

Evaluation of Typhidot test in the diagnosis of enteric fever in symptomatic children keeping blood culture as gold standard

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Objective: To evaluate the validity of typhidot test in the diagnosis of enteric fever in symptomatic children keeping blood culture as gold standard

Methodology: This descriptive cross sectional study was conducted at pediatric ward of Liaquat National Hospital, Karachi, Pakistan from July 30, 2013 to January 31, 2014. Patients of either gender with age between 1-12 years with fever 38°C and above lasting for at least 3 days were included. All had Typhidot and blood culture. Provisional diagnosis of enteric fever was made on the basis of history of fever ? 38°C lasting at least 3 days with or without abdominal pain, coated tongue, vomiting, constipation/diarrhea, splenomegaly, hepatomegaly, and rose spots.

Results: Total number of patients was 129. Mean age was 7.75±4 years. Mean duration of fever was

6.73±1.99 days. There were 89 (69%) male patients and 40 (31%) females. Vomiting was observed in 44 (34.1%) patients, coated tongue 64 (49.6%), constipation 11 (8.5%), diarrhea 31 (24%), splenomegaly 35 (27.1%), Hepatomegaly 58 (45%) and rose spots 75 (58.1%). Typhidot IgM was positive in 94 (72.9%) and blood culture was positive in 108 (83.7%) patients. Overall validity of typhidot showed that sensitivity was 83%, specificity 81%, PPV 96% and NPV 49%.

Conclusion: The validity of typhidot test in the diagnosis of enteric fever in symptomatic children was found to be satisfactory. (Rawal Med J 201;43:220-223).

Keywords: Typhidot test, enteric fever, fever in children.

INTRODUCTION

Enteric fever is termed for both typhoid fever and paratyphoid fever. Typhoid fever is caused by salmonella typhi, whereas paratyphoid fever is caused by S. paratyphi A, B and C. In 2000, it was estimated that over 2.16 million episodes of typhoid occurred worldwide, which resulted in 216,000 deaths, of which more than 90% morbidity and mortality occurred in Asia.^{1,2} According to WHO, the incidence of typhoid fever in Pakistan is 421 cases per 100,000 populations per year and it represents fourth most common cause of death in Pakistan.³ A study from Karachi claims the prevalence of the typhoid fever in symptomatic cases as 61.5%.⁴

The presenting signs and symptoms of typhoid fever in children differ significantly from those in adults. The diagnosis in emergency department is usually based on clinical signs and symptoms with basic or no laboratory testing.² Blood culture is the gold standard for the diagnosis and gives information about antibiotics sensitivity of isolate but in best of

the circumstances it carry 70-75% diagnostic yield. The widespread use of antibiotics in the community makes it difficult to isolate the organism on blood culture and alternative methods of diagnosis such as bone marrow culture may be required.⁵ Therefore, there is a real need for simple and rapid serological diagnostic test for enteric fever.

Culture of bone marrow aspirate is 90% sensitive.³ Blood, intestinal secretions (vomit or duodenal aspirate), and stool culture results are positive for S typhi in approximately 85%-90%.⁴ The dot-enzyme immunoassay (dot-EIA) is a new serological test that shows specific IgM and IgG antibodies against salmonella typhi strains. It separately identifies IgM and IgG antibodies.⁶ Typhidot test has been reported to be highly sensitive and specific test in diagnosing typhoid fever in some studies, other studies report variable results.⁷ Its sensitivity and specificity of has been reported as 92.85% and 90%.⁸ Therefore the rationale of this study to evaluate the validity of typhidot test in the diagnosis of enteric fever in

symptomatic children keeping blood culture as gold standard.

METHODOLOGY

This descriptive cross sectional study was conducted at pediatric ward of Liaquat National Hospital, Karachi, Pakistan from July 30, 2013 to January 31, 2014 through Non probability consecutive sampling technique. With prevalence as 61.5%⁴ to 90%⁸ using 95% level of confidence and 7% absolute precision total sample size calculated was 129. Inclusion criteria were patients of either gender with age between 1-12 years with fever 38°C and above lasting for at least 3 days. Patients with fever of 38 °C or above with clear focus of infection, patients with MP positive, those with history of recent typhoid immunization, with history of immunosuppression and taking any type of antibiotics during this illness were excluded from the study. Informed consent was taken from legal guardians of each child.

Patient's history and physical examination was conducted and the responses were marked on a pre-designed Performa (annex) comprising of demographic features and clinical diagnostic features of enteric fever and its duration. Typhidot was collected within 24 hours and the Blood Culture was followed for the maximum of 10 days until it turns to be positive for salmonella.

Data were analyzed using SPSS version 17. Sensitivity, Specificity, Positive predictive value, and Negative predictive value and Accuracy of clinical diagnosis were calculated for typhidot (Ig M) positive, taking positive blood culture as gold standard. Effect modifiers were controlled through stratification of age, gender, duration of fever to see the effects of these on outcome.

$p < 0.05$ was taken as significant.

RESULTS

Total numbers of patients were 129. Mean age was 7.75 ± 4 years. Mean duration of fever was 6.73 ± 1.99 days. 77 (59.7%) patients were in >7 years age group. There were 89 (69%) males and 40 (31%) females. Vomiting was observed in 44 (34.1%) patients, coated tongue in 64 (49.6%), constipation in 11 (8.5%), diarrhea in 31 (24%), splenomegaly in 35 (27.1%), Hepatomegaly in 58 (45%) and rose

spots in 75 (58.1%). Typhidot IgM was positive 94 (72.9%) and blood culture positive in 108 (83.7%) patients (Table).

Table. Clinical Features and validity of Test (n=129).

Clinical Features	Yes n (%)	No n (%)	P-Value
Vomiting	44 (34.1%)	85 (65.9%)	-----
Coated Tongue	64 (49.6%)	65 (50.4%)	-----
Constipation	11 (8.5%)	118 (91.5%)	-----
Diarrhea	31 (24%)	98 (76%)	-----
Splenomegaly	35 (27.15%)	94 (72.9%)	-----
Hepatomegaly	58 (45%)	71 (55%)	-----
Rose Spots	75 (58.1%)	54 (41.9%)	-----
Typhoid IGM Positive	94 (72.9%)	35 (27.1%)	-----
Blood culture positive	108 (83.7%)	21 (16.3%)	-----
Overall Validity of Typhoid			
Yes	90	18	0.001
No	18	17	
Age group ≤ 7 years and validity of typhoid			
Yes	46	2	1.00
No	4	0	
Age group >7 years and validity of typhoid			
Yes	42	4	0.001
No	14	17	
Duration of fever ≤ 5 days and validity of typhoid			
Yes	22	4	0.003
No	7	11	
Duration of fever >5 days and validity of typhoid			
Yes	68	0	0.001
No	11	6	

Overall validity of typhidot showed that sensitivity was found to be 83%, specificity 81%, PPV 96% and NPV 49% ($p=0.001$). Age group ≤ 7 years sensitivity was 92%, specificity 0%, PPV 96% and NPV 0% ($p=1.00$). Age group >7 years sensitivity was 75%, specificity 81%, PPV 91% and NPV 55 ($p=0.001$). With duration of fever ≤ 5 days sensitivity

was 76%, specificity 73%, PPV 85% and NPV 61% ($p=0.003$). With duration of fever >5 days sensitivity was 86%, specificity 100%, PPV 100% and NPV 35% ($p=0.001$).

DISCUSSION

In this study, overall sensitivity was found to be 83%, specificity 81%, PPV 96% and NPV 49%. Chi-square test was applied and sufficient evidence of significant relationship was observed as p -value was less than level of significance. Typhidot was positive in 72.9% children. In a study from Rawalpindi, Typhidot was positive in 55.2% and negative in 44.8% children.⁸ This difference may be due that they included adolescents and adults along with children in their study. In another local study Typhidot was positive in 856 (42.9%) children⁹. In another local study Typhidot was positive in 266 (48.36%) children¹⁰. 16 (4.5%) were positive in the age group 0-1 year whereas in 1-5 years age positive with 17.12% prevalence. patients of 5-10 years of age had 22.2% prevalence. While patients of 10-15 years of age were found positive with 26.9% prevalence. In Adolescent group, 27(25%) were positive.

An unsimilar study from India revealed 15.6% children were culture positive and in 31.1% Typhidot was positive.¹¹ In a local study, only 25.26% samples were positive for Typhidot test. The peak seropositivity rates were found during the months of April-June, while fewer cases were observed from January to March. Age wise distribution of typhoid fever reflected that age groups of 10-15 years were at higher risks of developing enteric fever.¹²

A study from India showed the overall sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the Typhidot-IgM test and Enter screen-IgM test considering blood culture as gold standard were 97.29% and 88.13%, 97.40% and 87.83%, 98.18% and 92.03%, 96.15% and 82.27%, respectively.¹³ While in another study, in 41 children diagnosed with typhoid fever, 37 were positive for IgM anti *S. typhi*, but only 18 were positive for *S. typhi* in blood culture. IgM anti *S. typhi* (cut-off ?4) test had an Area under the Curve (AUC) of 59%, sensitivity of 100% and

specificity of 17.39%. IgM anti *S. typhi* with cut-off >8 showed the highest AUC with sensitivity of 55.56% and specificity of 73.68%.¹⁴

In another study, *Salmonella typhi* was isolated from 82 (30.4%) and the remaining 188 (69.6%) were blood culture negative. Typhidot-M was positive in 136 (50.4%). Typhidot-M test had a sensitivity of 81.7%, specificity of 84.6%, PPV of 69.8%, and NPV of 91.4%.¹⁵ In our study, Rose Spots were common findings; present in 58.1% cases, vomiting in 65.9%, coated tongue in 49.6%, constipation in 91.5%, diarrhea in 76%, splenomegaly in 76% and hepatomegaly in 55% children. A study from India showed anorexia was the common symptoms along with toxic look, coated tongue.¹¹ Another study from Bangladesh reported abdominal pain in 21%, loss of appetite in 58% and coated tongue in 18%, myalgia was in 15%, headache in 12% and loss of appetite was in 58% children.¹⁶

CONCLUSION

The validity of typhidot test in the diagnosis of enteric fever in symptomatic children was found to be satisfactory. Even though Typhidot is rapid, easy and affordable, its use should be followed with care and should have backup test in certain circumstances.

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