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Original Research Article

Comparison of Typhidot IgM test and blood culture in children with clinically compatible enteric fever

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ABSTRACT

Background: The often-non-specific presentation of typhoid fever makes clinical diagnosis difficult. The blood culture is time consuming, affected by often given prior antibiotics and has low sensitivity (60%). Typhidot IgM gives quick results in early stage of disease. Pediatric data are scarce. So, we studied and compare Typhidot IgM test and blood culture in children with clinically compatible enteric fever.
Methods: This was retrospective observational study done in Department of Pediatrics from the 1st October, 2017 to 30 September, 2018. 42 children with clinically compatible enteric fever (aged 6 months to 18 years); with either typhidot IgM or blood culture positive for Salmonella species were sampled and analyzed.
Results: Typhidot IgM test had sensitivity of 92.7% (N = 39/42) compared to blood culture with sensitivity of 79.4% (N = 27/34). 2 out of 3 typhidot negative cases were *S. Paratyphi* positive in blood culture. Typhidot IgM had positive predictive value = 97.4% due to 1 false positive case. 19 (79.2%) out of 24 blood culture positive patients had not received any antibiotic prior test, 3 (60 %) out of 5 blood culture negative patients had received antibiotics.
Conclusions: Typhidot IgM is a highly sensitive quick diagnostic tool for diagnosing enteric fever in children with sensitivity of 92.3% and PPV of 97.4% compared to blood culture (sensitivity= 79.4%). It is more sensitive to diagnose *S. typhi* enteric fever (sensitivity= 97.3%) then *S. paratyphi* (sensitivity= 50%). Antibiotic administration prior to blood culture testing reduces its positivity rate but not significantly statistically. Larger studies are needed to change the current recommendations on typhidot IgM.

Keywords: Blood culture, Children, Enteric fever, Typhoid fever, Typhidot IgM

INTRODUCTION

Problem: Enteric fever is endemic disease and is a major public health problem in developing countries including India. Global estimates of typhoid fever burden range between 11 and 21 million cases and approximately 1,28,000 to 1,61,000 deaths annually.[1] In India, Reported data for the year 2013 shows 1.53 million cases and 361 deaths.[2] Children are disproportionately affected by typhoid fever, with peak incidence long known to occur in individuals aged 5 to <15 years of age.[3] It is a systemic infection caused by *Salmonella typhi*, usually through ingestion of contaminated food or water (faecal-oral route). A similar but often less severe disease, paratyphoid fever, is caused by *Salmonella paratyphi* A, B or C.[4]

The often-non-specific presentation of typhoid fever makes clinical diagnosis difficult as it may be confused with a wide range of other common febrile illnesses in regions where typhoid fever is endemic. There is no 100% sensitive or ideal test available for enteric fever. The sensitivity of a single blood culture is approximately 60% and is affected by the volume of blood obtained for

culture. Sensitivity of blood culture is further reduced by the common practice of starting treatment with antibiotics prior to confirmation of the diagnosis. Blood culture is not performed for the majority of cases in low-middle income countries, especially among those treated in non-hospital settings.[5] Blood culture is not always available and, when it is, it takes at least 2 to 3 days. As a result, diagnosis may be delayed or overlooked and patients without typhoid fever may receive unnecessary and inappropriate antimicrobial treatment. For this reason, typhoid rapid antibody tests can facilitate diagnosis and disease management.[6] Typhidot IgM is widely used serological test

WHO study in 2007 proved typhoid rapid antibody tests appear to correlate poorly with blood culture results in sub-Saharan Africa, The World Health Organization (WHO) has issued no recommendations on the use of typhoid rapid antibody tests.[6] In latest, a Cochrane database systematic review study has been published in May, 2017. It has conducted a meta-analysis of 37 studies with total 5080 participants (mostly from Asia) with the aim to assess the diagnostic accuracy of commercially available rapid diagnostic tests (RDTs) and prototypes for detecting *Salmonella typhi* or *paratyphi* A infection in symptomatic persons living in endemic areas.

It concluded that these tests had moderate diagnostic accuracy. Across all forms of the Typhidot test, the average sensitivity was 84% (95% CI 73% to 91%) and specificity was 79% (95% CI 70% to 87%).[5] Another study of diagnostic tests of enteric fever in children from Brazil, published in November 2010 suggests that Typhidot M test had the highest sensitivity, specificity, PPV and NPV of 90% (95% CI = 74.4-96.5), 100% (95% CI = 90.1-100), 100% (95% CI = 87.5-100), and 92.1% (95% CI = 79.2-97.3) respectively.[7] Other studies give similar data but most of these studies are based on adult data and exclusive pediatric studies and further Indian data are scarce.

The objectives of this study were to study and compare the sensitivity of Typhidot IgM and blood culture for diagnosis of enteric fever in clinically compatible children in urban population and to analyze the effect of antibiotic taken prior to testing, on sensitivity of Typhidot IgM and blood culture.

METHODS

This was retrospective observational study done in Department of Pediatrics from the 1 October 2017 to 30 September 2018. 42 children (aged 6 months to 18 years); with clinically compatible enteric fever (The acute illness with high-grade fever (95%), coated tongue (76%), anorexia (70%), vomiting (39%), hepatomegaly (37%), diarrhea (36%), toxicity (29%), abdominal pain (21%) with blood leukocyte counts are frequently low in relation to the fever and toxicity)with either Typhidot IgM or blood culture positive for Salmonella species were sampled and analyzed.[8] Children with alternative proven diagnosis or incomplete details were excluded. Epidemiological data, clinical features, blood culture, Typhidot IgM test and other laboratory parameters from all the patients were collected and it was analyzed by using the Statistical package for social sciences (SPSS) version 21 Fisher's exact test. P-value of less than 0.05 was considered as statistically significant. The study was conducted after getting ethical approval from the Bhaktivedanta Hospital and Research Institute, Mira Road, Thane.

RESULTS

In the study, 42 children with clinically compatibility for enteric fever, aged 6 months to 18 years; with either Typhidot IgM or blood culture positive for Salmonella species were sampled from the 1 October 2017 to 30 September 2018 in the Department of Pediatrics, Bhaktivedanta Hospital and Research Institute, Mira Road, Thane.

Age ranged from 1.5 year to 18 years, with median age of 10 years. 73.8% (N = 31/42) were between 5 to 15 years of age. There was male preponderance with 69.1% (N = 29/42). 38 cases were positive, 3 negative and 1 was false positive for Typhidot IgM test. Hence Typhidot sensitivity was found to be 92.7% with positive predictive value of 97.4%. Two of three Typhidot negative were *Salmonella paratyphi* and both received antibiotics prior. In one of them, test was done after 30 days. Total Typhidot is negative in 50 % of S Paratyphi. Typhidot IgM sensitivity in *S. typhi* was found to be 97.3% and in *S. paratyphi* it was 50%.

The false positive patient was diagnosed of pneumonia with blood culture negativity and the clinical features were not compatible with enteric fever. Blood culture was done in 34 cases, of which 27 were positive (23 were *S. Typhi*, 4 for *S. paratyphi* positive) and 7 were negative. Blood culture had sensitivity of 79.4%. Fisher's exact test was applied for testing correlation between Blood culture and Typhidot; the two-tailed P value was 1.0000. The association was considered to be not statistically significant.

19 (79.2%) out of 24 blood culture positive patients had not received any antibiotic prior test, but only 5 (20.8%) had received. 3 (60%) out of 5 blood culture negative patients had received antibiotics. Although there is negative correlation between blood culture positivity and receiving antibiotics prior testing, but it was not statistically significant.

DISCUSSION

Enteric fever is endemic disease and is a major public health problem in developing countries including India. It has non-specific presentation, which makes clinical diagnosis difficult as it may be confused with a wide

range of other common febrile illnesses in regions where typhoid fever is endemic. There is no 100% sensitive or ideal test available for enteric fever. The sensitivity of a single blood culture is approximately 60% and is affected by volume of blood obtained for culture, common practice of starting treatment with antibiotics prior to confirmation of the diagnosis.[5]

Many rural places, they are not available, and even if available, delayed results cause delayed and inappropriate treatment. The serological tests like Typhidot IgM can give quick results but universal acceptance and recommendations are lacking in children. Hence present study aimed to compare Typhidot IgM test and blood culture as a diagnostic tool in children with clinically compatible enteric fever in urban setting.

In present study, Typhidot IgM test had sensitivity of 92.7% (N= 38 out of 41 cases). In three cases it was negative. 2 out of 3 cases were *S. paratyphi* and 1 was *S. typhi* positive in blood culture. Although 2 another S. *paratyphi* culture proved cases were Typhidot IgM positive too, making Typhidot IgM 50% sensitive to pick up *S. paratyphi*.

Typhidot IgM's sensitivity to detect *S. typhi* was 97.3%. Typhidot IgM had positive predictive value= 97.4% due to 1 false positive Typhidot case in study as patient was diagnosed of pneumonia with blood culture negativity and the clinical features were not compatible with enteric fever. Brazilian study on Typhidot M test in children also found its sensitivity of 90%, PPV of 100%.[7]

Typhidot test study from RIMS hospital also found its usefulness in clinically suspected cases of typhoid fever and has observed the sensitivity of 93.75%, PPV of 75%.[9] In present study, blood culture had sensitivity of 79.4% (N= 27 positive and 7 negative). Fisher's exact test was applied; the two-tailed P value equals 1.0000. The association between Blood culture and Typhidot was considered to be not statistically significant. There were six patients positive for Typhidot IgM but negative for blood culture, responded well to anti Salmonella treatment. A systematic literature review published in 2016 observed that blood culture sensitivity was 66 % (95% CI 56-75 %) when compared with bone marrow culture results and it underestimated the burden of disease.[10]

In the present study, 19 (79.2%) out of 24 blood culture positive patients had not received any antibiotic prior test, but only 5 (20.8%) had received. In a study from Mumbai, published in 2008 observed that Fifty-five blood culture positive for salmonella patients (46.2%) received antibiotics prior doing test.[11] 3 (60 %) out of 5 blood culture negative patients had received antibiotics. Although there is negative correlation between blood culture positivity and receiving antibiotics prior testing, but it was not statistically significant).

CONCLUSION

Typhidot IgM is a highly sensitive quick diagnostic tool for diagnosing enteric fever in children with sensitivity of 92.3% and PPV of 97.4% compared to blood culture (sensitivity = 79.4%). It is more sensitive to diagnose *S. typhi* caused enteric fever with sensitivity of 97.3% and poorly sensitive for *S. paratyphi* with sensitivity of 50%. Antibiotic administration prior to blood culture testing reduces its positivity rate but not significantly statistically. Larger studies are needed to change the current recommendations on Typhidot IgM.

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