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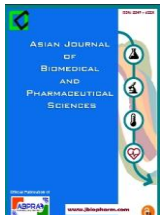

RESEARCH ARTICLE

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Prevalence of Enteric fever in patients with Pyrexia of Unknown origin

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Abstract
The study was undertaken to analyse the prevalence of Enteric fever in patients with suspected enteric fever, presenting with Pyrexia of unknown origin (PUO), utilizing slide agglutination test (Tydal-Tulip Diagnostics). Out of 1985 samples received, 542 (27.3 %) were positive for Enteric fever. The agglutinins to S.typhi were the most prevalent among the sera of various dilutions (47% for O antigen and 46.7% for H antigen). The levels of agglutinins for Salmonella paratyphi AH and BH were very low (only 4.8% and 1.5% for the AH and BH antigens respectively).Though statistically insignificant, the incidence of Enteric fever was found to be highest in age group 21-40 years (36%) followed by <20 years (30.4%) with a slight female predominance (p value≥0.05).
Keywords: Antibody titre, Enteric fever, Prevalence, Pyrexia of unknown origin, Salmonella, Slide agglutination.

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INTRODUCTION

Enteric fever is a systemic infection caused by *Salmonella t*yphi (*S. typhi*), Salmonella paratyphi A (S.paratyphi A), Salmonella paratyphi B (S.paratyphi B), and Salmonella paratyphi C (S.paratyphi C). The disease remains an important public health problem in developing countries. The disease has been described as endemic in tropical and sub tropical countries, with estimated annual incidences of 540 per 100,000 (1). The world wide incidence was estimated to reach up to 17 million cases (2) and about 600,000 deaths per annum (3). Areas with high disease burdens include South and East Asia, Africa south of the Sahara, and Latin America.

Transmission of the infection is by faecal-oral route, when contaminated food or water is consumed or from contaminated hands (5). Symptoms are non specific, but may range from headache to severe complications like haemorrhage and perforation of the intestine (4). Death may result due to destruction of the intestine, bone marrow or other organs (6). Antibiotic treatments have reduced the infection burden over the years especially in developed countries(7), despite the fact that resistance is very common (8).

Clinical diagnosis of typhoid is not specific because the presenting signs and symptoms are diverse and similar to those of other common febrile illnesses, such as malaria and dengue fever. The definitive diagnosis of Enteric fever requires the isolation of S.typhi or paratyphi from the blood of the patient concerned. Since the patients often receive antibiotics prior to a confirmatory diagnosis there is doubt that bacteria can be isolated from the blood cultures. Besides this, the facilities for blood culture are not always feasible in resource-poor regions. All these limitations have made widal test (a rapid slide agglutination test) the most utilized diagnostic test for Enteric fever.

The present study reports the prevalence of the disease in the southern part of Tamilnadu and highlighted the extent to which individuals of different age and gender among the studied population were infected. This is with intention of creating awareness among public, local and regional authorities to allow them to take effective measures for prevention and control of the infection.

Materials and Methods

A total of 1985 blood samples were collected from patients with PUO visiting Chennai Medical College Hospital and Research Centre, Trichy, Tamilnadu, India during January 2010 to December 2013.The samples were collected after getting an verbal consent and analyzed by using rapid Slide Agglutination Test (Tydal-Tulip Diagnostics). All the positive sera were semi quantitatively analyzed for the determination of antibody titre. The Widal test kits containing O,H, AH and BH antigens were supplied by Tulip Diagnostics (P) Ltd.Goa. Positive and negative controls were included in each batch of tests. The test and interpretation of results were done according to the guidelines of the kits manufacturer. The titre was taken as the highest dilution of serum with a visible agglutination. The results were analyzed using chi-square test.

Results

A total of 1985 patients with suspected enteric fever presenting with PUO were screened for agglutinins against Salmonella typhi , paratyphi A and B by the rapid Widal slide agglutination test. Table -1,2 and 3 show the results of Widal test . Based on the unpublished data from our same institution, the baseline titre for the widal test is 1:80 for S.typhi and S.paratyphi. A titre of >1:160 was considered positive for all the Salmonella species tested. A total of 542 (27.3%) were positive with $\geq$1:160 titre. Among the positives, S.typhi O agglutinins were the most prevalent 255 (47%) followed by S.typhi H agglutinins 253 (46.7%).The levels of agglutinins to S.paratyphi AH and BH were 26 (4.8%) and 8 (1.5%) respectively. Though statistically insignificant, the highest prevalence was seen in 21-40 (36%) years age group followed by 0-21 years age group (30.4%) with a slightly female predominance (p value $\geq$ 0.05).

As per Table-1, the overall positive samples were 542 (27.3%) with females being predominant (27.8%).

In Table -2, different age groups showed varying number of positivity. Higher prevalence were recorded in samples between 21-40 (36%) followed by 0-20 years age range (30.4%).

Year	Male tested	Male positives	Female tested	Female positives	Total tested	Total positives
2010	412	136(33%)	289	95(32.9%)	701	231(33%)
2011	218	60(27.5%)	155	42(27.1%)	373	102(27.3%)
2012	247	64(26%)	226	65(28.8%)	473	129(27.3%)
2013	246	42(17%)	192	38(19.8%)	438	80(18.3%)
Total	1123	302(26.9%)	862	240(27.8%)	1985	542(27.3%)

Table-1. Gender wise Prevalence of Enteric fever

Year	0-20yrs		21-40yrs		41-60yrs		>60 yrs		Total	
	Tested	Positives	Tested	Positives	Tested	Positives	Tested	Positives	Tested	Positives
2010	247	90	269	127	147	12	38	2	701	231
2011	124	33	125	45	97	22	27	2	373	102
2012	155	46	173	55	115	22	30	6	473	129
2013	106	23	171	39	113	13	48	5	438	80
Total	632	192(30.4)	738	266(36%)	472	69(14.6%)	143	15(10.5%)	1985	542(27.3%))

Table-2.Year of investigation and age group positive for Enteric fever

Antigen	No. Of positive samples (≥ 1in 160) (%)	Titre (1:20)	Titre (1:40)	Titre (1:80)	Titre (1:160)	Titre (1:320)	Titre (1:640)
S.typhi O	255(47%)	10(2.1)	65(13.5)	150(31.3)	97(20)	153(31.9)	5(1)
S.typhi H	253(46.7%)	9(2.2)	36(8.6)	120(28.7)	78(18.7)	171(41)	4(1)
S.paratyphi AH	26 (4.8%)	0	3(8.3)	7(19.4)	6(16.7)	20(55.6)	0
S.paratyphi BH	8 (1.5%)	0	5(25)	7(35)	2(10)	6(30)	0

Table: 3 Number and percentage of sera with end titres in patients with PUO

Discussion

A total of 1985 patients with PUO, that presented to the department of Microbiology were screened for enteric fever by using slide widal test. A titre of ≥1:160 was taken as cut-off value. A total of 542 (27.3%) were positive for enteric fever. This means the safety of drinking water and sanitation have not improved much or a large number of carriers are present in this area.

Another similar study in southern Nepal, Terai in 2005 (9) and in Kathmandu, Nepal in 2012 (10) also reported 28.9 % and 27% prevalence respectively in patients with febrile illness and suspected of having enteric fever. A study by Bhattacharya SS et al, Rourkela, India in 2008, obtained 5.58% Salmonella culture positivity (11). Khattak MI et al (12) and Naseen et al (13) observed a lower prevalence of enteric fever among PUO cases (7% and11.8% respectively).

From our data it is evident that typhoid fever is predominant over paratyphoid fever with the ratio of 7:1. It has been reported from various studies that the ratio of the diseases, typhoid fever and paratyphoid fever in most countries is found to be 10:1 (21). A possible explanation for the increasing prevalence of paratyphoid fever is consumption of food from street vendors. Because paratyphoid require a higher infective dose which is more likely to be present in food from street vendors.

Similar prevalence was found in a study carried out in Khathmandu in 2003(14) and in Kathmandu, Nepal in 2012 (10).Our study contradicts the study reports of Mendiratta et al in 2003 (53.3%) and Aggarwal A et al in 2005(52.94%) which showed higher isolation of S.paratyphi from PUO cases (15, 16). Lower prevalence of S.paratyphoid AH, and BH agglutinins in our study highlighted the low endemicity of paratyphi infection compared to typhi infection.

In acute enteric fever, a rise in O agglutinin titre followed by a slow increase of H agglutinin occurs. The H agglutinin response persists longer than O agglutinin response. From Table-3, it is evident that, our study results are also in agreement with this fact.

Our study found slightly higher seroprevalence in females than males. Similar findings were also reported by some other studies (10,17,18).This could be attributed to the fact that outdoor activities are more obvious in females like males in rural communities in Irungalur, Trichy exposing them to high risk of infection. Females get more in contact with sources of causative organisms such as contaminated vegetables, fruits and

shellfish obtained from contaminated water, more than males (20).

Our study observed a higher prevalence in samples between 21-40 (36%) followed by 0-20 years age range (30.4%). It concurs with study reports of Isa MA et al (19) and WHO-2003(20). This may be due to their depressed immune status and higher rate of exposure to contaminants.

Nearly 1% of the positive samples having agglutinins against S. typhi O (5) and H (4) showed more elevated titre of 1:640.

In addition to the unsafe drinking water, unhygienic practices by most food sellers are another major contributing factor as there are no health regulations governing their business. Improper and inadequate treatment of acute illness is contributing significantly to the spread of the infection, as patients will continue to shed the organisms in stool and urine for quite some time.

Conclusion

Although improved water quality and sanitation constitute ultimate solutions to this problem, vaccination in high-risk areas is a potential control strategy recommended by WHO for the short-to-intermediate term. However, typhoid vaccination has not been implemented as a routine public health measure in most typhoid-endemic countries despite the low price of the vaccine and the high cost of treating the disease. Policy-makers in several developing countries have indicated that updated data on the incidence of typhoid in their countries are essential before they introduce the vaccines into programmes.

To conclude proper sanitation, public health education, and vaccination are the long-term preventive measures that would improve this situation.

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