]	~5.5–7[b]
Chen et al [10]	Shanghai, China	249	51 (36–64)	2	0.8	7.2	8.3–8.7[a]
Young et al [11][c]	Singapore	18	47 (31–71)	0	0	3.6	~4.1[a]
Pan et al (in press)	Hubei, China	204	52.9 (SD, 16)	0	0	9.2	11.1[a]

Abbreviations: COVID-19, coronavirus disease 2019; HBV, hepatitis B virus; SD, standard deviation.

[a]Li et al. [12]; Wang et al. [13]; Ji et al. [14]; Ang et al. [15]; She et al. [16].

[b]No data specific to the Wuhan area were noted and so general rates in China were used here.

[c]Personal communication from the authors.

Several of these studies reported 0% incidence of HBV among individuals infected with COVID-19. We matched the HBV rates in COVID-19 subjects to age-specific rates of HBV reported in the respective geographic areas of origin (Table 1). The median age of COVID-19 infected individuals in the evaluated studies ranged between 47 and 51 years, corresponding to HBV rates ranging from 7% to 11%, whereas the HBV rates of those with COVID-19 remained between 0% and 1.3%. It is unclear whether this is a simple epidemiological "misconnection" or if being chronically infected with HBV impacts the chances of clinically significant infection with SARS-CoV-2 leading to fewer hospital admissions, in a similar fashion as that reported by Zhao et al to HIV and HCV. In this regard, research has documented that chronic HBV infection leads to a reduced or absent virus-specific T-cell reactivity (although HBV-specific T cells). This phenomenon, known as "immune exhaustion," is manifested by an impaired ability of T-lymphocytes to produce appropriate cytokines secondary to years of continuous, yet inefficient, immune reaction to the virus [3]. Immune exhaustion is also frequently observed in chronic HCV infection [4]. In this setting, it is plausible that the exhaustion of T lymphocytes may affect their ability to respond to other viruses and reduce the degree of "cytokine storm" that has been noticed in COVID-19 patients, thus culminating in a less severe disease. Similar patterns of immune cointeraction with consequences in clinical presentation and prognosis have been reported in individuals infected with HBV and schistosomiasis [5]. Further research is needed to elucidate if this epidemiological outlier is a consequence of immune dysregulation or just coincidence. If it is indeed the former, it could provide important insights in to the immunopathology of COVID-19 and open potentially unique venues for prevention and treatment.

Notes

Acknowledgments. The authors thank Drs Lanjuan Li (Wuhan, China) and Barnaby Young (Singapore) for providing information from their manuscripts regarding hepatitis B virus.

Financial support. This work was supported by the Robert Wood Johnson Foundation's Harold Amos Medical Faculty Development Program (to J. D. D.); and the National Cancer Institute of the National Institutes of Health (grant number R21 CA215883-01A1 to J. D. D.).

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

Chimaobi M. Anugwom,[1,2] Elizabeth S. Aby,[1,2] and Jose D. Debes[1,2,3]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, University of Minnesota, Minneapolis, Minnesota, USA, [2]Division of Infectious Diseases, Department of Medicine, University of Minnesota, Minneapolis, Minnesota, USA, and [3]Division of Gastroenterology, Hennepin Healthcare, Minneapolis, Minnesota, USA

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Correspondence: J. D. Debes, University of Minnesota, 420 SE Delaware St, MMC 810, Minneapolis, MN 55455 (debes003@umn.edu).

Clinical Infectious Diseases® 2021;72(1):180–2

DOI: 10.1093/cid/ciaa592

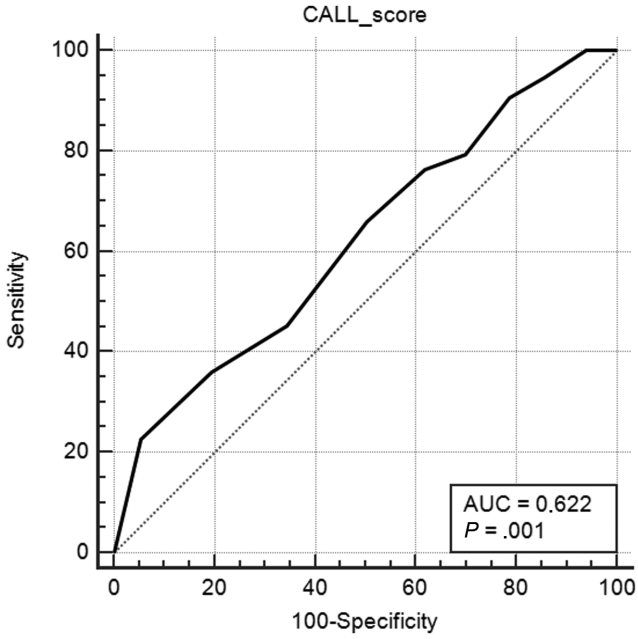

Figure 1. ROC curve showing the predictive power of the CALL score for predicting progression to severe COVID-19. Abbreviations: AUC, area under the ROC curve; CALL, comorbidity, age, lymphocyte count, lactate dehydrogenase; COVID-19, coronavirus disease 2019; ROC, receiver operating characteristic.

The CALL Score for Predicting Outcomes in Patients With COVID-19

To the Editor—Defining prognosis of patients affected by coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is of utmost importance for planning appropriate setting of care and treatment. Therefore, we read with great interest the article by Ji and colleagues that was recently published in *Clinical Infectious Diseases* [1]. After exclusion of patients presenting with severe COVID-19 syndrome and by using data records of 208 patients suffering from COVID-19, with mean age ± standard deviation [SD] 44.0 ± 16.3 years, the authors derived and validated a novel score, named CALL, based on 4 variables (C = comorbidity, A = age, L = lymphocyte count, L = lactate dehydrogenase [LDH]) aimed at predicting progression toward clinical deterioration. The CALL score ranges from 4 (absence of comorbidity, age under 60 years, lymphocyte count over 1.0×10^9/L, LDH under 250 U/L) to 13 (presence of comorbidity, age over 60 years, lymphocyte count under 1.0×10^9/L, LDH over 500 U/L). The prognostic power for predicting progression toward clinical worsening, defined as respiratory rate ≥30 breaths/min, resting oxygen saturation ≤93%, paO2/FiO2 ratio ≤300 or requiring of mechanical ventilation, was excellent with an area under the receiver operating characteristic (ROC) curve (AUC) of 0.91 (95% confidence interval [CI] .86 to .94). Using a cutoff value of 6 points, the authors found positive and negative predictive values of 50.7% (38.9%–62.4%) and 98.5% (94.7%–99.8%), respectively. Therefore, after exclusion of patients requiring immediate intensive care unit admission, we tested the predictive power of the CALL score in an Italian COVID-19 population admitted to hospital from 12 March to 20 April 2020 and consisting of 210 patients, 112 males (53.3%), with mean age 67.3 ± 16.8 years. Of them, 97 patients (46.2%) met criteria for progression to severe COVID-19 syndrome, and 37 patients (17.6%) died. Median CALL score was 10 (IQR 8–12). One hundred and fifty-four patients (73.3%) had comorbidity, 144 (68.6%) were over 60 years, 100 (47.6%) had lymphocyte count under 1.0×10^9/L, and 54 (25.7%) had LDH over 500 U/L. Progression to severe COVID-19 syndrome increased from 27.2% in patients with CALL score ≤6 points to 53.0% in patients with CALL score ≥11 points. The predictive power of the CALL score for predicting progression to severe COVID-19 was low with an AUC of 0.622 (95% CI: .533–.688) (Figure 1). Instead, the predictive power of the CALL score as prognosticator for in-hospital mortality was good (AUC 0.768, 95% CI: .705–.823). In conclusion, in our COVID-19 population the CALL score seems to be a good prognosticator for in-hospital mortality but not for progression to severe COVID-19. Other external validations are warranted.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.