Leptospira Serovar as Prognostic Factor

To the Editor: Herrmann-Storck et al. (1) investigated prognostic factors of leptospirosis and concluded that infection with Leptospira interrogans serovar Icterohemorrhagiae was linked to severe outcomes. We have concerns about this conclusion.

These researchers were comparing clinical severity of disease among patients for whom serovars of infecting isolates had been identified. However, in that study, blood culture was performed for only 88 (52%) of 168 case-patients, and serovars were identified for 40 (73%) of 55 Leptospira strains isolated. Expecting these 40 patients (24% of total) to represent all case-patients in the study is unjustified.

Also, the authors evaluated potential risk factors among these patients by applying a multivariable logistic regression model. This process is questionable. First, the sample size of 40 is not large enough to warrant multivariable analysis with 9 independent variables. Actually, only 8 case-patients had severe disease, although at least 10 outcomes are required for variables in a logistic regression model (2).

Second, the model selected is inappropriate. Variables such as thrombocytopenia, hyperneutrophilia, hyperamylasemia, and elevated aspartate aminotransferase levels are laboratory findings of severe leptospirosis (and not risk factors of disease). These factors should not be included in a multiple logistic regression model as confounders. We believe it is premature to reach a conclusion about the association between Leptospira serovars and clinical severity from the data presented by Herrmann-Storck et al.

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References

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In response: We thank Suzuki and Ariyoshi for their letter (1). Identification of serovar and species can only be accomplished by isolating Leptospira strains, and obtaining isolates and identifying the serovar and species are especially difficult for human cases of leptospirosis. The bacteria are present in blood for only 1 week after the onset of the disease; they also are fastidious and difficult to grow. Serologic testing gives only a possible serogroup, but it is the only diagnostic tool for confirming patients’ infection after 1 week of disease. A strength of our study (2) is that it contains extensive epidemiologic, clinical, and biological data and provides a broad collection of identified strains.

Including laboratory findings such as thrombocytopenia, hyperneutrophilia, and hyperamylasemia in the model was appropriate for the following reasons. First, they were not used to establish the definition of severity. Second, the variables included in the model were defined, not according to the norms but at a given level far above the norms (thrombocytopenia <50 g/L, hyperneutrophilia >12 g/L, amylase >285 U/L), which have been recently suggested as possible predictors of severity in other reports.

We are aware that the statistical model has its limits in the context of this retrospective study. We must point out that the conclusion of the independent involvement of Leptospira serovar Icterohemorrhagiae in severity is made in the context of Guadeloupe with its particular ecology and insular features, and results were compared with those for given cocirculating strains that are sometimes different in other areas of the world. The real implication of our study is the opportunity it presents to explore some virulence factors in this particular serovar, to compare the results with those of other studies conducted in other areas with the same tools of identification, and to pave the way for a much larger prospective study in the region.

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References

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