

DRUG SUSCEPTIBILITY AND COMPARISON OF ENTEROCHECK AND WIDAL TEST WITH BLOOD CULTURE IN THE DIAGNOSIS OF TYPHOID FEVER IN THE AGE GROUP OF 1- 15 YEARS

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ABSTRACT

Background: Typhoid fever and paratyphoid fever (also known as enteric fever, but collectively referred to as typhoid fever here) are severe systemic illnesses characterized by sustained fever and abdominal symptoms. The objective is to assess the sensitivity and specificity of the Enterocheck for the diagnosis of typhoid fever. **Materials and Methods:** This Observational study was conducted among 120 children in the age group of 1 year to 15 years, admitted in Masonic medical centre with history of fever of 5 days or more, with clinical symptoms and signs suggestive of Typhoid fever were included for study. **Results:** A total of 120 children in the age group of 1 to 15 years with fever ≥ 5 days with signs and symptoms suggestive of typhoid fever were studied. Among 120 children, blood culture was positive in 59 children. Blood culture is the gold standard in the diagnosis of typhoid fever. Blood culture was positive predominantly in the age group between 1- 5 years. Blood culture positivity was seen predominantly among males. Blood culture positive children were all sensitive to Ceftriaxone, except in one child. Amikacin was sensitive in all children. Resistance to Fluroquinolones (Ciprofloxacin, Ofloxacin) was predominant in the present study. Only 5 children were resistant to Chloramphenicol. **Conclusion:** Typhoid fever is an important cause of febrile illness in children. Fever with anorexia, diarrhoea, headache, hepatosplenomegaly were the common clinical manifestations. The Enterocheck WB test, with its higher sensitivity and specificity, can be effectively used in the rural setup, wherein blood culture facilities are not available.

INTRODUCTION

Typhoid fever is a systemic infection caused by the bacterium, *Salmonella enterica*, serotype typhi.^[1] The socio-economic impact of the disease is huge, because the typhoid survivors may take several months to recover and to resume work.^[2] An early and accurate diagnosis is necessary for a prompt and effective treatment. One has to rely on serological diagnosis, since many diagnostic laboratories in the developing countries, especially in the rural areas, do not have facilities for blood culture and thus serological diagnosis becomes an important diagnostic tool. The Widal agglutination test usually detects the IgM and the IgG antibodies to *S.typhi* in the patient's serum from the second week of the onset of the symptoms of typhoid fever. The early rising antibodies to the lipopolysaccharide (LPS) O are predominantly IgM in nature. The *S.typhi* specific IgM antibodies can be used as an early marker to detect a recent infection. So, this study was

undertaken to assess the sensitivity and specificity of the Enterocheck for the diagnosis of typhoid fever.

MATERIALS AND METHODS

This Observational study was conducted among 120 children in the age group of 1 year to 15 years, admitted in Masonic medical centre with history of fever of 5 days or more, with clinical symptoms and signs suggestive of Typhoid fever were included for study.

Sample Size: 120 children in the age group of 1 to 15 years with history of fever of 5 days or more with clinical symptoms and signs suggestive of typhoid fever.

Inclusion Criteria

Fever of 5 days duration or more Age group between 1 to 15 years.

Headache, Vomiting, Abdominal pain, Diarrhoea, Coated tongue, Hepatosplenomegaly

Any 3 out of 6 clinical manifestations mentioned above.

Exclusion Criteria

Children with already diagnosed typhoid fever within 1 year Children who were vaccinated for typhoid fever

Method of Collection of Data

This study was conducted in Masonic medical centre for children, Coimbatore. The study included children with fever of five days' duration or more, with clinical features as mentioned in inclusion criteria, in age group between 1- 15 years. Detailed history, clinical examination was done in this children. Consent was taken from the parents before sample collection. The blood samples were collected for blood culture on day 5 of fever. Widal test and the Enterocheck test, were done on 8th day of fever. Under universal aseptic precaution, right cubital fossa is cleansed with povidone iodine, Later spirit, and once again povidone iodine is applied and made sterile. Using 5 ml sterile Syringe, blood is drawn and put in automated blood culture medium. (Bactec method). Blood culture results are obtained in 48-hour interval and interpreted.

The Widal test was done by using the standard procedure. The Widal test was confirmed by tube agglutination method and it was considered positive when a titre of equal to or more than 1:160 was observed.

The Entero check test is a rapid, qualitative sandwich immunoassay for the detection of the IgM antibodies to S.typhi in human serum/plasma or whole blood specimens. It detects the presence of IgM class of antibodies to a lipopolysaccharide(LPS) which is specific to S. Typhi in the specimens. Positive and negative test results.

RESULTS

A total of 120 children in the age group of 1 to 15 years with fever ≥ 5 days with signs and symptoms suggestive of typhoid fever were studied.

Among 120 children, blood culture was positive in 59 children. Blood culture is the gold standard in the diagnosis of typhoid fever. Blood culture was positive predominantly in the age group between 1- 5 years. Blood culture positivity was seen predominantly among males.

Hepatomegaly was seen predominantly in the present study; Headache was predominantly among children in the age group between 11- 15 years. Diarrhoea, Vomiting and Abdominal pain were prominent clinical features in age group between 1- 10 years. Step ladder pattern of fever was not noticed in children in the present study. Coated tongue was present in 19 children in the present study.

Blood culture has grown Salmonella typhi in 57 children and 2 children has grown Salmonella para typhi A. None of them has grown Salmonella para typhi B.

None of the children developed complications of typhoid fever as in the form of intestinal ulcer, perforation, meningitis.

Blood culture positive children were all sensitive to Ceftriaxone, except in one child. Amikacin was sensitive in all children. Resistance to Fluroquinolones (Ciprofloxacin, Ofloxacin) was predominant in the present study. Only 5 children were resistant to Chloramphenicol.

Table 1: Age Distribution

Age Group	No of Blood Culture Positive Cases	Percentage
1- 5 Years	28	47%
6- 10 Years	26	44%
11-15 Years	5	9%

In the present study, about 47% of blood culture positive cases were seen in the age group between 1- 5 years

Table 2: Sex Distribution

Sex	No of Blood Culture Positive Cases	Percentage
Males	37	63%
Females	22	37%

In the present study, blood culture positive cases were seen in about 63% in male children.

Table 3: Clinical Features at Admission

Clinical Features	No Of Individuals
Headache	31
Abdominal Pain	23
Vomiting	20
Diarrhoea	18
Anorexia	26
Coated Tongue	19
Hepatomegaly	33
Splenomegaly	18
Myalgia	11
Rash	2

Table 4: Drug Susceptibility in Blood Culture Positive Typhoid Fever

Blood Culture Sensitivity Pattern In 59 Blood Culture Positive Children		
Drugs	No of Sensitive Cases	No of Resistant Cases
Eftriaxone	58	1
Cefixime	58	1
Azithromycin	57	2
Ciprofloxacin	10	49
Ofloxacin	39	20
Nalidixic Acid	55	4
Chloramphenicol	54	5
Amoxycillin	58	1
Amoxycillin- Clavulanic Acid	58	1
Amikacin	59	0

A total of 120 children in the age group of 1 to 15 years with fever ≥ 5 days with signs and symptoms suggestive of typhoid fever were studied.

Among 120 children, blood culture was positive in 59 children. Blood culture is the gold standard in the diagnosis of typhoid fever. Enterocheck was positive in 53 blood culture positive cases, Widal test was positive in 38 blood culture positive cases.

Blood culture was negative in 61 children. Enterocheck was negative in 57 blood culture

negative children and 4 children were positive among blood culture negative children.

Widal test was negative in 37 blood culture negative children and 24 children were positive among blood culture negative children.

Sensitivity and specificity of Enterocheck and Widal test were calculated as per statistical methods.

Positive predictive value and Negative predictive value of Enterocheck and Widal test were calculated as per statistical methods.

Table 5: Comparison of Diagnostic Tests

Blood Culture	Enterocheck WB		Widal Test	
	Positive	Negative	Positive	Negative
Positive(n=59)	53	6	38	21
Negative(n=61)	4	57	24	37

Sensitivity of Enterocheck WB= 89.80% Specificity of Enterocheck WB= 93.40%.

Positive predictive value of Enterocheck WB= 92.90% Negative predictive value of Enterocheck WB= 90.40%.

Sensitivity of Widal Test= 64.40% Specificity of Widal Test= 62.71%.

Positive predictive value of Widal test=61.29%. Negative predictive value of Widal Test= 63.79%.

DISCUSSION

In the present study, conducted in Masonic Medical Centre for children, Enterocheck Test was Positive in 57 children, among which 53 were Positive in Blood Culture Positive Children and 4 were Positive in blood culture Negative children. Enterocheck were Negative in 63 children, among them 6 were Negative in Blood Culture Positive children and 57 were Negative in blood culture negative children.

The sensitivity and specificity of the Enterocheck WB were found to be 89.80 % and 93.40 % respectively. This was comparable to other studies for the rapid diagnosis of typhoid fever. D. Narayanappa et al reported the sensitivity of typhidot-M as 92.60 percent.^[3]

Anush R compared the Enterocheck WB test to automated blood culture for typhoid fever and found its sensitivity and Specificity as 85.50% and 88.60% respectively.^[4] Kinikar Anagha et al, assessed the usefulness Of Enterocheck WB test for the easy and

early diagnosis of typhoid fever and its sensitivity and Specificity were found to be 89.47% and 96.87% respectively.^[5]

In the present study, Widal test was positive in 62 children, among them 38 were Positive in blood culture positive children and 24 were positive in blood culture negative Children. Widal test was negative in 58 children, among them 21 were negative in blood Culture positive children and 37 were negative in blood culture negative children.

The sensitivity and specificity of Widal test, were found to be 64.40% and 60.60% respectively.

In a developing country like INDIA, the Widal test has been used extensively in the neurodiagnosis of typhoid fever. Lateef A et al reviewed the significance of the Widal agglutination test and concluded that its use should not be encouraged in Endemic areas.^[6] Ideally in the Widal test, a fourfold rise of the antibody titre in paired sera is considered as diagnostic of typhoid fever. However, paired sera are often difficult to obtain and as a specific chemotherapy, it has to be instituted on the basis of a single Widal test only.

Kulkarni M et al and Rasaily et al revealed that a single Widal test, in association with relevant clinical findings, can still be used as a useful diagnostic tool for typhoid fever.^[7,8]

In the present study, 120 children with fever of 5 days or more with clinical symptoms and signs suggestive of typhoid fever were included. Among them blood culture was positive in 59 children. Salmomella typhi was grown in 57 children. Salmonella para typhi A

was grown in 2 children. *Salmonella para typhi* B was not grown. This is comparable with literature.^[9]

There are few studies on the clinical manifestations of typhoid fever in the Pediatric age group. In previous studies most common age group affected was more than 5 years¹⁰., while in the present study 47% of blood culture positive cases were in the age group Between 1- 5 years.

Relative bradycardia, rose spots were considered to be the salient features of Typhoid fever, were not seen in the present study. Step ladder pattern of fever could not be demonstrated in any of the children in the present study, probably because most of them were receiving anti pyretics.

In the present study hepatomegaly was present in 27.5 % of children, splenomegaly in 15 % of children. A recent study from Nepal also found that hepatomegaly was present 43% of cases.^[11]

There was no case of complicated typhoid fever in the present study, the reason being easy access to medical facilities and early initiation of antibiotic therapy.

In the present study, all blood culture positive children were sensitive to Ceftriaxone, except one child. Present study showed a high prevalence of resistance to Fluoroquinolones (Ciprofloxacin, Ofloxacin), with a return of sensitivity to Amoxicillin Chloramphenicol as seen in other studies.^[12] Recent reports of in vitro and in vivo Resistance to Ciprofloxacin have raised this concern as reported by Ravindran et al.^[13]

The sensitivity to Chloramphenicol, Amoxicillin in all the isolates was very high, which is in agreement with recent studies. In the present study only one Multidrug resistant strain was isolated, sensitive to Amikacin alone. Thus it is likely that drug resistance to these drugs may be seen in the future and there may be emergence of multidrug drug resistant strain in Typhoid fever has been reported by J Garhane et al.^[12]

CONCLUSION

Typhoid fever is an important cause of febrile illness in children. Fever with anorexia, diarrhoea, headache, hepatosplenomegaly were the common clinical manifestations. The Enterocheck WB test,

with its higher sensitivity and specificity, can be effectively used in the rural setup, wherein blood culture facilities are not available.

The early detection of the IgM antibodies by the Enterocheck WB test will serve as a marker of recent infection. The Widal test can be used as a complimentary serological diagnostic tool in rare circumstances.

The Blood culture should preferably be done in all susceptible child and antibiotic Susceptibility testing of the isolated strains is equally important in the prevention of emergence of Multidrug resistance.

There is re-emergence of strains with high sensitivity to first line antibiotics Like Chloramphenicol. A high prevalence of resistance is seen to fluoroquinolones.

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