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Original Article

Blood Culture in Clinically Suspected Typhoid Fever

Promukh Bhattacharya[1], Bikram Kumar Saha[2], Uttam Kumar Paul[3], Arup Bandyopadhyay[4]

[1]Assistant Professor, Department of Microbiology, MGM Medical College, Kishanganj, Bihar, India, [2]Assistant Professor, Department of Medicine, North Bengal Medical College, Siliguri, West Bengal, India, [3]Professor, Department of Medicine, MGM Medical College, Kishanganj, Bihar, India, [4]Professor, Department of Physiology, MGM Medical College, Kishanganj, Bihar, India

Abstract

Background: Typhoid fever, caused by the bacterium "*Salmonella enterica* serovar *typhi*" is still today a globally threatening disease even after the disease has been known for so many years. This is more so in developing countries such as Bangladesh, Pakistan, Nepal, African countries, and India of course. Ours being a tertiary care medical college hospital in rural area, we ventured to go for a study as to how typhoid diagnosis and treatment are done in these areas where typhoid is prevalent. Having found that almost cent percent cases of enteric fever are clinically diagnosed and empirically treated, we did a study by doing blood culture for 67 newly diagnosed cases of typhoid fever by clinical methods.

Materials and Methods: A total of 67 adult patients of fever of both sexes, clinically diagnosed as typhoid, without a history of prior antibiotic therapy, usually by the third day of fever, were chosen for the study. All these patients were subjected to blood culture for salmonella, and the results were analyzed.

Results: The results of the study showed that out of 67 clinically diagnosed typhoid patients only 8 had culture positive typhoid and 3 had culture-positive paratyphoid A.

Conclusion: The practices of diagnosing and empirically treating typhoid fever though hugely practiced in rural, semi-urban and even urban areas of developing countries, is definitely improper, and learned medico-social community and appropriate health authorities should come forward and find out an acceptable solution.

Key words: Blood culture, Clinical diagnosis of typhoid, Typhoid

INTRODUCTION

By typhoid fever, we mean an acute febrile infectious disease whose causative organism is the bacterium "*Salmonella enterica* serovar *typhi*."[1] Studies[2] are done In urban Slums in three South-East Asian countries, viz., India, Pakistan, and Bangladesh. In India, the incidence is 493.5 cases per 100,000 population per year. In Bangladesh, it is 18.7 per thousand per year in pre-school children and 2.1 per 1000 per year in older patients. In Pakistan, the same is 451.7 cases per 100,000 per year in children aged 2-15 years. These high incidences obviously suggest that further studies are required to explore typhoid situations particularly in developing countries. In Africa, typhoid is less understood than in Asia. This is due to lack of proper infrastructure to conduct clinical or epidemiological studies there. Crump *et al.* could get only the crude incidence rate in Africa, viz., 50 cases per 100,000 population per year where the total population is about 820 million.[3] However, Buckle *et al.* got a higher incidence rate in Africa, that is 724.6 cases per 100,000 population per year.[4] A confounding factor in these studies is the presence of non-typhoidal salmonellosis that mimics typhoid which is progressively rising and may be fatal in some cases.[5]

Regarding diagnosis, typhoid imposes confusion in Afro-Asian countries. Detection of causative organism in blood by polymerase chain reaction is probably the most suitable method. Next to that, bone marrow culture is the most sensitive and reliable method. Recently, the third method is being used in only a few developed

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Corresponding Author: Arup Bandyopadhyay, Department of Physiology, MGM Medical College, Kishanganj - 855 107, Bihar, India.
E-mail: arupbanerjee1953@gmail.com

countries because its sensitivity is 100%. In it, typhoid-specific immunoglobulin A is estimated in blood using ELISA through amplification of signal by isolation and incubation of peripheral blood lymphocytes.[6] Unfortunately, all the above-mentioned methods are too expensive, tedious, complicated or time-consuming to be applied in developing countries even in urban areas, let alone in remote places and villages. The Widal test has been marked unreliable as also the newer generation serology tests such as typhidot and tubex.[7-9]

We performed a study on knowledge, attitude, and practices of general practitioners in several underdeveloped places in India and found the noticeable poverty of infrastructure for diagnosis and management of typhoid.[10] Under these circumstances, we have ventured to study the sensibility and acceptability of blood culture as a diagnostic tool in this part of globe wherefrom we might get a deeper insight to develop new novel but feasible and acceptable diagnostic strategies which need to be implemented in this type of background.

MATERIALS AND METHODS

A total of 67 patients (40 males and 27 females) with complaints of fever of more than 3 days duration were enrolled for the study. The patients were in the age range from 18 to 76 years. Most of the patients were from rural and semi-urban backgrounds. The patients who had been treated with any antibacterial drug for the recent ailment were excluded from the study population.

About 10-15 ml of blood was collected with standard aseptic precautions from each patient and was inoculated into 40-45 ml of brain heart infusion broth. Incubation was done at 37°C. Subculturing was performed on days 1, 2, 3 and 7 days on MacConkey agar plates which were incubated at 37°C for 18-24 h. Lactose nonfermenting colonies, if any, on subculture plates were picked up and were examined by microscopy after Gram-staining of the smears. Standard biochemical tests including motility test were performed for identification of *Salmonella* spp.

RESULTS

Table 1 shows age and sex-wise distribution of isolates in blood culture of patients. Figure 1 shows age and sex-wise distribution of patients. Figure 2 shows sex-wise distribution of isolates in blood culture of patients.

DISCUSSION

This study envisaged toward determining the blood culture reports for detection of *S. typhi* shows that out of 18 patients in the age group of 18-30 years *S. typhi* was isolated in 3 patients and only 1 *S. paratyphi* was detected. In the 31-40 years, age group where the total number of patients was 19, 2 and 1 were the *S. typhi* and *S. paratyphi,* respectively.

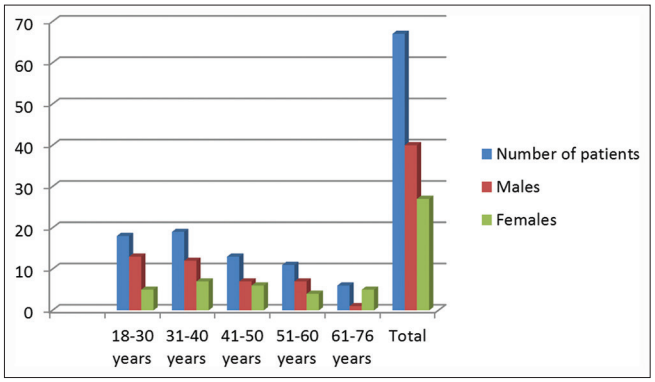

Figure 1: Age and sex-wise distribution of patients

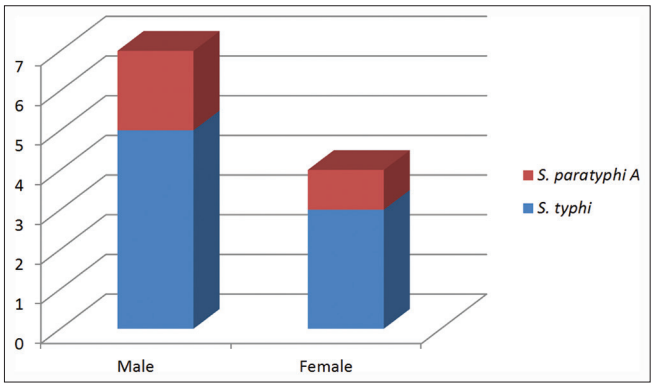

Figure 2: Sex-wise distribution of isolates in blood culture of patients

Table 1: Age and sex-wise distribution of isolates in blood culture of patients

Age group (years)	Number of patients	Males	Females	*S. typhi* isolated		*S. paratyphi* A isolated	
				Male	Female	Male	Female
18-30	18	13	5	2	1	1	-
31-40	19	12	7	1	1	-	1
41-50	13	7	6	1	-	1	-
51-60	11	7	4	1	1	-	-
61-76	6	1	5	-	-	-	-
Total	67	40	27	5	3	2	1

S. typhi: Salmonella typhi, S. paratyphi: Salmonella paratyphi

Similarly, in the age group 41-50 years out of 13 patients, 1 was *S. typhi* and1 was *S. paratyphi*. Again, in the 51-60 years age group, 2 were detected *S. typhi* and none belonged to *S. paratyphi*, the total number of patients being 11. In the oldest age group (>60 years), which consisted only 6 patients, none was detected positive for either *S. typhi* or *S. paratyphi*. In total, out of 67 patients of all adult age groups (>18 years) 8 patients belonged to *S. typhi* and 3 patients to *S. paratyphi*. This shows that blood culture is positive in only 16.4% cases of clinically suspected typhoid/paratyphoid patients.

Diagnosis of typhoid fever is normally made in all developed countries principally by blood cultures and also by stool/urine culture and serological testing.

In one study, out of 273 blood cultures from clinically typhoid fever patients, *S. typhi* was detected in 7 (2.6%) and *S. paratyphi* was detected in 4 (1.5%) patients.[11] In the same study, in Widal test, TO antigen was positive (i.e., dilution >1/80) in 47% of febrile patients, and 26% TH antigen positive (cutoff value >1/160). 24.4% had positive results for both TO and TH. To perform blood culture a bacteriological laboratory has to be present on site or else, it can be transported to the main laboratory. However, interestingly for proper blood cultures, it is essential to inoculate the media immediately after drawing blood, keeping proper temperature of the specimen, the media, and the inoculated media. Furthermore, blood for culture should be drawn very meticulously and in highly aseptic manner for which a properly trained and experienced technician is extremely difficult to obtain. The volume of blood required for blood culture is also highly variable and hence confusing. For example, 10-15 ml of blood is required for culture in adults and school children, whereas only 2-4 ml of blood is sufficient in preschool children and toddlers. This is because children show a much greater number of bacterial colonies compared to adults. One cannot compromise on volume of blood to be inoculated because that effort drastically brings down the sensitivity of the test. Therefore, obtaining this amount of blood is sometimes so difficult that only for that reason the blood culture test has to be discarded and an alternate reliable and acceptable diagnostic method may have to be sought after. Keeping the specimen collecting bottle highly aseptic is also another challenge in conducting a proper blood culture. Even the slightest flaw in the process may lead to highly noticeable pseudo-bacteremia. The volume of the culture media required is also extremely crucial. If that volume is not strictly maintained the possibility of false positive or false negative reports is expected.

S. typhi infection frequently occurs in endemic areas because of poor sanitary hygiene. Open passage of stool and urine by infected persons or carriers and then carriage of bacteria by insects, principally flies and cockroaches to food is an important mode of transmission of typhoid in developing countries. Even then, consumption of contaminated water is the principal cause in the developing countries, compared to developed countries where contaminated food due to droplet infection imparted by so-called healthy carriers is the commonest cause of typhoid fever. Hence, improvement of hygiene and cleanliness of the whole country particularly the rural areas and urban slums is the most important preventive step against typhoid. Construction of sanitary latrine in each and every household and frequently in the roadside should be the first step to prevent typhoid in this country. Beggars and vagabonds are very common in this subcontinent, for most of them begging are a profession or religious ritual. They do not have any habitat and they also won't spend a farthing to use a paid toilet.

Thus, extremely poor hygienic environment in developing countries, particularly in rural areas and urban slums, remains a disastrous cause of yearlong endemicity in these sects of the globe.

Interestingly, even then there is least scope of scientific diagnostic or treatment approach or the feasibility of that. There is no blood culture facility for typhoid throughout the rural and semi-urban areas of the country; even though the said test (viz., blood culture) is supposed to be the gold standard in the diagnosis of typhoid fever.

We have shown in our study that out of 67 patients who were clinically marked as typhoid fever, only 11 patients (16.4%) did have a positive culture out of which only 8 patients (11.9%) had true typhoid fever and 3 patients (4.5%) had paratyphoid fever.

In practice, however, all these patients would have got treatment for typhoid fever, sometimes with wrongly chosen antibiotics and more often with a wrong dose of the antibiotic chosen leading ultimately to drug resistance and many untoward side-effects.

Under these situations, it is obviously understood that in our conditions, which is also a vast area of the globe and hence not negligible; there are a great responsibility and burden to the scientific communities who should come forward, get united and find a solution to these challenges so that brethren of this vast weaker society get justified and enlightened service suitable for their environment but acceptable by general scientific community.

CONCLUSION

As an inference, it can be told that being a small study, but at the same time, covering a very sensitive community,

our study shows that a very minor portion (16.4%) of the patients deemed clinically as typhoid and treated likewise are actually typhoid fever (including paratyphoid fevers also). This improper treatment which is hugely prevalent does not seem becoming in a scientific world. The enlightened scientific community having come to know this medico-social malady should come forward to find out a remedy suitable for these environmental situations.

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