

How Useful is the Widal Test in Modern Clinical Practice in Developing Countries? A Review

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ABSTRACT

It has been over a century since the Widal test was developed for diagnosing enteric fever. Yet, the test remains the major means of diagnosing the disease in many of the developing countries where it remains endemic. This review appraises the Widal test in regard to its performance techniques, its various drawbacks and the available alternative diagnostics methods. Extensive literature search was conducted through Google search engine and PubMed for relevant published articles in peer-reviewed academic journals. Relevant text books were also consulted. The following conclusions were reached at the end of the review: the Widal test is grossly inadequate to be relied upon as a diagnostic tool for typhoid fever in an endemic area, culture isolation of the causative organism remains the gold standard for the disease diagnosis, there is still no sufficiently reliable alternative rapid diagnostic test (RDT) for typhoid fever and the quest to develop highly effective RDTs for the disease should continue.

Keywords: Widal test, Typhoid fever, Enteric fever, Typhoid rapid diagnostic tests

1. INTRODUCTION

The Widal test was developed by Georges-Fernand-Isidore Widal, a French physician and bacteriologist, in 1896 [1,2]. It is a serological agglutination test which has been used for over a century in the diagnosis of enteric fever [2]. Despite the availability of alternative diagnostic methods, the Widal test continues to be the commonest diagnostic test for typhoid fever in many of the poor developing countries where the disease is endemic. This review, therefore, appraises the Widal test, the alternative diagnostic methods and their applicability in modern clinical practice. It is our hope that it will serve as an education material for the clinician, the laboratory worker and the general population at large.

2. METHODS

Extensive literature search was made through Google search engine and PubMed for relevant published articles in peer-reviewed academic journals. Relevant text books were also consulted. Keywords employed for the search were “Enteric fever”, “Typhoid fever”, “Widal test”, “How to perform Widal test”, “Usefulness of Widal test”, “Alternatives to Widal test” and Typhoid rapid diagnostic tests.” The references of the articles at hand were used to find other relevant references. References were stored in an electronic reference manager (Mendeley) and kept for subsequent use. Forty-eight (48) relevant articles and texts were reviewed and cited in the final draft of the review.

3. ENTERIC FEVER

Enteric fever, also known as typhoid fever, is a potentially fatal acute systemic illness characterized by fever and abdominal symptoms [3]. Though now rare in the industrialized countries of the world as a result of improved sanitation and food hygiene, the disease is still an important cause of morbidity and mortality in the developing countries [3].

The disease was initially called typhoid fever because of its clinical similarity to typhus fever [4]. The term “enteric fever” was proposed as a name for the disease in 1869 due to the anatomical site of the infection [4]. The two terms are, however, being used interchangeably. Enteric fever is primarily caused by *Salmonella enterica serovar typhi* (*Salmonella typhi*). A less severe illness is caused by *Salmonella paratyphi* A and, less commonly by B and C [5]. *Salmonella typhi* is a gram-negative, non-encapsulated, facultative anaerobic, flagellated motile bacillus [6]. It has somatic (O), flagellar (H) and virulence (Vi) antigens [6]. The *S paratyphi* also have similar antigens denoted by AH, BH and CH.

Typhoid fever is related to rapid population growth, increased urbanization, overcrowding, inadequate human waste treatment, limited water supply and overburdened health care systems. Majority of cases are sporadic, although large outbreaks do occur commonly resulting from breakdowns in water supplies and sanitation systems [3,6]. In 2004, the WHO estimated the global burden of the disease at 21 million cases per annum, leading to an estimated 216,000–600,000 deaths annually [6]. The disease is endemic in the developing regions of the world: Indian subcontinent, South and Central America, Asia and Africa [3,6]. The world is divided into three regions according to the annual incidence of typhoid fever: high incidence (>100/100,000 cases/year) includes south-central Asia and south-east Asia; medium incidence (10-100/100,000 cases/year) includes the rest of Asia, Africa, Latin America and the Caribbean, and Oceania, except for Australia and New Zealand; and low incidence (<10/100,000 cases/year) includes Europe, North America, and the rest of the developed world. [7]

66 Man is the main reservoir of the organism, largely current cases and chronic carriers who
67 disseminate the organism in their feces [6]. The disease is acquired predominantly via the
68 feco-oral route by ingestion of contaminated food or water [5]. Less common modes of
69 transmission include sexual transmission (oral-anal, oral-penile, and receptive anal
70 transmission) and transmission through the use of unsterilized instruments (endoscopes,
71 polyvinyl duodenal tube or rectal tube) [8–10]

72 **4. THE WIDAL TEST**

73 The Widal test is an agglutination test that measures specific antibody titers in the serum. It
74 involves the detection of *Salmonella* antibodies in the patient's serum by the use of bacterial
75 suspensions of *S typhi* and *S paratyphi* A and B that have been treated to retain only the O
76 (somatic) and H (flagellar) antigens [2]. The test, therefore, operates on the premise that
77 patients with typhoid fever have antibodies in their sera that can agglutinate homologous
78 antigens in killed *Salmonella* suspensions. The O agglutinins which are immunoglobulin M
79 (IgM) antibodies appear early and represent the initial serological response in acute enteric
80 fever while the H agglutinins which are immunoglobulin G (IgG) antibodies usually develop
81 slowly and persist for a longer duration [2,11] Killed colored suspensions of the *S typhi* O
82 antigen, *S typhi* H antigen, *S paratyphi* AH antigen and *S paratyphi* BH antigen are routinely
83 used for the test.

84 **4.1 Widal test performance and methods**

85 Two methods can be employed to perform the Widal test: the slide agglutination test and the
86 tube agglutination test [2, 12] Though the tube agglutination test has better accuracy, the
87 slide test is commonly used because it is easier and faster to conduct.

88 **4.1.1 Slide agglutination Widal test**

89 The slide agglutination test could either be a qualitative or a quantitative test [2].
90 The qualitative test is used as a rapid screening test to determine the presence of
91 *Salmonella typhi* and *paratyphi* antibodies in the serum of patients. A drop of the patient's
92 serum is added to an equal drop of each of the standard bacterial antigens (O, H, AH, BH)
93 on a slide and thoroughly mixed with an application stick [2,12]. The slide is rotated gently
94 and observed for agglutination. Physiologic saline and a previously reactive serum are used
95 as negative and positive controls [12]. The appearance of agglutination to any of the antigens
96 infers a positive test while non-agglutination implies a negative test. Agglutinations are
97 visualized as clumps.

98 The quantitative test is usually done after the qualitative test (rapid screening test) has been
99 performed. Only the previously detected *salmonella* antibody/antibodies in the patient's
100 serum are then tested to determine their titers. A drop (0.03ml) of the antigen suspension
101 which previously showed agglutination is added to aliquots of 40µl, 20µl, 10µl, and 5µl of the
102 patient's serum on a slide and thoroughly mixed with an applicator stick. The slide is then
103 rotated gently and observed for reactions. Tests' results are scored from 0 to 4+ [0 (no
104 agglutination), 1+ (25% agglutination), 2+ (50% agglutination), 3+ (75% agglutination) or 4+
105 (100% agglutination)] [2,13] The smallest quantity of serum that shows a 2+ or 50%
106 agglutination is chosen as the antibody titer of the test sample [2,13] The presence of
107 agglutination in 40µl corresponds to 1:40, 20µl to 1:80, 10µl to 1:160 and 5µl to 1:320 titers
108 respectively.

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110 **4.1.2 Tube agglutination Widal test**

111 This is a more accurate but more cumbersome and time-consuming quantitative test in
112 comparison to the quantitative slide test. It can be used to clarify ambiguous agglutination
113 reactions gotten by the more rapid slide test [2].

114 Four sets of 8 test tubes are prepared for each antigen (O, H, AH, BH). The first test tube of
115 each antigen set is then filled with 1.9ml of physiological saline [12]. Next, 1ml of
116 physiological saline is added to the other tubes (tubes 2-8). To the first tube, 0.1ml of the test
117 sample (serum) is added and properly mixed. From tube 1, 1ml of the diluted sample is
118 transferred to tube number 2 and mixed properly. The dilution is continued serially up to the
119 7th tube in each set of the four antigens. From tube 7 of each set, 1ml of diluted serum is
120 discarded. Hence, the dilution of the serum sample from tubes 1-7 respectively in each
121 antigen sets are: 1:20, 1:40, 1:80, 1:160, 1:320, 1:640, 1:1280 [12]. Tube 8 serves as a negative
122 control. To one set of test tubes, 50µl of the O antigen is added (i.e. tubes no 1-8). Then,
123 50µl of the H, AH and BH antigens are added to the 2nd, 3rd and 4th set of test tubes
124 respectively and thoroughly mixed. The tubes are then covered and incubated overnight at
125 37°C for up to 20 hours [2,12]. After incubation, the sediments are dislodged and observed
126 for agglutination. The control tubes are firstly examined and they must contain no
127 agglutination. The results are scored from 0 to 4+ agglutinations as described above for the
128 slide test. The highest dilution of serum to produce agglutination is taken as the titer. The
129 titer for each of the antigens is noted and recorded.

130 **4.2 Pitfalls of the Widal test**

131 The Widal test is a relatively cheap and readily available test, especially in developing
132 countries where more sophisticated tests like culture and polymerase chain reaction (PCR)
133 are either not available or unaffordable where available. It is, however, difficult to interpret
134 because of the various reasons that may cause either a false positive (Table 1) or a false
135 negative result (Table 2).

Table 1: Causes of false positive Widal test

1	Vaccination against <i>Salmonella typhi</i> or <i>paratyphi</i>
2	Previous enteric fever
3	Substandard quality reagent
4	Cross-reaction with non- <i>Salmonella</i> infections like malaria
5	Cross-reaction with non-typhoidal <i>Salmonella</i> antibodies
6	Infection with other <i>Enterobacteriaceae</i>
7	Anamnestic reaction
8	Non-infectious chronic illnesses like rheumatoid arthritis and ulcerative colitis
9	Laboratory error

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Table 2: Causes of false negative Widal test

1	Antibiotics use before test
2	Wrong timing e.g. test before the end of first week of infection
3	Substandard quality reagent
4	Laboratory error
5	“Hidden organisms” in bone and joints
6	Poorly immunogenic strains of infecting organism

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138 *Salmonella* are grouped into different serotypes (A – E) based on the somatic O antigen (the
139 Kaufmann-White scheme) [11,14,15] There are at least 78 organisms in the serotype D to

which *S typhi* belongs. While all the 78 group D organisms have O antigen 9, about 60 including *S typhi* possess O antigen 12 [14,15] Hence, infection by any of the group D serotypes could lead to the production of antibodies that can agglutinate the O antigen used in the conduct of the Widal test. Also, because all the groups A and B organisms possess O antigen 12, they could produce O antibodies that can agglutinate the Widal test O antigen. This cross-reaction with non-typhoidal *Salmonella* antibodies significantly reduces the specificity of the test and is a cause of false positive results. Several other non-Salmonella infectious diseases in the typhoid endemic regions like malaria, infective endocarditis, chronic viral hepatitis, dengue, brucellosis, miliary tuberculosis etc. have been demonstrated to exhibit this cross-reactivity that increases the false positive rate of the Widal test [2]. Cross-reaction with other *Enterobacteriaceae* also exists [2].

A study was conducted by Olopoenia *et al* to determine Widal agglutinin titers among a Nigerian population who had no prior typhoid immunization [2]. Among participants who had a positive malaria smear and a negative *S typhi* culture 85% had 1:40, 12% had 1:80, and 3% had 1:160 Widal titers respectively. Whereas, of the participants that had both malaria smears and *S typhi* cultures negative results 45% had 1:40, 15% had 1:80, and 10% had 1:160 Widal titers respectively. In essence, all the participants in the former group had at least a 1:40 Widal agglutination titer while 70% of the latter group had a similar response. This study further corroborates the fact that patient with malaria fever tend to have false positive Widal agglutination reaction.

Non-infectious chronic illnesses like rheumatoid arthritis and ulcerative colitis can also give a false positive result [11]. Patients who have received vaccines against *Salmonella* may have false positive reaction but this can be differentiated from true infection by a repeat test. True untreated infection usually results in a titer rise whereas vaccinated individuals do not demonstrate any titer rise. Individuals who had suffered from repeated exposure to small inocula of *S typhi* or to other *Salmonella* species that contains type 9 or 12 O antigens could have a false positive result [2]. This can also be differentiated from true infection by lack of any rise in titer on test repetition. It should be noted, however, that the mandatory repeat Widal test after the initial positive test is usually not done in many of the places where typhoid fever is endemic. Also, individuals who had suffered from enteric fever in the past sometimes develop anti-*Salmonella* antibodies during non-typhoidal fever states. This is termed anamnestic reaction [11].

The timing of the test is very important as the antibodies begin to rise in the first week and titers increase through the second to fourth week after which they gradually decline. Hence, the test may yield a negative result in the early part of the first week. Patients who have been treated with antibiotics in the early stages may not give positive results [2,16] Such patients may also not show any rise in titer when they initially tested positive, instead there may be a fall in the titer. Occasionally, "hidden organisms" in bones and joints and poorly immunogenic strains of infecting organism may cause false negative results [16,17].

There seems to be poor standardization in the manufacturing process of the Widal antigens as variability in quality exists. DeVillier *et al* compared the *S typhi* O antigens obtained from different manufacturers by testing them against the same serum which initially tested positive by the slide agglutination test [2,18]. The study showed a significant variability in the agglutination titers of the antigens. This kind of variability could lead to either false positive or false negative results.

4.3 Interpretation of the Widal test

While several reports from certain developing countries have suggested that a single Widal test is enough to make the diagnosis of typhoid fever [19–26], others have disputed the

189 reliability of such a single test result [27–34]. However, it is generally agreed that the
190 reliability of the test improves if the interpretation is made against a local cut-off titer
191 [2,15,35].

192 Theoretically, a single Widal test may have some diagnostic relevance in an “unexposed”
193 febrile patient (unvaccinated or lack of active infection). In reality, however, such a single
194 test’s result does not have any diagnostic significance in an endemic area because repeated
195 subclinical exposures to *S typhi* may have occurred [2]. Even in cases of extremely high
196 single Widal agglutination titers, the causal organisms may be other species of *Salmonella*
197 and not *S typhi* [2,36].

198 A review by Olopoenia and King to determine the significance of the Widal test for typhoid
199 fever diagnosis in modern medicine concluded that the test cannot be expected to give a
200 reliable diagnostic result in endemic regions because of its several pitfalls; hence, its use
201 should be discouraged [2]. A study was conducted by Enabulele and Nyemike in a Nigerian
202 population to determine the validity of a single Widal test as a diagnostic tool for enteric fever
203 among febrile adults using blood culture as the reference standard [37]. Malaria parasite test
204 was also done on each sample. Of the 271 participants, 124 (45.76%) were positive for the
205 Widal agglutination test, 60 (22.14%) blood cultures grew *salmonella* and 55 (20.30%) had a
206 co-infection of enteric fever and malaria. Out of the 124 that were positive for Widal test, only
207 21(16.94%) of them had a positive blood culture. Whereas, of the remaining 147 that were
208 negative for Widal test, 39 (26.53%) of them had blood culture confirmation of enteric fever.
209 For Widal agglutination test, a sensitivity of 35%, specificity of 51%, positive predictive value
210 of 17% and negative predictive value of 73% were gotten. These values are too low than for
211 the test to be considered reliable. From the foregoing, it is obvious that a single Widal test
212 cannot be reliably used to diagnose enteric fever in an endemic area. Disregard for this fact
213 probably accounts for the seemingly high rate of diagnosis and treatment of typhoid fever in
214 the endemic areas which are mainly developing countries.

215 It is generally considered that the Widal test is helpful in the diagnosis of typhoid fever in
216 endemic regions only if the patient has a four-fold or more increase in the O or H agglutinin
217 titers of serum specimens taken during the acute and convalescent period of infection (2-3
218 weeks apart) [2,15]. This again is a major obstacle to its use because antibiotic therapy often
219 needs to be commenced at the early stage of the infection in order to prevent the patient
220 from developing serious complications like gut perforation and gastrointestinal bleeding.
221 Thence, no reasonable physician would wait for 2-3 weeks without treating a patient with
222 suspected enteric fever. Again, once antibiotics have been commenced there may be no
223 further rise in the agglutinin titer, rather, it may decrease.

224 4.4 Misuse of the Widal test

225 Misuse of the Widal test is rife in many of the developing countries of the world [2,15,38].
226 This is probably due to the fact that the test is cheap and readily available in contrast to the
227 more reliable but sophisticated diagnostic methods. This is particularly so because patients
228 often do not go to the appropriate medical facilities with competent hands for medical
229 attention because of ignorance and poverty. A report from Libya shows that clinicians
230 depend on the Widal test for the diagnosis of enteric fever despite that locally acceptable
231 threshold titer has not been determined because their laboratories lack skilled and
232 experienced personnel and appropriate facilities to detect and serotype *Salmonella* isolates
233 [38]. Due to the weak nature of institutional regulation in these countries there is proliferation
234 of quack medical and laboratory practices. The laboratories often perform the test, make the
235 diagnosis and prescribe the antibiotics [2]. Many diagnostics centers use just a single
236 positive result for diagnosis not taking into account the reality of cross-reaction between S

237 *typhi* and malaria parasites or other *Salmonella* species that are also endemic in their areas
238 and the generally low diagnostic accuracy of the Widal test. These practitioners often
239 disregard the fact that a negative Widal test result may be more useful than a positive one
240 thereby contributing to unnecessary use of antibiotics.

241 It is imperative that laboratory personnel desist from usurping the role of the physician. Their
242 role is to perform and report the test. It is the responsibility of the requesting physician to
243 utilize the information supplied by the laboratory in conjunction with the clinical information at
244 his/her disposal to arrive at appropriate diagnosis. There is a need for close communication
245 between the requesting physician and the laboratory so as to clarify ambiguous laboratory
246 reports before use. Laboratories should desist from reporting test results in descriptive terms
247 (negative or positive) as this may lead to wrong interpretation of results by the physician [2].
248 The results should rather be reported as either 'no agglutination' or in titers (1:20, 1:40, 1:80,
249 1:160 etc.) if agglutination is present [2].

250 **4.5 Alternative rapid diagnostic tests to the Widal test**

251 As a consequence of the drawbacks attendant to the Widal test, several alternative rapid
252 diagnostic tests (RDT) have been developed. These tests include the indirect
253 hemagglutination assay (IHA), indirect enzyme-linked immunosorbent Assay (ELISA) for
254 immunoglobulin M (IgM) and IgG antibodies to *S typhi* polysaccharide, indirect fluorescence
255 Vi antibody assay, counter immunoelectrophoresis (CIEP) and monoclonal antibody against
256 *S typhi* flagellin etc [35].

257 Some of the commercially available RDTs kits for typhoid include- Tubex TF (IDL, Sweden),
258 Typhidot (Malaysian Biodiagnostic Research, Malaysia), Multi-Test Dip-S-Ticks (Panbio
259 INDX, US), Typhidot-M (Malaysian Biodiagnostic Research, Malaysia), SD Bioline (Standard
260 Diagnostics, Korea) and Mega *Salmonella* (Mega Diagnostics, US) etc [39] Tubex TF and
261 Typhidot are among the most commonly used of the recent generation of RDTs for typhoid
262 fever [39]. Mostly, these tests have not been found sufficiently superior in performance to the
263 Widal test to be recommend as lone reliable diagnostic tests for typhoid fever in endemic
264 areas [40,41,42,43].

265 Thriemer *et al* conducted a meta-analysis to determine the performance of Tubex TF and
266 Typhidot in typhoid endemic countries [39]. A total of seven studies were included per test.
267 The meta-analysis showed average sensitivity and specificity of 69% (95%CI: 45%–85%)
268 and 88% (95%CI: 83%–91%) respectively for Tubex TF. A formal meta-analysis could not be
269 conducted for Typhidot because of data limitation but across the extracted studies,
270 sensitivity and specificity estimates ranged from 56% to 84% and 31% to 97% respectively.
271 It was concluded that the observed performance does not support the use of either of the
272 RDTs exclusively as the basis for diagnosis and treatment of typhoid fever.

273 In another meta-analysis of 37 studies that evaluated three RTDs and their variants (TUBEX
274 in 14 studies, Typhidot in 22 studies and Test-It Typhoid immunochromatographic lateral
275 flow assay in 9 studies), Wijedoru *et al* obtained an average sensitivity of 78% (95%CI: 71%-
276 85%) and specificity of 87% (95%CI: 82%-91%) for TUBEX; an average sensitivity of 69%
277 (95%CI: 59%-78%) and specificity of 90% (95% CI 78% to 93%) for all Test-It Typhoid and
278 prototype tests (KIT); and an average sensitivity of 84% (95%CI: 73%- 91%) and specificity
279 of 79% (95%CI: 70%-87%) for Typhidot test. The authors concluded that few of the 37
280 studies were at a low risk of bias, the three main RDTs and their variants had moderate
281 diagnostic accuracy, the tests did not show any evidence of superiority to one another in
282 terms of their average sensitivity and specificity and there is need for more robust
283 evaluations of alternative RDTs for enteric fever [44].

284 However, an immunodiagnostic assay for enteric fever, called typhoid/paratyphoid diagnostic
285 assay (TPTest), has been developed lately [45]. The test is centered around the detection of
286 anti-Salmonella enterica antibodies secreted by activated lymphocytes in the peripheral
287 blood of acutely infected patients. [45]. TPTest had a sensitivity of 100% compared to blood
288 culture, and specificity that ranged from 78-97% (95% CI: 73%-100%), depending on the
289 definition of true negative among Bangladeshi patients [45]. In a study that compared the
290 diagnostic accuracy of TPTest to Tubex and Typhidot, the sensitivity of TPTest, Tubex and
291 Typhidot were estimated at 96.0% (95% CI: 87.1%-99.8%), 60.2% (95% CI: 49.3%-71.2%),
292 and 59.6% (95% CI: 50.1%-69.3%), respectively; while specificity was estimated at 96.6%
293 (85%CI: 90.7%-99.2%) for TPTest, 89.9% ((5% CI 79.6%-96.8%) for Tubex, and 80.0%
294 (67.7%-89.7%) for Typhidot [46]. This indicates that TPTest has a superior diagnostic
295 accuracy compared to Tubex and Typhidot. Nevertheless, it takes 24-48hrs to obtain the
296 result of the test at the moment and moderate laboratory capacity is required to conduct it
297 [46].

298 5. HOW IS TYPHOID FEVER DIAGNOSED

299 The gold standard for the diagnosis of enteric fever remains culture isolation of the organism
300 [2,35]. It is considered 100% specific [2,35]. The blood, bone marrow, stool, urine, rose spot,
301 gastric and intestinal secretions may be cultured. Culture efficacy varies with the type of
302 specimen being tested. Bone marrow culture yield is about 90% sensitive at any point in the
303 course of the disease to as long as five days after the initiation of antibiotic therapy [35,47].
304 The test is not the preferred option because the procedure is extremely painful. The
305 sensitivity of blood culture approaches 90% in an untreated patient in the first week of
306 infection but the figure drops to less than 50% by the third week. Large volume (10-30ml)
307 and multiple samples (>3 times) improve the diagnostic yield [35]. The sensitivity of stool
308 culture alone is less than 50% while urine culture is lesser [35]. A single rectal swab during
309 hospital admission has a sensitivity of 30-40% [35]. However, the high rate of antibiotics use
310 by patients before hospital presentation in the developing countries tends to interfere with
311 the isolation of infectious agents from clinical specimens, particularly blood culture. Though
312 blood culture is currently the preferred diagnostic method, it is expensive; the result is only
313 available after more than 48 hours; and requires elaborate laboratory equipment and rare
314 technical expertise.

315 The polymerase chain reaction has varying success. The nested PCR has a sensitivity of
316 82.7% and a specificity of 100% when blood and urine assays are combined [48]. The test is
317 not readily available in the endemic areas and where available, it is mostly used for research
318 purpose because it is generally too expensive for patients.

319 Common nonspecific laboratory findings in patients with typhoid fever include moderate
320 anemia, thrombocytopenia, relative lymphopenia and elevated erythrocyte sedimentation
321 rate (ESR) [Table 3] [35]. Depending on the stage of the disease at the time of diagnosis,
322 there could be slight elevation of the prothrombin time (PT) and activated partial
323 thromboplastin time (aPTT), a reduction in fibrinogen levels and elevation in the levels of the
324 fibrin degradation products. The liver transaminases and serum bilirubin values could rise to
325 as twice the reference range.

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Table 3: Nonspecific laboratory findings in patients with typhoid fever

1	Moderate anemia
2	Thrombocytopenia
3	Relative lymphopenia
4	Elevated erythrocyte sedimentation rate (ESR)
5	Elevated prothrombin (PT) and activated partial thromboplastin time (aPTT)
6	Reduced fibrinogen levels
7	Elevated fibrin degradation products levels
8	Elevated liver transaminases and bilirubin

332

333 The question then comes to mind: “How is enteric fever to be diagnosed in the absence of a
334 rapid, reliable and cost-effective diagnostic method?” The fact is that accurate diagnosis of
335 typhoid fever remains a challenge in resource-poor settings because the disease does not
336 have specific clinical features. The diagnosis is often made by the exclusion of other
337 common febrile illnesses in the locality. In many of the areas where malaria is endemic,
338 typhoid fever is usually suspected whenever a febrile patient gives a history of repeated
339 standard malaria treatment without abatement of the fever. Features that may suggest the
340 development of complications such as generalized abdominal tenderness with guarding and
341 hematochezia are also sought for. Apart from fever and abdominal pain, nonspecific
342 symptoms such as headache, diarrhea or constipation, anorexia, body weakness and
343 muscle pains are often associated with the disease [3]. Neuropsychiatric manifestations
344 (known as typhoid psychosis) ranging from confusion to frank psychosis could occur in 5%
345 to 10% of patients with enteric fever [3]. Rose spots (red macules of 2-4 millimeters
346 diameter) may be observed in light skinned persons. It is not uncommon for physicians to
347 commence empirical antibiotic therapy while awaiting culture results once a clinical
348 impression of typhoid fever has been made.

349 6. CONCLUSION

350 The Widal test cannot be relied upon to accurately diagnose typhoid fever due its glaring
351 inadequacies. Therefore, its use should be discouraged by all means. The general
352 population, laboratory workers and clinicians need to be adequately enlightened on the
353 limitations of the Widal test as this will go a long way to reducing the rate of unnecessary
354 diagnosis and treatment of typhoid fever in the endemic populations. The quest for the
355 development of effective typhoid RDTs should continue until they could perform at levels
356 comparable to the malaria RDT. Since culture isolation of the causative organism remains
357 the definitive diagnosis of enteric fever, there is an urgent need for the provision of
358 appropriate laboratory equipment and training of more laboratory personnel on microbiology
359 culture techniques in the developing countries where the disease is endemic.

360

361 COMPETING INTERESTS

362

363 Authors have declared that no competing interests exist.

364

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