Assessment of knowledge of Typhoid fever diagnosis and management amongst the interns and residents in the teaching hospital of India

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Abstract-

Introduction-There are estimates that typhoid fever occurs between 10/100,00 and 100/100,00 times a year, making it an important global health issue, hence the accurate diagnosis of typhoid fever at an early stage is very important for proper management. India is endemic for typhoid fever and widal is the most commonly prescribed diagnostic test in cases of fever.

Objectives-The present study was undertaken to evaluate the knowledge about the diagnosis and management of Typhoid fever amongst the interns and residents in the teaching hospital of Northern India.

Methodology-A semi-structured, self-administered questionnaire, was used in this cross-sectional study. The study population comprised of interns and postgraduate students of a medical college situated in northern India.

Results-The study included 101 participants. Data analysis showed, only 11% of the participants had good knowledge, 55.4% had moderate knowledge and 33.6% had poor knowledge about the test and the disease. However, most of the participants had good knowledge about the clinical features, treatment and availability of the diagnostic tests but only a few had thorough awareness of the proper implementation and utilization of the available diagnostic tests. Only 25% knew about the right time to order widal test for diagnosis of typhoid fever and just 60.4% knew about blood culture as the confirmatory test during the first week of illness.

Conclusion-Majority of the participants had a fair knowledge of clinical features and treatment. However, for proper patient management, correct diagnosis at the right time plays a crucial role. Education and training are essential for the utilization and application of the available diagnostic tests which are an essential component of antimicrobial stewardship.

Keywords- Typhoid fever, widal test, knowledge

INTRODUCTION-

There are estimates that typhoid fever occurs between 10/100,00 and 100/100,00 times a year, making it an important global health issue (1). Asystemic prolonged febrile illness, caused by various Salmonella serotypes like *Salmonella typhi*, *S. paratyphi A, S. paratyphi B* and *S. paratyphi C* (2). Disease is transmitted by faecally contaminated water and food in endemic areas, especially by carriers handling food, as human are the only reservoir host for typhoid fever (2). This disease is usually associated with low socio-economic status and poor hygiene. For finding the etiological agent and potential carriers, that may be responsible for acute typhoid fever outbreaks, an accurate diagnosis of typhoid fever at an early stage is very important (3). A French physician and bacteriologist, Georges Fernand-Isidore Widal, developed the Widal test in 1896 (4,5). Most hospitals in the tropics cannot perform cultures owing to lack of material, equipment, expertise, and finances (2), hence, the Widal test, a serological agglutination test, has been used in the diagnosis of typhoid fever for decades (4,5), even now, the test's value for diagnosing typhoid fever has been debated for as long as it's been available (5) In endemic regions, ideally a fourfold rise of antibodies in paired sera is considered diagnostic, however, a positive single acute-phase serum sample, with clinical signs and symptoms may also suffice (6). Widal test has been reported creating huge problem, in having different cut-offs for different places (7,8). Hence, when antibody titres of the normal population are unknown, doctors practicing in endemic regions find it difficult to interpret widal test results (9). False positive reactions have been also observed due to non- typhoidal fevers (10). Widal test's requiring low training in comparison with tests such as culture and polymerase chain reaction (PCR), in addition to sheer habit (11), it is very overprescribed in India. The purpose of this present study is to evaluate the knowledge about the widal test among intern and resident doctors in teaching hospital in India, which are generally the first medical personnel encountered by the patients, and to bring light on various pitfalls and limitations of the test.

Methodology-

Study design- A semi-structured, self-administered questionnaire, cross-sectional study was used to assess the knowledge of Typhoid fever diagnosis and management amongst the interns and residents in a teaching hospital of India. Ethical clearance was obtained from the Institutional Ethical Committee, JNMCH, AMU.

Participants: The study population comprised of Medical undergraduate students currently doing internship (MBBS, BUMS) and medical postgraduate students of a medical college situated in northern India. A total of 101 responses were recorded.

Questionnaire- The questionnaire consisted of 21 questions assessing the knowledge regarding epidemiology, clinical manifestations, treatment, and prevention. These questions consisted of three types of formats i) single correct answer ii) multiple correct answer iii) one-word answer; for questions that had single correct answer, 1 point was given for a correct response and 0 was given for a wrong response. In multiple correct answer type questions, 1 point were given for all correct responses, 0.5 points for partially correct response and 0 points were given when all responses were wrong.

Results-

A total of 101 participants consisting of medical undergraduates including interns and medical postgraduate students of a medical college situated in northern India were included in the study to access knowledge about the widal test and typhoid fever. When the questionnaire data were analyzed only 11% of the participants had good knowledge, 55.4% had moderate knowledge and 33.6% had poor knowledge. (Table 2) (Figure 1)

It was good to see that 75(74.3%) doctors were able to make provisional diagnosis of the clinical case scenario as a patient of typhoid fever, however, only 25(25%) knew when to order widal test for diagnosis of typhoid fever(figure2). 70(69.3%) doctors knew about the significant titre of widal test and 81(80.2%) interpret the widal test report of a positive case correctly however, only 11(10.9%) were able to interpret the post TAB vaccination widal test report correctly. Participants who answered correctly the causes of false positive and false negative results in widal test, was 52(51.5%) and 3(3%) respectively and it was surprising to see that nearly 88(87.1%) lacked

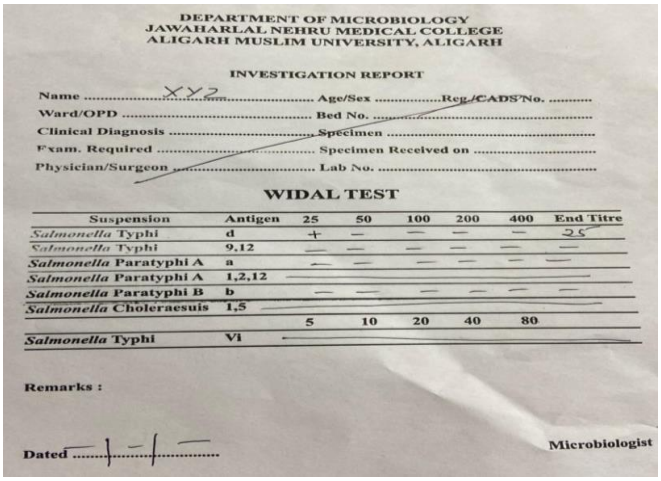
knowledge of the amnestic response. Only 61(60.4%) of the participants answered correctly about the utilization of blood culture as the confirmatory diagnostic test during the first week of fever.

Regarding typhoid carriers diagnosis, 69(68.3%) knew about the correct antigen for which antibodies to be tested; however, only 43(42.6%) knew about the drug of choice for the same (Table 1)

It was good to see, that 86(85.1%) participants correctly answered, how to treat typhoid fever in admitted patients, although only 73(72.3%) knows about the outpatient care treatment of typhoid fever.

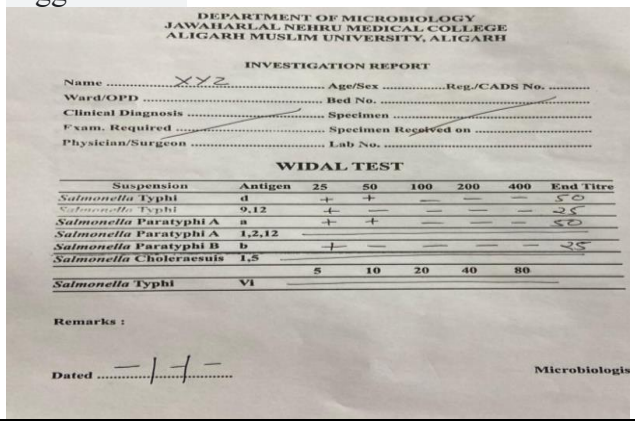
Table 1- Questionnaire and responses

S.NO.	**QUESTIONS**	**OPTIONS**	**RESPONSE(%age)**
1.	What is the principle on which widal test is based?	Don't know	10(9.9)
		Agglutination reaction	83(82.2)
		Wrongly answered	8(7.9)
2.	Mr. Rakesh, comes to your clinic with complaint of high-grade fever, headache, abdominal pain and diarrhoea for last 6 days. He also has decreased appetite for 3 days. O/E you find, temperature-101.5-degree F, pulse rate – 90bpm, abdominal tenderness, white coated tongue and rashes on his body. What will you suspect in this pt.?	Don't know	1(1.0)
		Typhoid fever	75(74.3)
		Typhoid fever and other diseases	19(18.8)
		Other than typhoid fever	6(5.9)

3.	Tests for typhoid fever confirmation?	**CBC, blood culture, LFT**	1(1.0)
		Wrongly answered	41(40.6)
		Other tests along with CBC, blood culture and LFT	59(58.4)
4.	After how many days of symptoms, a doctor should advice widal test in the patient?	Don't know	1(1.0)
		After 2-4 days of symptoms	15(14.9)
		After 5-7 days of symptoms	60(59.4)
		After 8-10 days of symptoms	25(24.8)
5.	 Based on this report, whether you'll prescribe antimicrobial therapy for this pt.?	Don't know	3(3.0)
		Yes	10(9.9)
		No	81(80.2)

		May be	7(6.9)
6.	What is the significant titre of the widal test- TO AND TH antibodies respectively?	Don't know	2(2.0)
		>1/100 &>1/200	70(69.3)
		>1/60 &>1/30	22(21.8)
		>1/40 &>1/20	5(5.0)
		>1/20 &>1/10	2(2.0)
7.	Paired testing should be done after how many weeks of initial testing and how much fold increase in titre should be present to called as positive?	Don't know	1(1.0)
		2^{nd}&4^{th} week	51(50.5)
		1^{st}& 2^{nd} week	31(30.7)
		1^{st}& 3^{rd} week	10(9.9)
		2^{nd}& 3^{rd} week	8(7.9)
8.	False positive results in widal test can be due to-	SLE, vaccination post typhoid vaccine	5(5.0)
		SLE, vaccination post typhoid vaccine, malaria	11(10.9)
		SLE, vaccination post typhoid vaccine, cross	33(32.7)

		reaction to non-typhoidal salmonella	
		SLE, vaccination post typhoid vaccine, malaria, cross reaction to non-typhoidal salmonella	52(51.5)
9.	False negative results in widal test can be due to-	Don't know	3(3.0)
		Early presentation, carrier status, following a typhoid relapse	6(5.9)
		early presentation, carrier status, technical errors, following a typhoid relapse	82(81.2)
		Early presentation, technical errors	3(3.0)
		carrier status, technical errors, following a typhoid relapse	7(6.9)
10.	Typhoid fever caused by what all species of salmonella?	**S. typhi and S. Para typhi A+B+C**	16(15.8)
		wrongly answered	9(8.9)

		s. typhi and s. Para typhi A/B/C	76(75.2)
11.	WIDAL TEST report given below. This is suggestive of-  DEPARTMENT OF MICROBIOLOGY JAWAHARLAL NEHRU MEDICAL COLLEGE ALIGARH MUSLIM UNIVERSITY, ALIGARH INVESTIGATION REPORT Name ..... XYZ ..... Age/Sex ..... Reg./CADS No. ..... Ward/OPD ..... Bed No. ..... Clinical Diagnosis ..... Specimen ..... Exam. Required ..... Specimen Received on ..... Physician/Surgeon ..... Lab No. ..... WIDAL TEST Suspension Antigen 25 50 100 200 400 End Titre Salmonella Typhi d + + — — — 50 Salmonella Typhi 9,12 + — — — — 25 Salmonella Paratyphi A a + + — — — 50 Salmonella Paratyphi A 1,2,12 Salmonella Paratyphi B b + — — — — 25 Salmonella Choleraesuis 1,5 5 10 20 40 80 Salmonella Typhi Vi Remarks : Dated — / — / — Microbiologis	Don't know	14(13.9)
		Post TAB vaccination	11(10.9)
		wrongly answered	76(75.2)
12.	Antibodies to which antigen you'll check in typhoid carriers?	Don't know	9(8.9)
		Vi antigen	69(68.3)
		d antigen	9(8.9)
		a and b antigen	14(13.9)
13.	What is the doc for typhoid carriers?	Don't know	4(4.0)
		azithromycin	25(24.8)
		ciprofloxacin	43(42.6)
		cefixime	19(18.8)

		amoxicillin	10(9.9)
14.	Which of the following tests can be used for diagnosis of typhoid fever?	Don't know	5(5.0)
		blood culture, bone marrow culture, IgM typhidot assay, widal test, bile culture, co-agglutination test	6(5.9)
		blood culture/ bone marrow culture/ IgM typhidot assay/ widal test/ bile culture/ co-agglutination test	90(89.1)
15.	A patient (MR. X) presented with fever and rashes, was advised malaria, dengue and widal test. His results are as follows – A. MPQBC: +ve B. NS1Ag: NON-REACTIVE C.TYPHOID TITRE: H- 100; O-50; What will be the most suitable diagnosis in this pt.(MR. X)?	Don't know	26(25.7)
		malaria	44(43.6)
		wrongly answered	31(30.7)
16.	How will you confirm false positive widal test or dual infection in pt. (MR.X)?	Don't know	13(12.9)

		repeat mpqbc	16(15.8)
		repeat widal titre	33(32.7)
		repeat both mpqbc and widal titre	39(38.6)
17.	What is the best suitable explanation of such widaltiters in above pt. (MR.X)?	Don't know	53(52.5)
		amnestic response	13(12.9)
		wrongly answered	35(34.7)
18.	Confirmatory diagnostic test for typhoid fever during first week?	Don't know	2(2.0)
		BLOOD CULTURE	61(60.4)
		widal test	19(18.8)
		urine culture	2(2.0)
		stool culture	17(16.8)
19.	Are you aware of National antibiotic policy?	yes	62(61.4)
		no	39(38.6)
20.	What is the recommended antibiotic for INPATIENT CARE of pt., suffering from typhoid fever?	Don't know	1(1.0)
		ceftriaxone i.v.	86(85.1)
		ciprofloxacin oral	8(7.9)

		azithromycin oral	1(1.0)
		cefixime oral	5(5.0)
21.	What is the recommended antibiotic for OUTPATIENT CARE of pt., suffering from typhoid fever?	Don't know	4(4.0)
		cefixime	73(72.3)
		ofloxacin	19(18.8)
		ampicillin	5(5.0)

Table 2- Level of knowledge of participants

Level of Knowledge	**score**	**Total n(%age)**
Poor	<10	34(33.6)
Moderate	10-15	56(55.4)
Good	>15	11(11)

Figure1-Pie chart showing level of knowledge of participants

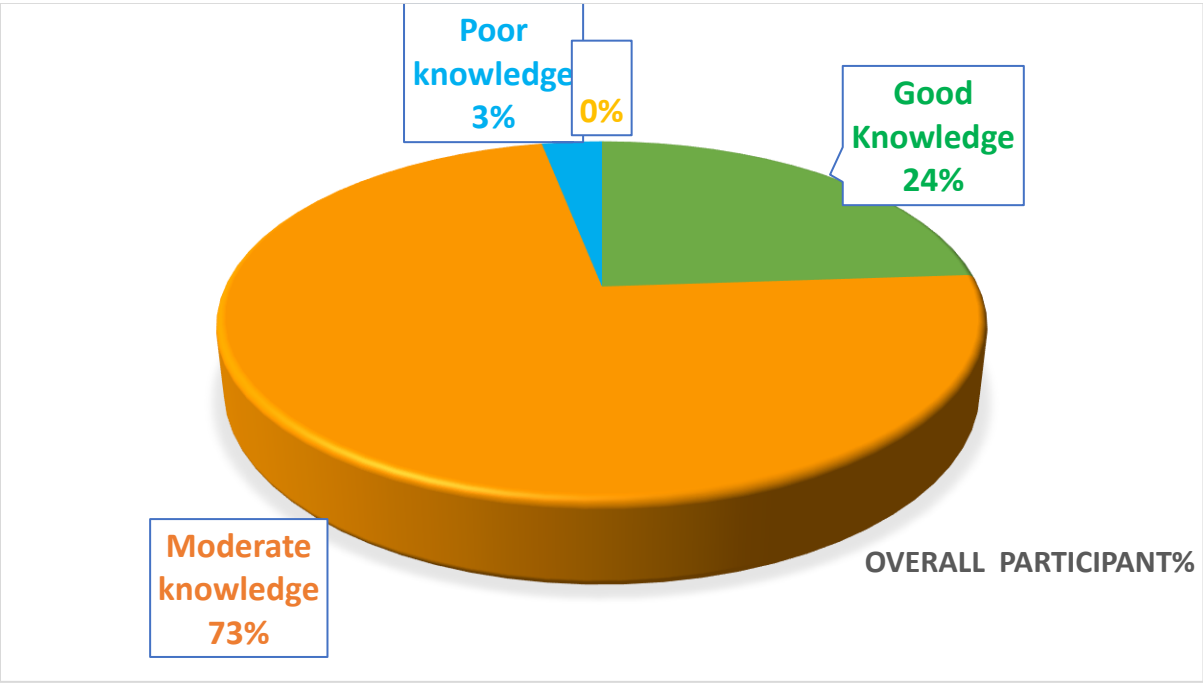
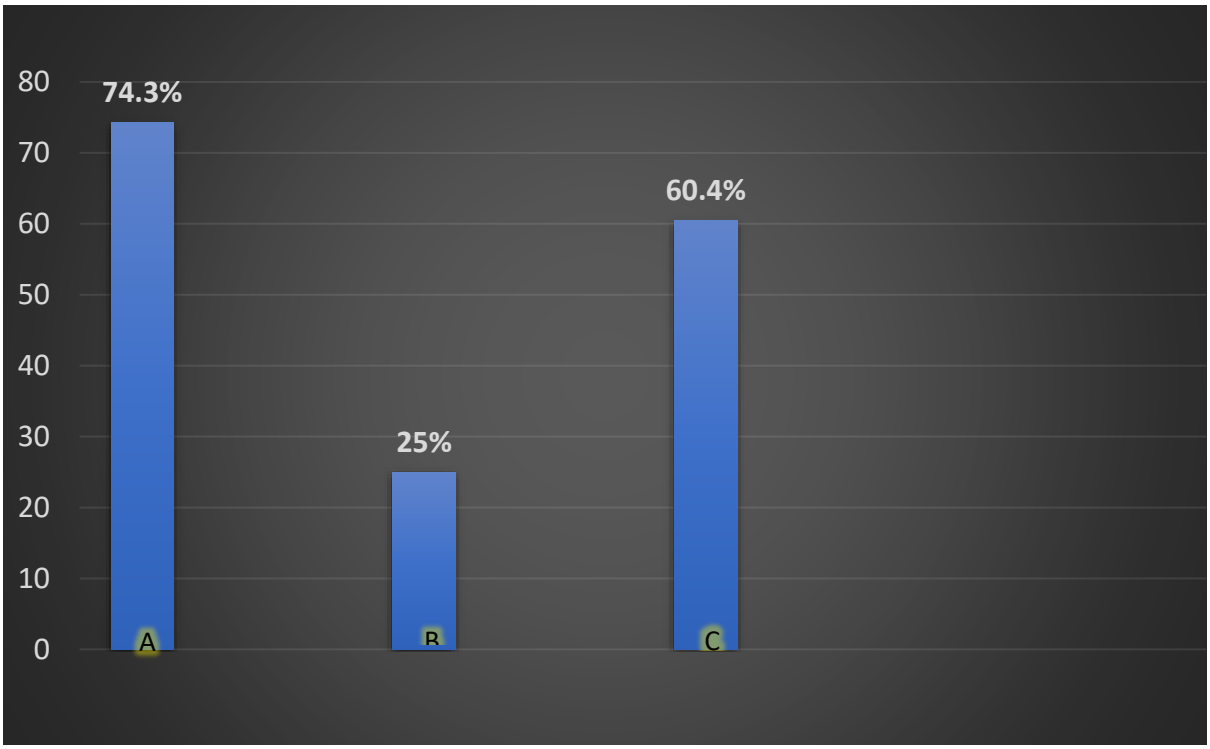


Figure 2- Bar Graph showing responses reagarding widal test



A- number of participants were able to make, provisional diagnosis of the clinical case scenario as a patient of typhoid fever

B- number of participants knew about when to order widal test

C- number of participant knew about confirmatory test during the first week of illness.

Discussion-

Endemic infections continue to be a major problem for healthcare, in a country. There are many endemic diseases in India, which accounts for high mortality and having impact on country's expenditure on health infrastructure. Typhoid fever is one among them, it continues to be a global health problem, especially in the tropics and subtropics part of the world (1). An attempt has been made to assess the knowledge about the diagnostic tests for typhoid fever, especially most prescribed test, the Widal test in an area where *Salmonella typhi* is endemic by various different clinical scenarios, several factors, which have led to confusion in the interpretation of the test.

In order to make the healthcare personnel aware of the diseases and diagnostic tests, it will be necessary to assess their knowledge of the diseases and diagnostic tests. In the present study

medical undergraduate students currently doing internship (MBBS, BUMS) and medical post graduate students of a medical college situated in northern India answered a questionnaire regarding the Typhoid fever diagnosis and management.

It was seen that only 11% of the participants had good knowledge, 55.4% had moderate knowledge and 33.6% had poor knowledge.

The widal test is based on agglutination principle, which measures specific antibody titres in patient's serum. By using the bacterial suspensions of *Salmonella typhi* and *S. paratyphi A and B*, it detects the antibody against salmonella O(somatic) and H(flagellar) antigen in patient's serum (5). This test therefore, work on the principle that antibody present in the patient's serum can agglutinate the homologous antigens in killed *Salmonella* suspensions. Early appearing antibody, IgM, represent acute typhoid fever which is targeted against O agglutinins and late appearing antibody, IgG, persist for longer time and targeted against H agglutinin (5)

In developing countries, like India, where there is a shortage of more complex test like PCR, blood culture, widal test comes out to be a relatively cheap and readily available test, though it has its own pitfalls, making it difficult to interpretate because of many factors, because of which, either results comes out to be a false positive or false negative result as listed below (list not exhaustive) (2,3,5,12,13).

Factors leading to false positive widal test

1. Prior Vaccination against *Salmonella typhi* or *Paratyphi*
2. Past history of typhoid fever
3. Cross-reaction with infections like malaria
4. Cross-reaction with non-typhoidal *Salmonella* antibodies
5. Anamnestic reaction
6. SLE, rheumatoid arthritis and ulcerative colitis
7. Technical error

Factors leading to false negative widal test

1. Use of antibiotics before test

2. Test before the end of first week of infection
3. Technical error
4. "Hidden organisms" in bone and joints
5. Poorly immunogenic strains of infecting Organism

Titres of antibodies begin to rise in first week and keep on increasing through the second to fourth week, after which they begin to decline gradually, hence, timing of the order of widal test is very important, otherwise test may show negative result, which is a unnecessary burden on patient being financially and also according to health perspective. Prior use of antibiotics before collecting the sample for widal test, might show a false negative result (2,3,5). "Hidden organisms" in bones and joints and poorly immunogenic strains of infecting organisms, sometimes shows false negative results (3,13).

Undoubtedly, culture isolation of the organisms, remain the gold standard for diagnosis (5,14), as it considered to be 100% specific(14). Samples that can be used for culture are namely blood, bone marrow, stool, urine, rose spot, gastric and intestinal secretions.

To ensure the good and genuine results of widal test, some factors have to be taken into account: 1. One should know about baseline antibody titre in their area of practising, and titre, therefore, should be interpretated in relation to the baseline antibody titre; 2. Do not always decide the diagnosis according to one widal test report, always repeat the widal test and the titre should be increased significantly, 4 fold rise; 3. If patient has signs and symptoms of disease, a negative test should not be used as exclusion of typhoid fever; 4.Always ensure to take out the sample for culture, before starting the antimicrobial therapy (15).

We used our study as an opportunity to find out, whether the budding physicians know about the National antibiotic policy or not, and 62(61.4%) participants do know about that.

Participants were having good knowledge about the inpatient and outpatient care of typhoid fever patient, which is the ultimate goal desire by a patient and as well as community.

Overall, the results of this study were unsatisfactory, as most of the participants did not have proper knowledge of widal test, which either lead to underdiagnosed or overdiagnosis of the disease. Both the scenarios have their pitfalls, underdiagnosis lead to worsening of the patient condition because

of not getting proper treatment at required time, while overdiagnosis lead to irrational use of antibiotics in the patient.

Conclusion-

Majority of the participants had a fair knowledge of clinical features and treatment. However, for proper management of the patient diagnosis plays a crucial role, we can thus determine that in regions where typhoid fever is common, the widal test can still be useful if it is interpreted carefully and with knowledge of relevant data, particularly regarding the amount of agglutinin present in healthy people and those suffering from other non-typhoidal fevers in the area. Education and training are essential for utilization and application of the available diagnostic tests which are an essential component of antimicrobial stewardship.

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