The accuracy rate of laboratory reports of typhoid fever

Ranjbar R.1 PhD, Izadi M.1 MD, Joneydi Jafari N.2 MD, Panahi Y.1 PhD

1Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran;
2Molecular Biology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran;
3Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran;
4Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran;

Abstract
Aims: Salmonellae organisms are a large group of enteric bacteria and their infections present an important public health problem worldwide particularly in developing countries. Regrettfully, Diagnosis and laboratory report of Salmonellae organisms is not performed correctly, due to a variety of reasons. This study was designed to determine the accuracy of laboratory reports of typhoid fever in Tehran during a two year period.

Methods: This descriptive study was carried out on clinical samples diagnosed as Salmonella typhi received from a number of hospital laboratories in Tehran in years 2007 and 2008. Bacterial strains were diagnosed and identified by standard differential biochemical and serology tests using poly and mono specific Salmonella antisera. Results were then compared to those reported from the hospital laboratories.

Results: Among 161 samples which were suspected to contain Salmonella typhi, 60 were reported as Salmonella typhi. Standard biochemical and serology test results revealed that although samples belonged to serogroup D of Salmonella, none of them had reacted with specific Salmonella antiserum; therefore, all non-typhoidal group D Salmonella strains had been misdiagnosed as Salmonella typhi.

Conclusion: The precise laboratory identification of Salmonella typhi should be emphasized, because laboratory reports with misdiagnosed Salmonella typhi may prevent physicians from taking proper supportive and curative measures and impair the treatment process.

Keywords: Typhoid fever, Salmonella typhi, Non-Typhoidal Salmonella

Introduction
Infections resulted from Salmonella has been left as a very important health problem all around the world [1]. Salmonella organisms are a large group of enteric bacteria. Most serotypes of Salmonella are considered as potential pathogens for humans and animals [2]. These bacteria are established in digestive system of vertebrates including mammals, birds, and poultry and depending on serotype, condition, and various factors of host, they create diseases with different symptoms and complications [3]. Generally, Salmonella infections can present as acute enterocolitis, intestinal fever, and septicemia in humans [4].

Among the diseases resulting from infection with Salmonella bacterium, typhoid fever is highly important. Typhoid is usually created by Salmonella typhi and is always achieved from human repositories. In most of the cases, typhoid happens when water or food polluted by human’s stool or urine is consumed. This is a systemic disease and is caused by Salmonella enteric serogroup typhi. This bacterium has been human-specific pathogen; however, it had not been recognized until the nineteenth century. The classic form of this disease presents acutely with symptoms such as fever of about 39 to 40 centigrade, sore throat and abdominal pain. Diarrhea occurs more than constipation in adults while Diarrhea and constipation are mostly observed in children. During the second week, a rash called “rose spots” witch are small red spots appear on the chest and epigastrium. This skin rash is temporarily and disappears after three to four days. Typhoid-like fever has the similar symptoms, yet milder than those typhoid’s. The complications are not severe and recovery is achieved rapidly. About one-third of those with typhoid fever suffer from other complications as well [4, 5, 6].

Antimicrobial resistance among Salmonella typhi and non-typhoidal species is increasing [7, 8]. Moreover, in endemic areas, rather than typhoid fever many other factors are involved in long-term fever. Therefore, the early and accurate diagnosis of this disease is difficult and highly important [9]. Serology tests are available in most laboratories, yet they have low sensitivity and specificity [10].

Laboratory diagnosis is mostly based on the bacterium culture from clinical samples. For definite diagnosis of typhoid fever and determination of sensitivity tests to antibiotics and epidemiologic studies, culture is necessary. The isolation of Salmonella typhi from bone marrow aspiration is the gold standard diagnostic
method for typhoid fever and is more sensitive than blood cultures. Of course, if one cultivates enough amount of blood, the sensitivity may reach to that of bone marrow cultures, and thereupon it is not necessary to do the bone marrow aspiration. Having the bacteria suspicious to \textit{Salmonella} isolated, one determines the serogroup through using the antisera. Serogrouping is based on the direct reaction of each of these isolates with antibodies of O, H, and Vi antigens. Clinical laboratories do not usually report the \textit{Salmonella} serogroups, but they report these isolates as breed-serotype [4, 5, 6, 11, 12, 13].

Definite diagnosis of specific serotypes happen through creating the agglutination reaction by the help of specific antiseraums of serotype, but it does not happen due to not easy availability of these antiseraums, except in referent laboratories or the researches.

The aim of this study was to analyze the accuracy rate of laboratory reports of typhoid fever in a two-year period in the laboratories of training hospitals of Tehran.

\textbf{Methods}

This descriptive study was performed on samples received from some training hospitals of Tehran in 2007-2008.

At first, different clinical samples such as stool, blood, joints fluid, and other secretions were cultivated in laboratories. In the next day, colonies suspicious to \textit{Salmonella} were isolated in specific and differential mediums such as \textit{Salmonella-shigella agar} (SS agar), Xylose lysine deoxycholate agar (XLD agar), and Mac Conkey Agar and then they were recognized by standard biochemical tests such as transmitting on TSI environment, citrate, Lysine Iron Agar, Urea, and MRVP, and by using Polyvalent antiseraums. Serotyping with monovalent antiseraums was done to confirm the results [14, 15, 16, 17]. Then the results obtained from this study were compared with that of had been reported by diagnostic laboratories related to these hospitals.

\textbf{Results}

According to the reports obtained from the studied hospitals, among the 161 isolates suspected with \textit{Salmonella}, 60 isolates (37.3\%) were reported as \textit{Salmonella typhi} (Typhoid fever factor). Although, these isolates were related to serogroup D \textit{Salmonella}, none of them reacted with specific antiseraum against \textit{Salmonella typhi}. Therefore, non-typhoidal \textit{Salmonella} were reported as \textit{Salmonella typhi} by mistake. In fact, when all of the isolated isolates were studied by the group antiseraums, to determine the specific serotype, they were tested by specific antiseraum of serotype. In conclusion, all of the isolated \textit{Salmonella} isolations were appertained to 14 different non-typhoidal serotypes.

\textbf{Discussion}

The results showed that in all cases without any exception non-typhoidal \textit{Salmonella} isolates have been reported by mistake as \textit{Salmonella typhi} (Typhoid fever factor) by all of the laboratories of the studied hospitals. \textit{Salmonella} categorization is highly complex due to the many similarities between different species, because they produce a set of different species instead of one specific species. Members of the genus \textit{Salmonella} are categorized basically based on epidemiology, the type of host, biochemical reactions, and the structures of antigens O, H, Vi (if there is any). White established the first categorization in 1929, then Kauffman completed and corrected it and he introduced any serotype \textit{Salmonella} as isolated \textit{Salmonella}. Another categorization system was Edwards-Ewing that categorized \textit{Salmonella} in three species of (\textit{Salmonella choleraesuis}, \textit{Salmonella enteritis}, and \textit{Salmonella typhi}) and 100 serotypes [4, 5, 6, 9]. The last categorization was presented based on exact optimization analysis of DNA in 1989 that shows this fact that \textit{Salmonella} genus is including two types of \textit{Salmonella enterica}, and \textit{Salmonella bongori}. In this categorization, most of the human's pathogenic serovars are placed under the enterica species. \textit{Salmonella enteric} is sub categorized into 6 types that has the most human's pathogenic strains under the species of enteric [6]. However, historically the old naming ways have been used in many old books and articles. One has recognized about 2500 of \textit{Salmonella} serotypes based on O, H antigens [4].

Although the categorization of \textit{Salmonella} is based on surface antigens serotyping in the first level, one should know typhi serotype separated from other isolated serotypes, because the categorization of this serotype is based on neutral biochemical behaviors. \textit{Typhi} serotype shows negative results in all Simon Citrate, Ornithine Decarboxylase, gas production from glucose, Dulcitol fermentation, Arabinose, Rhamnose, Moissanite, and Acetate consumption. These properties are important, because this serotype is responsible for most of the intestinal fevers. Other serotypes usually cause enteritis [3, 5].
It is clear that the treatment strategy is different about Typhoidal and non-typhoidal infections. Therefore, paying attention to the type of isolated specimen is highly important in treatment adoption. False reports of serotypes can deflect the doctor from adopting suitable therapeutic and supportive methods and confront the patient treatment process with disturbance. Therefore, explaining the issue and its importance for officials and experts of laboratories and presenting proper protocols to determine the identity of this group of bacteria can solve this problem.

Conclusion

Hospitals studied in Tehran have only the ability to diagnose Salmonella at the level of A, B, C and D. Therefore, unfortunately the bacterium serotype is usually reported by mistake without doing complementary differential tests including using specific serotypes antisera. This false report make the physician not take proper therapeutic and supportive measures.

References