

Clinical Diagnosis Of Enteric Fever And The Potential Benefits In The Management Of Enteric Fevers In The Developing World

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Citation

G Jombo, M Enenebeaku, S Utsalo. *Clinical Diagnosis Of Enteric Fever And The Potential Benefits In The Management Of Enteric Fevers In The Developing World*. The Internet Journal of Parasitic Diseases. 2006 Volume 2 Number 2.

Abstract

Aim To examine the clinical presentations of enteric fever so as to aid their quick clinical diagnosis.

Methods A systematic literature review on clinical presentations of enteric fever was carried out. Relevant information from original articles, reviewed articles, short communications, letters to the editor, and case reports over a 30 year period (1977-2007) were compiled. Data obtained was analysed using simple descriptive methods.

Results Fever, headache, weakness, chills, anorexia, and fatigue were the most frequent symptoms encountered among patients with enteric fever. Also bradycardia, low blood pressure, weight loss, hepatomegaly and splenomegaly, and coated tongue were among the most frequent signs encountered among similar patients. Laboratory findings based on isolation of *Salmonella* spp. from specimens as well as significant titres in widal test could be used to establish diagnosis of enteric fever. Clinical presentations such as meningitis, myocarditis, splenic/hepatic abscess, psoas abscess, dysentery, haemorrhagic cystitis, pneumonia, glomerulonephritis and acute aphasia were found to be among the unexpected and unusual presentations of enteric fever.

Conclusion In view of the diverse and complex presentations of typhoid fever, physicians should approach patients with infective, psychiatric and neurologic clinical features with the belief that, *Salmonella* infection may not be that remote a possibility.

INTRODUCTION

Enteric fever is caused by *Salmonella typhi* and *Salmonella paratyphi*, and globally accounts for at least 16 million infections with not less than 600,000 deaths each year^{1,2,3}. The disease is quite of low prevalence in the developed parts of the world¹. The disease is however still of a significant public health importance in Africa, parts of Asia, central and south America and other developing regions of the world^{2,3}. In the west, the incidence of typhoid fever has been reported as low as 0.2 per 100,000 persons per year⁴. In the developing world on the other hand, though, accurate statistics may be lacking, the incidence of up to 13-22 per 100,000 persons per year has been documented⁵.

Typhoid infections have been found to present with quite diverse signs and symptoms which at times has challenged the professional competence of even the well experienced

medical personnel^{6,7}. In Poland⁸, typhoid was found to manifest as a respiratory tract infection in a five year old boy, while in Johannesburg, South Africa⁹, neonatal typhoid fever believed to have been transmitted vertically was noted with invariably fatal outcome. Also in Brazil¹⁰, an unusual form of typhoid fever with cholestatic hepatitis and jaundice was encountered; patient eventually survived only after appropriate treatment for typhoid fever with ciprofloxacin was instituted. And, in Jamaica¹¹, aphasia was unusually observed in a 20 year old adult female with typhoid fever.

In view of the rare and unusual symptoms and signs of enteric fever being encountered by medical experts worldwide¹². And, sometimes only at post mortem examination points to the fact that several of the available textbooks on infectious diseases have not yet told us the whole story about typhoid fever¹³. A proper understanding of

the disease with its unusual presentations would impact positively on its better and prompt management with much more encouraging outcomes¹⁴.

Typhoid fever at present is still a disease of major public health importance in Nigeria and indeed the rest of Africa^{15,16,17}. Clinical diagnosis, still useful in our hospitals, of typhoid fever could therefore pose a serious challenge among clinicians especially with complex clinical picture. This would be more pronounced and confusing especially when patients present late at the clinic as is often seen, when most of the classical features of the disease might have disappeared. Also, lack of adequate laboratory facilities for proper diagnosis of infectious diseases in several health centres in Africa makes clinical diagnosis a veritable adjunct to effective management of enteric fevers^{18,19,20}.

This study was therefore set up to review the diverse clinical presentations of typhoid fevers so as to widen the horizon of thought of possibilities among clinicians confronted with related clinical pictures. The study would therefore be useful for clinicians both in the developing world as well as those in the developed societies where typhoid fever is almost non-existent and clinicians might have forgotten about its clinical diagnosis²¹, hence the relevance of the study.

MATERIALS AND METHODS

A systematic literature search on clinical presentations of enteric fever was carried out on published articles in reputable journals from 1977 to 2007 (30 years). This includes original articles, review articles, letters to the editors, case reports, as well as short communications. Write-ups on symptoms, signs, laboratory findings and unusual presentations of enteric fever were given preference in the course of selection. Data obtained was analysed using simple descriptive methods.

RESULTS

Between 1977 and 2007, 755 published articles on a total of 3992 subjects were encountered on clinical presentations of enteric fever, out of which 676 subjects presented with unusual features. The male female ratio of enteric fever was found to be 1.18, while the age range of infection was 6 days to over 75 years. The age distribution pattern was inconclusive.

The commonest symptoms encountered among the subjects were: fever 72.4% (2,889), (range 68%-100%); headache 45% (1,798), (range 43%-87%); and weakness 40.7%

(1,624) (range 27%-62%). Other symptoms encountered include nausea 10.8% (431), fatigue 12.8% (511), chills 21.9% (875), coughing 3.1% (123), and anorexia 19.5% (777), (Table 1).

Evaluation of the signs of enteric fever among the subjects showed that: bradycardia 10.7% (427), low blood pressure 13.4% (536), splenomegaly 7.8% (312), and hepatomegaly 3.2% (127) were the commonest signs encountered. Other signs encountered were weight loss 0.6%, rales 4.4%, coated tongue 2.3%, icterus 6.1%, rose spots 3.1%, night sweats 1.8%, and psychosis 1.8%, (Table 2).

Analysis of the laboratory findings on enteric fever among the subjects showed that anaemia, leucocytosis, leucopenia, and elevated liver enzymes were found in 11% (4390), 14.5% (578), 9.9% (395), and 8.6% (342) respectively. Stool culture positive only, blood culture positive only, and both stool and blood culture positive were recorded in 46.1% (1841), 10.8% (432), and 4.9% (198) respectively. Widal test significance was recorded in 17.3% (689) while urine culture positivity was recorded in 0.4% (17) subjects. Isolation of *Salmonella* spp. from other body secretions such as cerebrospinal fluid, pleural effusion and pus was variable, (Table 3).

A review of the 676 subjects with unusual presentations of enteric fever showed that: meningitis 27.7% (187), splenic abscess 12.4% (84), hepatic abscess 10% (68), and acalculous acute cholecystitis 11.1% (78) were the commonest presentations. Pneumonia 8.7% (59), neonatal typhoid 7% (47), dysentery 5.8% (39), and palatal palsy 0.1% (1) were also encountered, (Table 4).

Figure 1

Table 1: Symptoms of Enteric fever among 3,992 subjects in 755 literature reviews.

Symptoms	Frequency	Percent (%)
Fever	2,889	72.4
Headache	1,798	45.0
Diarrhoea	166	4.1
Abdominal pains	283	7.1
Constipation	372	9.3
Nausea	431	10.8
Vomiting	301	7.5
Cough	123	3.1
Myalgia	272	6.8
Fatigue	511	12.8
Insomnia	98	2.5
Chills	875	21.9
Anorexia	777	19.5
Weakness	1,624	40.7
Unusual Presentations	676	16.9

Figure 2

Table 2: Signs of Enteric fever among 3,992 subjects in 755 literature reviews.

Signs	Frequency	Percent (%)
Splenomegaly	312	7.8
Hepatomegaly	127	3.2
Hepatosplenomegaly	63	1.6
Bradycardia	427	10.7
Blood Pressure Normal	673	16.8
Blood Pressure Raised	296	7.4
Blood Pressure Low	536	13.4
Rales	176	4.4
Psychosis	71	1.8
Icterus	244	6.1
Coated tongue	92	2.3
Rose spots	122	3.1
Night sweats	71	1.8
Weight loss	23	0.6
Purulent pleurisy	19	0.5
Unusual Presentations	676	16.9

Figure 3

Table 3: Laboratory findings on Enteric fever among 3992 subjects in 755 literature reviews.

Laboratory Findings	Frequency	Percent (%)
Anaemia	439	11.0
Leucocytosis	578	14.5
Leucopenia	395	9.9
Elevated Liver Enzymes	342	8.6
Elevated Serum Bilirubin	133	3.3
Faecal leucocytes (Mean 4,950/mm ³)	142	3.6
CSF, Other Secretions culture	Variable	Variable
Stool cultures Positive only	1,841	46.1
Blood cultures Positive only	432	10.8
Blood and Stool Culture Positive	198	4.9
Widal test significant	689	17.3
Urine culture Positive	17	0.4
Unusual Presentations	676	16.9

Figure 4

Table 4: Unusual Features among subjects with Enteric fever in 676 subjects.

Unusual Feature	Frequency	Percent (%)
Meningitis	187	27.7
Psoas abscess	2	0.3
Myocarditis	5	0.7
Splenic abscess	84	12.4
Hepatic abscess	68	10.1
Dysentery	39	5.8
Haemorrhagic cystitis	6	0.9
Neonatal typhoid	47	7.0
Typhoid hepatitis	59	8.7
Palatal palsy	1	0.1
Acalculous acute cholecystitis	75	11.1
Pneumonia	59	8.7
Acute aphasia	7	1.0
Glomerulonephritis	22	3.3
Cutaneous vasculitis	11	1.6
Pancreatitis	4	0.6
Total	676	100

DISCUSSION

Of the 3992 subjects with enteric fever reviewed, the frequency of fever, headache, weakness, chills and anorexia

was found to be 72.45 (92,889), 45% (1,798), 40.7% (1,624), 21.9% (875), and 19.5% (777) respectively. There were wide margin of reports among individual findings. Anand²² and Hoge, et al²³ recorded 100% of fever each in their respective studies, Idoko, et al²⁴ recorded 88% fever while Boomsma²⁵ reported 38%. Varied reports on headache were similarly reported, including, Secmeer, et al²⁵ 40%, Anand²² 55%, and Boomsma²⁵ 17%. Varied reports on other symptoms such as diarrhoea, constipation, anorexia and chills were similarly reported by different authors^{26,27}.

In Sub-saharan Africa and other tropical regions of the world where malaria is still endemic, similar symptoms may be encountered among patients with malaria as well as initial symptoms of several viral infections²⁸. Efforts should be made at excluding these diseases. Other symptoms such as myalgia, cough, insomnia, anorexia, weakness, constipation and nausea should be used, though not in isolation, to strengthen the suspicion of enteric fever. This suspicion could become stronger especially where both thin and thick blood films are negative for *Plasmodium* spp. The presence of signs such as bradycardia, coated tongue, rose spots, low blood pressure, hepatomegaly or splenomegaly and weight loss could as well be a pointer to enteric fever in the midst of the above mentioned scenario²⁴. Signs such as jaundice and psychosis should also be considered for enteric fever on patients with suspected psychiatric or viral hepatitis ailments²⁹.

The inability to isolate *Salmonella* spp. from stool, blood, urine or any other potential body secretions could be complemented by a quality controlled widal test. Enteric fever should be strongly considered especially where the titre is significantly high in the midst of at least a few clinical features³⁰.

The presentation of enteric fever in the form of psoas abscess, myocarditis, hepatic abscess, meningitis, palatal palsy, and acute Glomerulonephritis among others pose serious challenge in prompt diagnosis^{31,32,33}. It is also capable of ridiculing the clinical expertise of even the most experienced of physicians. Though some of these unusual presentations could be attributed to the complications of enteric fever; the obvious late presentation of such cases at the clinic where most of the common clinical features will have cleared further compounds the challenge of the attending physician³⁴.

Physicians practicing in Sub-Saharan Africa and other

tropical regions of the world where enteric fever is still endemic should consider typhoid, not too much a distant possibility in clinical presentations such as cutaneous vasculitis, acute aphasia, and haemorrhagic cystitis among others. Treatment for typhoid could be instituted in the absence of a reliable laboratory confirmatory test where other common causes have been ruled out. This approach may rescue at least a few of such patients who present in resource poor countries with ill equipped diagnostic facilities. Physicians practicing in regions of the world where typhoid has been controlled should as well be on a watch out for such bizarre presentations especially among travelers from endemic regions^{6,8,10,12}.

In conclusion, we have found out that, apart from the usual clinical features of enteric fever the disease can trick the physician and present in quite unusual forms. This could be more confusing in the absence of reliable laboratory facilities to establish accurate diagnosis. Physicians practicing in typhoid prone regions of the world should assess patients with such unusual presentations as hepatitis, Glomerulonephritis, haemorrhagic cystitis, meningitis, and acute aphasia among others with the possibility that, *Salmonella* could be the culprit after all.

CORRESPONDENCE TO

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