

Relationship between Blood Volume and Diagnostic Sensitivity of Blood Culture for Typhoid Fever: a Systematic Review and Meta-Regression Study

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Background: Blood culture is the standard approach for diagnosing typhoid fever in epidemiologic studies. We performed a meta-analysis to quantify the relationship between the amount of a suspected typhoid patient's blood inoculated into media and blood culture sensitivity for typhoid fever, a relationship that has been postulated but whose functional form has never been determined.

Methods: A systematic literature review was performed to identify all studies that report the sensitivity of blood culture in bone-marrow culture-confirmed cases of typhoid fever (which is the current gold standard). We fit a meta-regression model to account for between-study heterogeneity and accommodating for repeated measures within some of the studies.

Results: The studies included in our analyses were representative of the patient populations in contemporaneous typhoid-endemic countries. A meta-regression model showed that across the studies, blood volume inoculation had a significant effect on culture sensitivity, even after inclusion of study-level random effects. During secondary analysis, we determined that the prevalence of antimicrobial use prior to seeking care and the time before diagnostic testing was unlikely to bias our results.

Conclusions: The relationship between the amount of blood inoculated into growth media and blood culture sensitivity should be rigorously taken into account in the interpretation of typhoid fever incidence studies and the evaluation of next-generation typhoid fever diagnostics.