ORIGINAL ARTICLE

AL-ANBAR MEDICAL JOURNAL
Anb. Med. J. 16(1): 12–16, 2020

Incidence of Typhoid Fever and the Validity of the Widal Test in Some Districts in Iraq

Mousa A. Shubbar[1,*] and Shakir M. Zighair[1]

[1] *National Focal Point of Measles/Rubella Surveillance, Directorate of Public Health/Communicable Diseases Control Center, Ministry of Health, Baghdad, Iraq*

(Received : 26 November 2019; Accepted : 28 January 2020; First published online: 4 February 2020)

ABSTRACT

Background: Typhoid fever is a serious infectious disease. In Iraq, the disease has a public health burden because it's endemicity and there is an overestimation of the cases because the diagnosis almost depends on the Widal test.
Objectives: The study aimed to determine the occurrence of typhoid fever in four sentinel sites in Iraq and to assess Widal test sensitivity and specificity.
Materials and methods: This cross-sectional observational study conducted in four districts in Iraq which has a population ranging from 170 000 to 431 000. A consecutive sample of (757) patients attended the outpatient or admitted to hospitals with any Widal positive case, probable typhoid case and suspected typhoid case were included in the study. A questionnaire including demographic, clinical, laboratory and exposure data was filled for each suspected case. Confirmation of the diagnosis of typhoid fever was done by serological examination and culture (blood, urine or feces) for each patient included in the study.
Results: The occurrence of typhoid fever (per 100 000 population) was 34, 9.4, 3.5, 0 in Al-Haweeja, Al-Hay, Al-Majar, and North Najaf districts respectively and this occurrence was lower in three study districts when compared with the same period of 2010 and 2011. The mean of the age of cases was 25.8 years ± 16.03 and the male to female ratio of confirmed cases was 0.7:1. Also, this study showed that the sensitivity of the Widal test was 16.7% and the specificity was 36.2% when compared with culture results.
Conclusion: The incidence rate of typhoid fever was low in the four selected sites except for the Al-Haweeja district. The sensitivity and specificity of the Widal test were low.

Keywords: Incidence; Typhoid fever; Widal test; Iraq.

DOI: 10.33091/amj.2020.170935

INTRODUCTION

Typhoid fever is an acute, life-threatening febrile illness caused by bacterium Salmonella Enterica serotype Typhi [1]. The global burden as estimated by WHO in 2004 was 21,000,000 cases and 216−600 thousand deaths/year [2]. The highest incidence of the disease in the world is in the Asia (274 cases/100 000 population/year), and with a mortality rate of 1-4% [2]. Early diagnosis is an essential step in this disease and serves 2 aims, diagnoses of the causative agent, and to identify the carriers who are responsible for the outbreak of the typhoid fever.

The principle of the Widal test is to detect the antibodies (agglutinins) in the serum of the infected individual, against both antigens, H (flagellar) and O (somatic) of the microorganism S. typhi [3]. However, this test is out of date in the diagnosis of the typhoid fever in developed countries owing to the following reasons, low rate of occurrence of the disease, drinking safe water, availability of modern techniques in the identification of the organism, in addition to low validity of the Widal test (low sensitivity and specificity) [4]. Anyhow, the test is still in use in developing countries, including Iraq, as a diagnostic tool in typhoid disease.

Raeeda Mahmoud [5] revealed in her study that there is a

* Corresponding author: E-mail: mousa.fetp@gmail.com
Phone number: +9647722629294

http://doi.org/10.33091/amj.2020.170935

variation in the distribution of typhoid fever in different years (2001-2004) and this variation might be due to lack of diagnostic facilities in medical laboratories in different years. There is a relatively common occurrence of typhoid and paratyphoid diseases in certain natives, e.g. South Asia, Southeast Asia, and sub-Saharan Africa, because of poor water supply and sanitation. Moreover, these diseases are considered a major reason for mortality and morbidity, especially among the pediatric population [6–9].

We aimed to determine the occurrence of typhoid fever in four sentinel sites in Iraq and compare it with the previous years and to assess Widal test validity (sensitivity and specificity).

MATERIALS AND METHODS

The present study is a cross-sectional observational study and conducted in four districts which has a population ranging from 170 000 to 431 000 and these districts are Al-Majar district in Misan, The North Najaf district in Al-Najaf, Al-Hay district in Wasit, and, Al-Haweeja district in Kirkuk province. These sites were non-randomly selected by the Ministry of Health to represent different Iraqi provinces. The study period was from January 1 to June 30 /2012 and the population size of the study districts was taken from directorates of health in the provinces as denominators for calculation of rates (198 462, 431 852, 170 131, 312 988). Data from Acute Enteric Diseases Control Section and Surveillance Section in the Communicable Diseases Control Center / Baghdad was used for comparison with previous years.

A consecutive sample of (757) patients attended the outpatient or admitted in the following district General Hospitals: Al-Haweeja General Hospital (156) patients, Al-Hakeem General Hospital (100) patients, Al-Shaheed Fayrooz General Hospital (485) patients, and Al-Mijar General Hospital (16) patients, were included in this study according to the inclusion criteria.

After an initial history and physical examination were completed by General Practitioner in the primary health care center, every patient suspected to have typhoid fever was referred to the General Hospital of the district. According to the regulation of Ministry of Health, serological test (Widal test) was done for every suspected case and culture (blood, urine or fecal) also done for every suspected case in the district hospital regardless the result of Widal test, then, a case investigation form was filled by the district hospital staff for every suspected case regardless the results of Widal test and the culture and this case investigation form includes information which was taken directly from the patient and includes four categories: demographic, clinical, laboratory, and epidemiological data. Finally, the patient classified into one of the following categories: laboratory-confirmed, clinically diagnosed or discarded. The inclusion criteria were any patient who met the standard case definition of the suspected case and the following standard case definitions were used in this study [7].

1. Suspected typhoid case was any patient from the four sentinel sites with insidious onset of sustained fever (more or equal to 3 days) with one or more of the following: marked headache, malaise, anorexia, relative bradycardia and splenomegaly.
2. A probable typhoid case was any suspected case with a positive Widal test (Widal positive case was any case with O and/or H antibody titer $\geq$ 1/160).
3. Laboratory confirmed typhoid case: any suspected typhoid case with positive culture (blood, feces, urine or bone marrow).
4. Clinically diagnosed typhoid case: any suspected typhoid case that the physician decides that it is a typhoid case.

The recommended way for the Widal test is a tube agglutination procedure, where serial 2-fold dilutions of the individual serum from 1:20 to 1:1280 are examined [10].

The data were entered, stored and analyzed using Epi Info software version 3.3.2 (US Centers for Diseases Control and Prevention, Atlanta, GA) and presented in simple measures of frequency and percentage of the occurrence.

RESULTS

Out of 757 suspected cases of typhoid fever, 130 (17%) were confirmed cases. Study hospitals reported no eligible patients refused to participate. Four hundred and eighty-five patients were from Al-Hay district, 156 from Al-Haweeja district, 100 from North Najaf district and 16 from Al-Majar.

The age of the studied cases ranged from 6-90 years with a mean of 25.8 years $\pm$16.03, while, the median was 25, and mode 30. Typhoid cases were mostly affected by the young age groups 10-39 years (496, 71%) Table 1.

The symptoms were distributed among patients as follows: fever in (627) patients, anorexia in (459) patients, the malaise in (546) patients, constipation in (114) patients, diarrhea in (119) patients, cough in (143) patients, and abdominal pain in (3) patients. While the fever was seen in all patients with typhoid fever Table 2.

A 323 (41.5%) from suspected cases were males, and 434 (57.5%) females with male to female ratio was 1/1.34 Table 3. While 54 (41.5%) from confirmed cases were males and 76 (58.5%) females Table 4.

Table 1. Frequency of suspected typhoid cases in regards with the age groups.

Age groups (years)	Number (%)
0-9	65 (9.3%)
10-19	153(22%)
20-29	217 (31%)
30-39	126 (18%)
40-49	82 (11.8%)
50-59	33 (4.7%)
60-69	12 (1.7%)
70-79	3 (0.4%)
$\geq$ 80	3 (0.4%)
Total	694 (100%)

Table 2. Distribution of symptoms reported by patients with typhoid fever (N=130).

Symptom	Frequency	Percentage
Fever	130	100%
Anorexia	27	20.7%
Malaise	27	20.7%
Constipation	15	11.5%
Diarrhea	7	5.4%
Cough	3	2.3%
Abdominal pain	1	0.8%

http://doi.org/10.33091/amj.2020.170935

Table 3. Distribution of final classification of suspected typhoid cases by gender.

Classification		Frequency	Percentage
Blood	Male	5	0.6%
culture-confirmed	Female	1	0.1%
Clinically	Male	88	11.6%
diagnosed	Female	36	4.9%
Not	Male	230	30.3%
confirmed	Female	397	52.5%
Total	Male	323	42.5%
	Female	434	57.5%

Table 4. Distribution of confirmed typhoid cases by gender.

Gender	Frequency	Percentage
Male	54	41.5%
Female	76	58.5%

In April, the suspected and confirmed cases of typhoid fever were the highest number recorded. Figures 1 and 2. Most of the typhoid cases 82.3%(107) were admitted to the hospital and 17.7% (23) of the cases weren't hospitalized. Most of the 107 cases detected from Al-Haweeja district Table 5.

These results reveal that the incidence of the disease declined through the study period when compared with data of 2010 and 2011. This decline was in 3 districts (North Najaf, Al-Majar, and Al-Hay districts) and there was a slight increase in Al-Haweeja district Table 6

A comparison of the results of the Widal test with the results of blood culture revealed the following findings of the validity of the test Table 7.

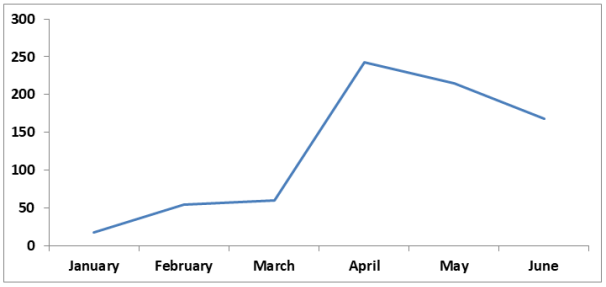

Figure 1. Distribution of suspected typhoid cases by months, January-June 2012.

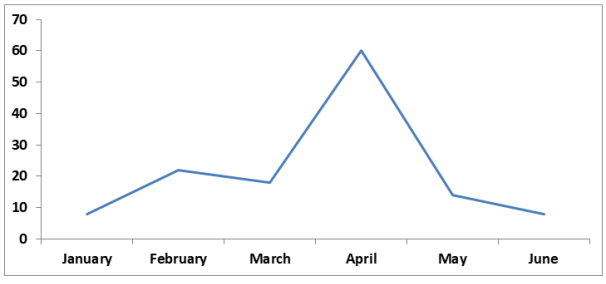

Figure 2. Monthly distribution of typhoid cases.

Table 5. Distribution of 130 confirmed typhoid cases according to the four sentinel regions.

Site	No. of confirmed cases	Population size	incidence of the disease during the study period (per 100000)
Al-Haweeja district	107	312988	34.2
North Najaf district	0	431852	0
Al-Majar district	7	198462	3.5
Al-Hay district	16	170131	9.4

Table 6. incidence (per 100000) of typhoid fever through the study period compared with data of 2010 and 2011.

Districts	2010	2011	2012
Al-Haweeja	37.7	30.6	34
Al-Hay	11.9	30.3	9.4
Al-Majar	50.8	65.9	3.5
North Najaf	28.3	9.31	0

Table 7. Comparison of Widal test with blood culture results*

	Culture positive	Culture negative	Total
Widal positive	1	455	456
Widal negative	5	258	263
Total	6	713	719

* Sensitivity = 16.7%, Specificity = 36.2%, Positive Predictive Value = 0.22%, Negative Predictive Value = 2%.

DISCUSSION

Despite the control and preventive measures implemented routinely targeting typhoid fever, the annual number of the cases recorded in the different Iraqi provinces is about 50 000 with a mean incidence of the last ten years of 151 per 100 000 population [11] that's because the diagnosis of typhoid fever in Iraq depends mainly on the Widal test.

The Mandatory Notification System in Greek [12] revealed that the mean monthly notification rate of typhoid fever increased during Summer. Comparing this result with that reported in Iraq, before the Gulf war in 1988-1989 it is shown that the rate of typhoid fever was much lower than that reported in the present study [6]. It was shown the rate of disease ranging from 11.3-11.6/100.000. That reflects that the people in Iraq during those years were enjoying a fairly good standard of living [6]. The same reports showed that the incidence of disease increased during economic sanction against the country it was found the rate of infection from 1991-1994 were 112.8, 119.9, 112.5, and 142.1/100.000 population respectively [6].

The lower occurrence of typhoid fever in three selected sites (North Najaf, Al-Majar and Al-Hay districts) during the 1st six months of 2012 compared with the same period of 2010 and 2011 may be because the surveillance in these sites depended during 2010 and 2011 only on Widal test and clinical diagnosis by general practitioner in a primary health care center while in 2012, this surveillance became culture and case-

http://doi.org/10.33091/amj.2020.170935

based surveillance using case investigation form and depended on clinical information taken by the specialist physicians in the hospitals.

The same incidence of fluctuation was illustrated in a study implemented in Korea [13]. This study showed that the annual incidence rate of typhoid fever from eleven provinces in that country shows certain fluctuation some provinces show an increased incidence rate by more than two folds when compared with an overall incidence rate of the previous nine years. Sunmi Yoo et al suggest the occurrence of an unnoticed outbreak.

Regarding the age and gender distribution, the results of this study were consistent with other studies; the highest incidence (44.6%) of typhoid fever in Greek [12] during the period from 2001-2004 was among the young age group (25-44) and the incidence was higher among women in different Korea provinces during the period 1992-2000 (women: 40/100 000 persons, men: 0.34/100 000 persons) [13].

The low result of the Widal test sensitivity and specificity of the current study was consistent with prior studies regarding the validity of the test [14–16]. In the endemic area where the population exposed to Salmonella organisms, elevated antibody titers may be present in a significant proportion of the normal population. This situation clarified by a study done by the college of medicine in Diyala university[17] revealed that the Widal test gave false-positive results for H antigen in 50% and O antigen in 55% of normal healthy people. Also, it showed that Widal test gave false-positive results for H antigen in 46% and O antigen in 40% of non-typhoid febrile patients and also it revealed that the prevalence of false-positive Widal test may imply subclinical infection with Salmonella typhi, also Salmonella typhi shares the same O and H antigens with many other Salmonellae. Another explanation of the false-positive Widal test is that the reading of rapid slide agglutination test after two minutes can give a false result or the specimen is not at room temperature [18].

In Iraq, many studies were done and various cut off titers was stated. Al-Rawi [19] considered an initial titer of 1/320 is the most reliable one in the consideration if Typhoid fever. Al-Abbasi [20] also considered an initial titer of 1/320 as a diagnostic value. Hameed [21] also considered the titer of 1/320 for both O and H antigens as a diagnostic value. Salah [22] mentioned that a titer of 1/160 is highly specific but less sensitive in the community of Basra. Al-Khushali [23] also considered an initial titer of 1/160 as a diagnostic value.

The limitation of our study was the Widal test validity according to titers were not assessed because of some missed data. Therefore, further investigation is needed to assess the validity of the test according to titers.

CONCLUSION

The occurrence of typhoid fever in the four selected sites except the Al-Haweeja district was low during the first six months of 2012 in comparison with the same period of 2010 and 2011. High prevalence of false-positive Widal test was found in our study. The sensitivity and specificity of the Widal test were low. The present situation underlines the importance of case-based surveillance and laboratory confirmation of typhoid fever.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

[1] G. W. Brunette. Cdc health information for international travel 2012. *The Yellow Book. Oxford University Press*, 2011.

[2] D. C. N. Wu. In this months bulletin. *Bull World Heal. Organ*, 98:1, 2020.

[3] W. W. C. Topley, G. S. Wilson, M. T. Parker, and L. H. Collier. Topley and wilsons principles of bacteriology, virology, and immunity. *London: Arnold*, 1990.

[4] E. C. Wam, C. N. Arrey, L. F. Sama, L. A. Agyingi, and A. N. Wam. Comparative study on the use of widal test to stool culture in the laboratory diagnosis of typhoid fever in holy family hospital akum, north west region of cameroon. *Open Microbiol. J.*, 13(1), 2019.

[5] R. M. Ebrahim. Seasonal variation of typhoid fever in kirkuk city. *Al-Taqani*, 23(5):94–98, 2010.

[6] J. Crump, S. Luby, and E. Mintz. The global burden of typhoid fever. *Bull. World Health Organ*, 82:346–353, 2004.

[7] T. Vos *et al.* Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 19902016: a systematic analysis for the global burden of disease study 2016. *Lancet*, 390(10100):1211–1259, 2017.

[8] S. Balasegaram *et al.* Guidelines for the public health management of typhoid and paratyphoid in england: practice guidelines from the national typhoid and paratyphoid reference group. *J. Infect.*, 65(3):197–213, 2012.

[9] G. C. Buckle, C. L. F. Walker, and R. E. Black. Typhoid fever and paratyphoid fever: Systematic review to estimate global morbidity and mortality for 2010. *J. Glob. Health*, 2(1), 2012.

[10] G. Ameya, E. Atalel, and B. Yohannes. Comparative study of widal test against stool culture for typhoid fever suspected cases in southern ethiopia. *Pathol. Lab. Med. Int.*, 9:1–7, 2017.

[11] J. Dworkin *et al.* Disease burden and epidemiology of typhoid fever in sulaimania, iraqi kurdistan. 2012.

[12] K. Mellou *et al.* A large waterborne gastroenteritis outbreak in central greece, march 2012: challenges for the investigation and management. *Epidemiol. Infect.*, 142(1):40–50, 2014.

[13] S. Yoo, H. Pai, J. Byeon, Y. H. Kang, S. Kim, and B. K. Lee. Epidemiology of salmonella enterica serotype typhi infections in korea for recent 9 years: trends of antimicrobial resistance. *J. Korean Med. Sci.*, 19(1):15–20, 2004.

[14] A. Adhikari, R. Rauniyar, P. P. Raut, K. Das Manandhar, and B. P. Gupta. Evaluation of sensitivity and specificity of elisa against widal test for typhoid diagnosis in endemic population of kathmandu. *BMC Infect. Dis.*, 15(1):523, 2015.

[15] S. Shukla, B. Patel, and D. S. Chitnis. 100 years of widal test and its reappraisal in an endemic area. *Indian*

J. Med. Res., 105:53–57, 1997.

[16] S. Sankar. Epidemiological profile and outcome in typhoid fever. *Stanley Medical College, Chennai*, 2018.

[17] A. Mussa. Reassessment of widal test in the diagnosis of typhoid fever. *Diyala J. Med.*, 1(2):13–25, 2011.

[18] M. L. Turgeon. Linne and ringsruds clinical laboratory science-e-book: The basics and routine techniques. *Elsevier Health Sciences*, 2014.

[19] A.R. D. T. Evaluation of the widal test in the diagnosis of typhoid fever. *Baghdad university*, 1992.

[20] A. M. Al-Abbasi and S. Al-Obaidi. The level of salmonella typhi antibodies among the iraqi subjects and their value in the diagnosis of typhoid fever. *J Comm Med*, 7(2):113–119, 1994.

[21] A. H. I. enteric fever clinical and diagnostic evaluation. *Baghdad*, 1993.

[22] H. Al-Hossani, H. Abouzeid, M. M. Salah, H. M. Farag, and E. Fawzy. Knowledge and practices of pregnant women about folic acid in pregnancy in abu dhabi, united arab emirates. *East. Mediterr. Health J.*, 16(4):402–407, 2010.

[23] M. N. Al-Khushali. Typhoid and paratyphoid fevers in salahaldin governorate. *Med. J. Tikrit*, 2(142):107–112, 2008.

http://doi.org/10.33091/amj.2020.170935