EOSINOPENIA AS A DIAGNOSTIC MARKER FOR ENTERIC FEVER: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

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ABSTRACT

Introduction

Enteric fever is produced by gram negative bacteria, Salmonella typhi and paratyphi A, B and C. Enteric fever presents with clinical features of fever, headache and abdominal pain, which are hallmarks of this disease. A positive culture is the only confirmative diagnostic test for enteric fever. Simple hematological tests like a complete blood count are commonly performed tests in any patient presenting with fever. Absolute eosinopenia, ie, an eosinophil percentage of 0 on peripheral smear, is a consistent finding seen with enteric fever. It has a high negative predictive value, therefore a high eosinophil count may help the clinician rule out enteric fever and think of another diagnosis. In this study, we aim to prove the value of eosinophil count as a guide towards the diagnosis of enteric fever.

Materials and Methods

This study was a one year hospital based cross-sectional study, done from 1st January 2020 to 31st December 2020. Sources of data were the patients admitted in the wards and visiting the OPD of KLES Dr. Prabhakar Kore Hospital, Belagavi, a tertiary care hospital in Karnataka, India, satisfying the inclusion criteria. The sample size was 45. The study included patients diagnosed as enteric fever by a positive blood culture for S. typhi/paratyphi or showing rising Widal titres.

Observation and Conclusion

In our study, 95.56% of the patients were under the age of 50 years. Males were more commonly affected compared to females in our study, 66.67% being males while 33.33% were females. Fever was a consistent complaint, present in all of our patients. Abdominal pain was present in 37.78% patients. 22.22% patients presented with relative bradycardia, while 35.55% had organomegaly in the form of

hepatomegaly, splenomegaly or both. Anemia was seen in 26.67% patients, 17.78% patients had leukopenia while 4.44% had leukocytosis. Thrombocytopenia was seen in 24.44% patients. Absolute eosinopenia, ie an absolute eosinophil count of 0 was seen in 42 out of the total 45 patients studied, ie 93.33% of the total study population. All the samples taken in our study were blood culture positive. 84.44% patients were infected with Salmonella typhi organism while 15.56% were infected with Salmonella paratyphi A. Out of the 45 samples, only 46.67% were sensitive to prototype fluoroquinolone (ciprofloxacin) while 44.44% showed complete resistance and 8.89% showed intermediate resistance. It was surprising to note that only 31.11% samples were sensitive to ceftazidime, while 6.67% were completely resistant. 62.22% samples showed evidence of production of ESBL (Extended Spectrum Beta Lactamase). Sensitivity to meropenem, imipenem and ertrapenem was 95.56%, 95.56% and 88.89% respectively. The Widal test was performed for a total of 41 out of 45 samples. Only 37.78% patients had a positive Widal test with high titres, ie at least 1 antibody titre was equal to or more than 1:160, 22.22% patients had a positive Widal test but low titres, ie none of the antibody titres were more than 1:160, and 31.11% patients had a negative Widal test, inspite having positive blood culture for S.typhi or paratyphi. Out of the 45 patients, 73.33% patients received 3rd generation cephalosporin, while 20% received both 3rd generation cephalosporin and azithromycin. 6.67% patients received other antibiotics like co-amoxiclav, piperacillin-tazobactam, meropenem, etc. The diagnosis of enteric fever is cumbersome, hence, a simple test like eosinopenia proves indespensible and accurate as a guide towards diagnosing this disease.

Keywords:

Enteric fever, Eosinopenia, Widal test, Culture

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INTRODUCTION

Enteric fever is a disease produced by gram negative bacteria, Salmonella typhi and paratyphi A, B and C. Enteric fever is used interchangeably with 'typhoid' and 'paratyphoid' fever. The only known host for enteric fever is humans. It spreads via the faeco-oral route, through contaminated food and water. Once ingested it spreads via ileal lymphatics and reaches reticuloendothelial system, where it affects multiple organs[1].

The incidence of enteric fever is rare in developed nations. It is endemic to the Indian population. It is a disease, which is more commonly seen in urban compared to rural areas. Young children and adolescents are much more likely to be affected compared to people of older age group[2]. The incidence of S. typhi in more than that of S. paratyphi (ratio = 4:1). S. paratyphi tends to have a milder clinical course compared to S. typhi.

Enteric fever presents with clinical features of fever, headache and abdominal pain, which are hallmarks of this disease.

Diagnosis of enteric fever poses a challenge due to its large list of differential diagnosis, which includes diseases like malaria, dengue, viral hepatitis, leptospirosis, etc. Due to this reason, one cannot rely solely on clinical findings, which tend to overlap between multiple acute febrile illnesses. Therefore, laboratory investigations remain the mainstay in order to label a patient as enteric fever.

A positive culture is the only confirmative diagnostic test for enteric fever. Most commonly used body fluid is blood, but bone marrow, intestinal secretions, stool and rose spots can also be cultured.

Other tests that give a diagnostic clue towards enteric fever but lack both sensitivity and specificity are serological tests like Widal tests[3], rapid serological tests

detecting Vi or O:9 antigens[4]. These tests are not useful, especially in endemic regions. ELISA test against polysaccharide Vi Ag maybe useful in detecting carriers, but should not be used for diagnosis.

Simple hematological tests like a complete blood count are commonly performed tests in any patient presenting with fever. Findings on complete hemogram in enteric fever are anemia, leukopenia, eosinopenia and thrombocytopenia. These findings are attributable to arrest of myeloid maturation, decrease in the number of erythroblasts and megakaryocytes and increased phagocytosis by histiocytes in the bone marrow[5].

Absolute eosinopenia, ie, an eosinophil percentage of 0 on peripheral smear, is a consistent finding seen with enteric fever. Eosinophil levels are regulated by glucocorticoids and adrenaline. In acute phase of the disease, there is rapid sequestration of circulating eosinophils in response to chemotactic factors like c5a and fibrin[6,7]. Absolute eosinopenia is not specific for enteric fever and may occur in other bacterial infections, but is a consistent finding seen in enteric fever which acts as a marker or clue to diagnose it. It has a high negative predictive value, therefore a high eosinophil count may help the clinician rule out enteric fever and think of another diagnosis.

Although blood culture is confirmatory, it is a time-consuming process. Moreover, in a country like India, there simply may not be resources available to culture the bacterium, and even if available, may not fulfil quality requirements in order to provide good yield of bacteria. Therefore, to fill the gap between the day of presentation of patient and the day of confirmatory diagnosis, which may take as long as 5 days in certain institutions, or sometimes, in absence of confirmatory diagnosis, a simple blood test, which is eosinophil count, is indispensable, and can help in

diagnosing the patient fast as well as starting early antibiotic therapy. This is crucial in preventing complications like gastrointestinal bleeding, perforation, secondary bacteremia, peritonitis, septic shock and encephalopathy.

In this study, we aim to prove the value of eosinophil count as a guide towards the diagnosis of enteric fever.

OBJECTIVES

To prove that eosinopenia is a diagnostic marker for enteric fever

REVIEW OF LITERATURE

Enteric fever is a disease produced by gram negative bacteria, Salmonella enterica serotype typhi and paratyphi A, B and C. A rare causative organism is Salmonella cholerasuis. The terms 'typhoid fever' and 'paratyphoid fever' are used synonymously with enteric fever. The term 'enteric' fever, introduced in 1800s, is used because of the involvement of Peyer's patches along with mesenteric lymph nodes. The term 'typhoid' was coined by Pierre Charles Alexander Louis in 1829. 'Typhoid' means typhus-like, as the disease was once thought to mimic epidemic typhus. The term 'paratyphoid' was coined by Raoul Bensaude and Emile Achard, who first isolated Salmonella paratyphi B. The only known host for enteric fever is humans.

Etiopathogenesis:

The credit for discovery for the transmission pattern of enteric fever goes to William Budd, who observed the same during the Taw Valley of England epidemic. It spreads via the faeco-oral route, through contaminated food and water. ID_{50} is 10^{5-7}, but as low as 10^3 can also produce infection. Once ingested it spreads via specialized microfold cells (M cells) to basolateral membrane. This entry of the bacteria into epithelial cells is regulated by the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. Therefore, CFTR polymorphism preventing protein expression provides protection against acquisition of enteric fever, found in a study done in Indonesia[8]. Then, via ileal lymphatics (mesenteric lymph nodes), the bacteria reach the reticuloendothelial system. In this phase, Peyer's patch hypertrophy and even necrosis can occur due to recruitment of monocytes and lymphocytes. This phase earns the disease its name 'enteric' fever. Eventually, it enters thoracic duct and finally reaches the bloodstream[1]. Since the invasive phase of the organism is short

lived, that is why it may be asymptomatic or only produce mild gastrointestinal symptoms like diarrhoea. Bacilli can get seeded into various organs like the liver, gall bladder, spleen, bone marrow, lymph nodes, lungs and kidneys. The bacilli possess a number of virulence factors like flagellar protein synthesis inhibition, resulting in induction of TLR5 responses, Vi capsule synthesis that avoids detection of lipopolysaccharide and other membrane components. Investigations into genomic sequencing of typhoid toxin are still underway; studies show that it contains two types of toxins: cytolethal distending-like and pertussis-like. These toxins show promising results with respect to vaccine production as well as diagnostic tests[56].

Risk factors for transmission include the following: consumption of water and ice contaminated with the organism; flooding; consumption of food and drinks bought from street vendors[9]; consumption of fruits and vegetables, especially raw, from fields fertilised with sewage; household contacts who are sick; improper handwashing and toilet access. An important risk factor found in studies is a higher predisposition to getting Salmonella typhi or paratyphi infection if prior infection by H pylori organism. S. typhi tends to spread more via contaminated water and due to unhygienic practices among members of a household while S. paratyphi more commonly spreads via contaminated food, especially through consumption of infected food from street vendors. In areas where enteric fever is sporadic, the disease is acquired mainly by travel to endemic areas. It can also spread in healthcare workers by handling specimens infected with Salmonella typhi or paratyphi, or by coming in contact with infected patients. Another rare method of transmission is sexual contact, in homosexual males[9]. There is no increase in incidence of enteric fever in immunocompromised hosts, however, the risk of non-typhoidal salmonellosis is increased in them[10].

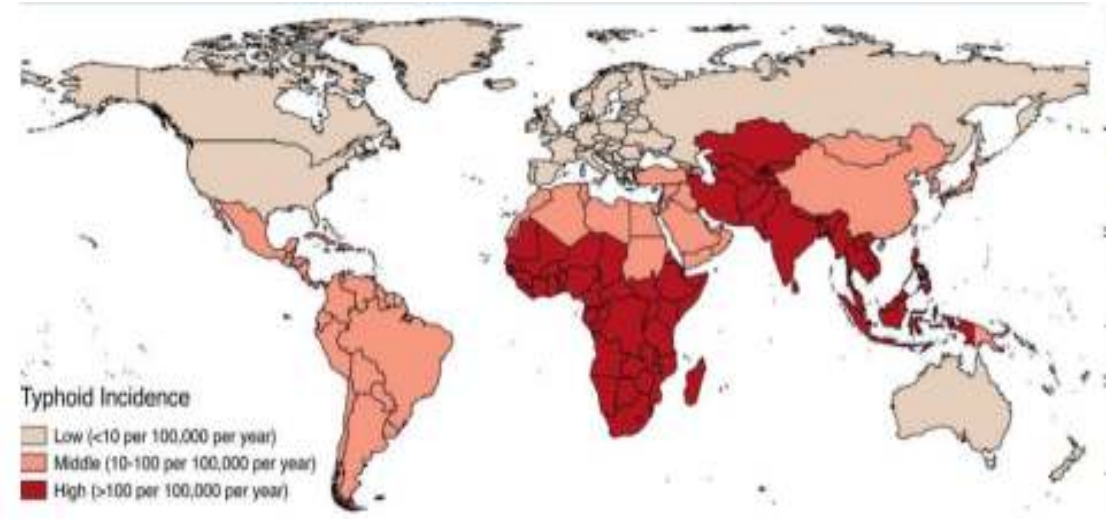


Figure 1: Incidence of enteric fever

Epidemiology:

The incidence of enteric fever is rare in developed nations. It is seen commonly in developing nations – the incidence being highest in South-Central and South-East Asia, followed by rest of Asia, Africa, Latin America, Oceania and then the rest of the world[11]. It is endemic to the Indian population, and amounts to a significant burden in the healthcare system, because although treatable, there are threats faced related to prevention, diagnosis and bacterial resistance[12]. It is a disease, which is more commonly seen in urban compared to rural areas[13]. Young children and adolescents are much more likely to be affected compared to people of older age group. In endemic regions, young children (< 5 years) are maximally affected[14], but the disease may take a more severe form in older children, that is school-going age group, requiring hospitalization. As age advances, Salmonella typhi bactericidal antibodies and anticapsular (Vi) antibodies increase, thus the incidence reduces. In less endemic regions, median age group of patients inflicted by enteric fever is higher compared to endemic regions. The incidence of S. typhi is more than that of S. paratyphi (ratio = 4:1). The most common cause of paratyphoid fever is S. paratyphi

A (~20-50% cases). Vaccination to S. typhi is available, therefore in vaccinated patients – incidence of S. paratyphi is more [15,16]. Before the era of antibiotics, enteric fever used to amount to a significant amount of mortality rate, almost more than 15%. After the advent of antibiotics, the mortality rate is less than 1%.

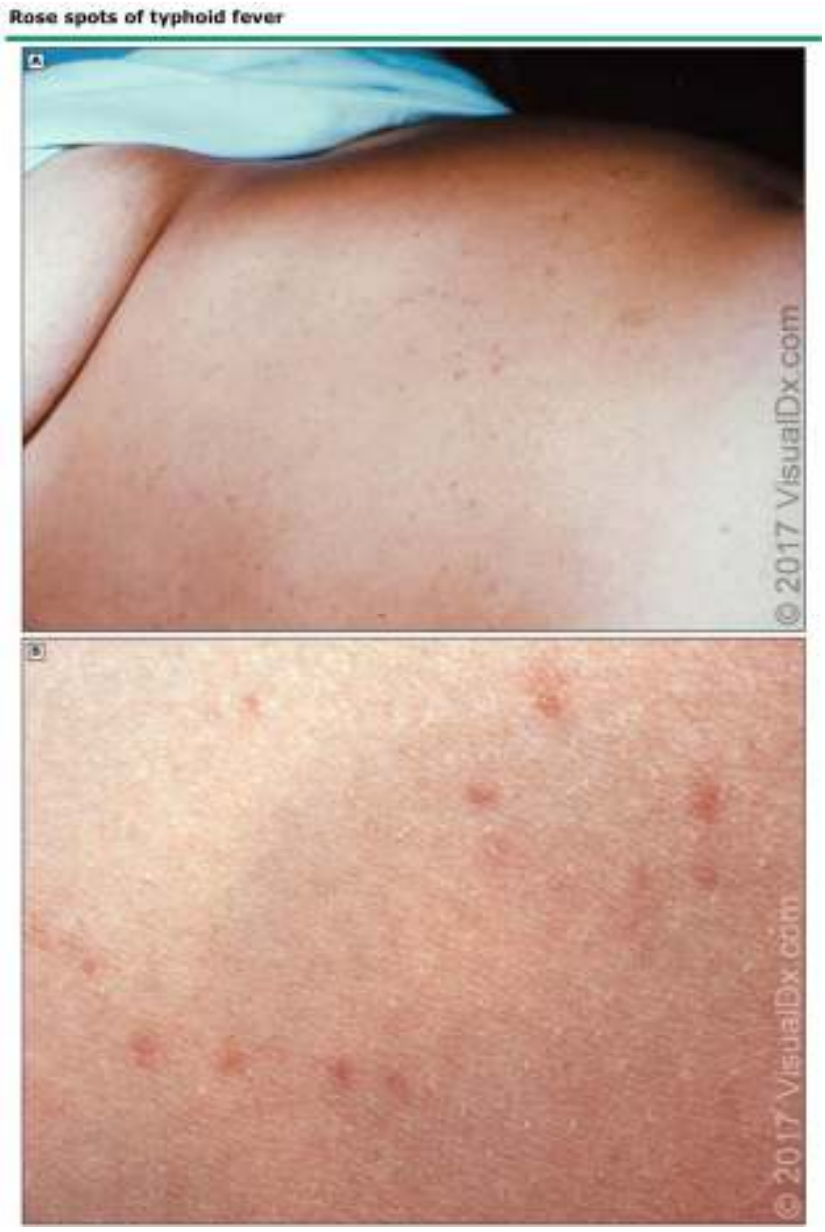


Figure 2: Rose Spots

Clinical features:

The period of incubation of enteric fever is 10-14 days (but can also be 5-21 days). The incubation period can be shorter for paratyphoid fever.

Enteric fever presents with hallmark features of fever, headache and abdominal pain. Patients usually present with prolonged fever, which may have a characteristic stepladder pattern, may be associated with chills and rigors. Fever can persist for upto 4-8 weeks if not treated. It may showcase relative bradycardia. Relative bradycardia, also called temperature – pulse dissociation or Faget's sign is a sign commonly seen in enteric fever, but it is also found in conditions like yellow fever, brucellosis, legionella infection, psittacosis, typhus, Q fever, leptospirosis, patients on beta blockers, lymphomas, drug fever and factitious fever. It refers to absence of rise in pulse in relation to temperature. Usually, with 1 degree Celsius rise in temperature, pulse rises by 10 beats per minute. This does not occur in the above listed conditions, hence it is called relative bradycardia. Other symptoms include – abdominal pain, headache, cough, sweating, myalgia, malaise, arthralgia and gastrointestinal symptoms, like anorexia, nausea, vomiting, diarrhea and/or constipation[17]. S. paratyphi tends to have a milder clinical course compared to S. typhi, although clinically it is difficult to distinguish between the two organisms[18]. Salmonella paratyphi A manifests as fever, jaundice with or without thrombotic features. Salmonella paratyphi B can also have presentation similar to paratyphi A, but can sometimes have presentation similar to non-typhoidal salmonella gastroenteritis. Salmonella paratyphi C, unlike its counterparts, instead of presenting with more local symptoms in the gastrointestinal tract, it comes with generalised manifestations like bacteremia and arthritis. Schistosomia haemotobium coinfection may also produce symptoms of dysuria.

Some signs associated with the disease are coated tongue, hepatosplenomegaly, rose spots and epistaxis. Coated tongue of enteric fever is classically white or yellowish-brown coated, sparing the edges. Rose spots are 1-4 mm pink blanching macules seen over back, chest, abdomen in the second week of illness. They occur during the first week and last only for two to three days. Rose spots are concentrated with bacilli, and culture samples can be taken from the same.

Presentation in neonates and children might differ. It occurs due to vertical transmission during late pregnancy. It may prove to be fatal. Symptoms can start upto 3 days after delivery, presenting with features like fever, diarrhea, vomiting and abdominal bloating. Apart from that, organomegaly, jaundice and seizures can occur. Children younger than 5 years usually present with a milder clinical course, with lesser chance of landing up with severe complications, and therefore can be treated mostly on outpatient basis.

The clinical course of an untreated disease is that, in the first week there is fever; second week has the features of abdominal pain and rose spots; third and fourth week, serious complications like gastrointestinal bleeding and perforation may arise which may progress to secondary bacteremia and peritonitis, eventually leading to septic shock and encephalopathy.

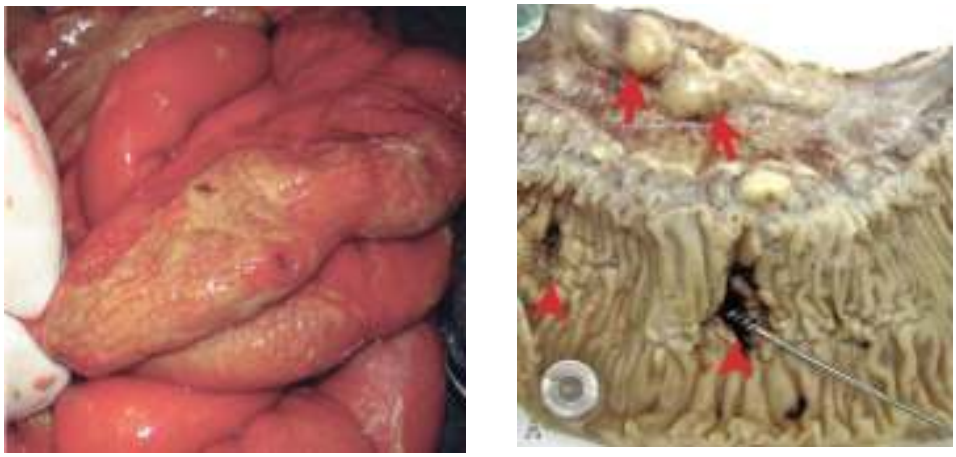


Figure 3: Intestinal perforation in enteric fever patient

Enteric fever can present with a large number of complications, incidence of these complications increases with the following risk factors: time gap between clinical disease and onset of treatment, antibiotic used, virulence of the organism, quantity of the inoculum, whether patient has had past infection by Salmonella typhi or paratyphi, whether patient has been vaccinated, host immunity, HLA typing of the host and chronic use of gastric acid suppressing agents. The complications of enteric fever include gastrointestinal bleeding and perforation – due to Peyer patch hyperplasia and necrosis – which can cause ulceration in the terminal ileum, most commonly, followed by ileocaecal valve, and then ascending followed by transverse colon. The most common site of perforation is the terminal ileum. Typhoid ulcers are usually ovoid and parallel to long axis of the bowel. Other gastrointestinal complications can occur resulting in pancreatitis, hepatitis, jaundice and acute cholecystitis. Neurological complications which can occur with enteric fever are meningitis, neuropsychiatric symptoms – called muttering delirium or coma vigil, Guillain Barre syndrome, neuritis, typhoid encephalopathy and seizures. Muttering delirium or coma vigil refers to a patient in a delirious state, where the patient is conscious but not oriented to time, place and person. He maybe in an oblivious state and also be incontinent. The patient may also have irrelevant speech. He may pick at random imaginary objects, bedclothes, etc. Along with these features, he may have twitching of the muscles of fingers, wrists, lips, tongue – called subsultus tendinum and carphologia. Historically, this complication used to be called ‘typhoid state’. Seizures are a rare complication of enteric fever, and even if they do occur, they are more commonly seen in children and neonates. Hematological complications include disseminated intravascular coagulation, hepatic or splenic abscess and granulomas, hemolytic uremic syndrome and hemophagocytic syndrome. Cardiovascular

complications include endocarditis, pericarditis and myocarditis: toxic myocarditis with fatty infiltration can present as arrhythmias or cardiogenic shock. The pulmonary organs can get affected resulting in severe pneumonia and empyema. Other complications include orchitis, glomerulonephritis, arthritis, osteomyelitis (Sickle cell anemia patients are susceptible to Salmonella typhi osteomyelitis), endophthalmitis, parotitis and even miscarriages. Complications are rare in the present day due to availability of good diagnostic methods and prompt and extensive use of antibiotics. They were more common in the pre-antibiotic era.

Relapse:

Recurrence of infection can occur 2-3 weeks after resolution of fever. Risk of recurrence is 10-25% with chloramphenicol, and 1-6% with newer antibiotics. It is usually the same strain with the same susceptibility profile which causes relapse. Although empirically 3rd generation cephalosporins are preferred drugs due to large scale emergence of fluoroquinolone resistant strains, the risk of relapse in fluoroquinolone sensitive strains treated with fluoroquinolones is much lesser compared to the fluoroquinolone sensitive strains treated with 3rd generation cephalosporins.

Chronic carriers:

2-5 % patients become chronic carriers. They are asymptomatic, and shed the organism in faeces / urine for > 1 year[19]. Chronic carrier state is commonly seen in women, infants, patients with biliary abnormalities and concurrent bladder infection with Schistosoma hematobium. They have an increased risk of gall bladder carcinoma via MAPK and AKT pathways[20], since S. typhi survives in gall bladder by forming biofilms, thus evading gall bladder epithelial cells[21].

An example from history is of the infamous Mary Mallon, or ‘Typhoid Mary’, a New

York cook in the 1900s, who, over a period of 15 years caused 7 outbreaks and infected 200 people.

Microbiology:

Salmonella typhi and paratyphi A, B, C belong to species S. enterica subspecies enterica. They are gram negative bacilli, which are aerobic and facultatively anaerobic. They are destroyed by boiling, chlorination of water and pasteurization of milk. Karl Eberth was the first to discover the agent Salmonella typhi, and called it Bacillus typhosus. The S. enterica species are classified using the Kauffman and White scheme, based on O, ie polysaccharide and H, ie flagellar antigens. Apart from serogrouping and serotyping, S. enterica species are identified using culture and biochemical techniques. The organisms possess 3 antigens – H antigen, which is the flagellar antigen, O antigen, which is the somatic antigen and Vi antigen, which is the surface antigen. Fimbrial antigens may also be present but are not useful in serotyping. H antigen-antibody complexes form loose, large, fluffy clumps. The O antigen-antibody complex forms chalky, granular, compact clumps. Vi stands for virulence factor and it inhibits complement activation, action of phagocytes and bacterial lysis. However, the Vi antigen is not highly immunogenic, and does not produce clinical disease in human volunteers. Due to its poor immunogenicity, it is not useful for diagnosis, and is not employed in Widal test.

All Salmonella species apart from S. typhi and paratyphi A, B, C are called non-typhoidal salmonella. They usually cause inflammatory diarrhea in patients, rarely mimicking enteric fever and causing an invasive disease with full blown bacteremia. Invasive disease is rarely seen in immunocompetent adults, and can be a rare finding in immunocompromised adults or children.

Diagnosis:

Diagnosis of enteric fever poses a challenge due to its large list of differential diagnosis, which includes diseases like malaria, dengue, viral hepatitis, leptospirosis, etc, as well as undue use of antibiotics and lack of optimal facilities and tests for diagnosis[22]. Due to this reason, one cannot rely solely on clinical findings, which tend to overlap between multiple acute febrile illnesses. Therefore, laboratory investigations remain the mainstay in order to label a patient as enteric fever. Diagnosis should be considered in any febrile traveller from an endemic region, like the Indian subcontinent[23], Phillipines, Latin America, etc. In India, it is an important differential diagnosis for any acute febrile illness.

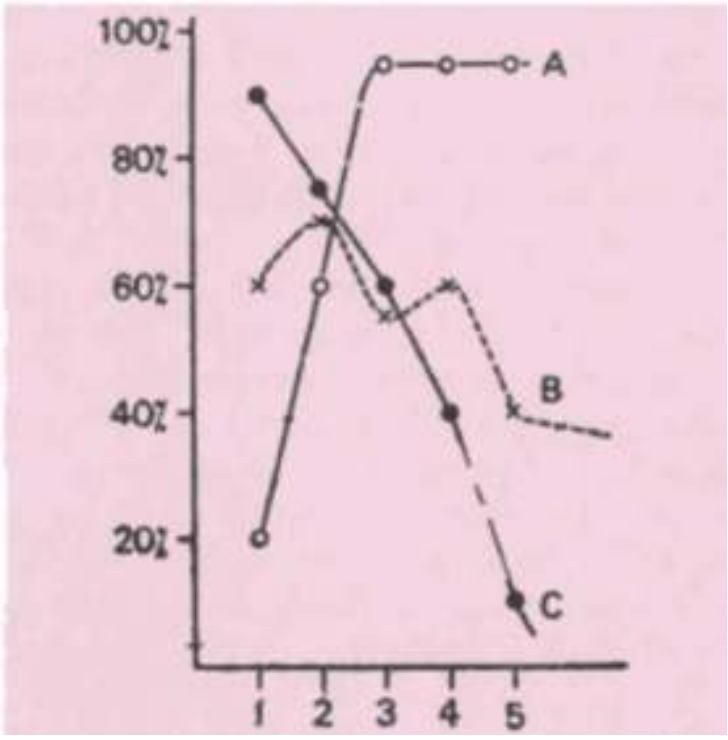


Figure 4: Laboratory Diagnosis of enteric fever

Back in 1884, the first ever organism was cultured by Georg Gaffky. A positive culture is the only confirmative diagnostic test for enteric fever. Organisms can be isolated from blood, bone marrow, stools, rose spots, intestinal secretions, urine, CSF, pus from suppurative lesions and sputum. Intestinal secretions can be cultured via duodenal string test. Blood culture is the most common in practice, although bone marrow culture is the most sensitive. Centrifugation of blood and buffy coat can be done to increase yield in culture[1]. Sensitivity of bone marrow culture is > 80%, blood is 40-80%, stools is ~30%. When intestinal secretions, blood and bone marrow, all are cultured, the sensitivity of all 3 together is more than 90%. The yield of bone marrow culture : blood culture is 5:1 in the first week, and then increases to 150:1 by the third week of the illness. Bone marrow can yield bacteria even after 5 days of initiation of antimicrobial therapy[24]. Stool culture is more sensitive in the third week[1]. While blood is the most commonly used fluid since it is easily obtained for culture, bone marrow culture is impractical in day to day practice, while stool and urine cultures give less yield[25]. Other tests that give a diagnostic clue towards enteric fever but lack both sensitivity and specificity are serological tests like Widal tests[3], rapid serological tests detecting Vi or O:9 antigens[4]. These tests are not useful, especially in endemic regions[26]. The Widal test is a widely used test, but has varied limitations. It detects agglutinating antibodies against O and H antigens of Salmonella typhi, and H antigens of Salmonella paratyphi A and B. The O antigen of S. paratyphi is not used as it shows cross-reactivity with S. typhi. Although used commonly for diagnosis, it is an unreliable test as false negative result can occur in the early weeks of the illness and false positive test result can be obtained in case of past infections, previous exposures or vaccination. There is no universally defined standard cut-off for the Widal test, leaving it to the physician to interpret. Due to these reasons, it should never be used

for diagnosis. ELISA test against polysaccharide Vi Ag maybe useful in detecting carriers, but should not be used for diagnosis[27]. Some rapid diagnostic tests available are Multi-Test Dip-S-Ticks, TUBEX and TyphiDot. The Multi-Test Dip-S-Test is a rapid dipstick test that detects 5 organisms, including S. typhi. It detects antibodies for the following antigens: O, H, Vi – IgM or IgG antibodies. TUBEX, a semiquantitative test, recognises IgM antibodies for O9 antigen. TyphiDot, via enzyme immunoassay, detects IgM/IgG against outer membrane protein of S. typhi[28]. These above tests, especially TUBEX and TyphiDot showcase better diagnostic capability, compared to Widal test. However, neither are they confirmatory nor are they easily available. Hence, it is difficult to rely upon the above, in the current scenario. PCR (Polymerase Chain Reaction) can be performed, flagellin, somatic gene and Vi gene can be detected by the same, but it is not sensitive. Simple hematological tests like a complete blood count are commonly performed tests in any patient presenting with fever. Findings on complete hemogram in enteric fever are anemia, leukopenia (leukocytosis can be present in children, perforation and secondary infection), eosinopenia and thrombocytopenia. These findings are attributable to arrest of myeloid maturation, reduction in the number of erythroblasts and megakaryocytes and enhanced phagocytosis by histiocytes in the bone marrow[5]. Absolute eosinopenia, ie, an eosinophil percentage of 0 on peripheral smear, is a consistent finding seen with enteric fever. Leukocytes are cells which are responsible for inflammation and immune reactions in the body. They consist of neutrophils, T and B lymphocytes, monocytes, natural killer (NK) cells, eosinophils and basophils. Eosinophils are chemotactic cells, which respond to a specific chemotactic agent called eotaxin. Eosinophils are raised, ie eosinophilia is seen in infections like helminthic infections, bronchial asthma, cutaneous allergic reactions and hypersensitivity reactions.

However, eosinopenia is a feature of acute bacterial infections, especially a consistent finding in enteric fever. Eosinophil levels are regulated by glucocorticoids and adrenaline. In acute phase of the disease, there is rapid sequestration of circulating eosinophils in response to chemotactic factors like c5a and fibrin [6,7]. Absolute eosinopenia is not specific for enteric fever and may occur in other bacterial infections[7], but is a consistent finding seen in enteric fever which acts as a marker or clue to diagnose it. It has a high negative predictive value, therefore a high eosinophil count may help the clinician rule out enteric fever and think of another diagnosis. Although blood culture is confirmatory, it is a time-consuming process. Moreover, in a country like India, there simply may not be resources available to culture the bacterium[30], and even if available, may not fulfil quality requirements in order to provide good yield of bacteria. Therefore, to fill the gap between the day of presentation of patient and the day of confirmatory diagnosis, which may take upto as long as 5 days in certain institutions, or sometimes, in absence of confirmatory diagnosis, a simple blood test, which is eosinophil count, is indispensable, and can help in diagnosing the patient fast as well as starting early antibiotic therapy, which is crucial to prevent complications. Other tests like liver function tests, renal function tests, serum electrolytes, amylase, lipase can be used to assess for other clinical manifestations and complications. Histopathological specimens reveal Peyer patch and mesenteric lymph node enlargement, containing infiltration by mononuclear cells, macrophages and lymphocytes. Eventually, necrosis occurs along with mixed cellular infiltration, leading to ulceration and sloughing off of mucosa, clinically manifesting as intestinal bleed or perforation.

Antibiotic resistance:

In 1948, Chloramphenicol was discovered as an antibiotic effective against enteric fever. This was discovered by Theodore Woodward, who belonged to the University of Maryland. Upto 1972, chloramphenicol became a widely used drug for the combat of this disease, which had previously resulted in a high amount of morbidity and mortality. In 1972, some reports emerged of chloramphenicol resistance, however, they were isolated strains. There came to effect a large force epidemic of chloramphenicol resistance in Mexico in the early 1970s, eventually followed by similar epidemics in Peru and Chile, in which typhoidal Salmonella contained incompatibility group H1 R factor plasmids, putting an end to extensive use of chloramphenicol and giving rise to the need for newer drugs[36]. Research showed that drugs like ampicillin and trimethoprim-sulfamethoxazole could replace chloramphenicol as the primary drug to treat enteric fever. MDR (Multi drug resistant) strains have resistance encoded by plasmids to chloramphenicol, ampicillin and trimethoprim-sulfamethoxazole[31]. These MDR isolates started appearing in South and Southeast Asia in late 1980s and 1990s. Some MDR isolates have been classified as 'clone H58' strains via genome sequencing, and this particular genome has spread throughout Asia and Africa[32]. Clone H58 strains carry resistance both via plasmids as well as integrated within the chromosomes. Travellers from the Indian Subcontinent are more likely to be infected with MDR strains[33]. The emergence of MDR strains led to the extensive use of fluoroquinolones, sometimes to the extent of abuse where they were used either suboptimally or for a shorter duration than recommended. Although excellent drugs, they came to be utilized so often, that it led to eventual development of resistance. In the Indian subcontinent, South Asia and South Africa, decreased susceptibility to ciprofloxacin (DSC) / ciprofloxacin resistant strains have started to

appear[34]. These strains have to be tackled by drugs like 3rd generation cephalosporins. XDR (extensively drug resistant) strains are exclusively seen in Pakistan and Iraq. It is called the 'Sindh strain'. The resistance is integrated into the chromosomes, as well as plasmids. They are resistant to – chloramphenicol, ampicillin, trimethoprim-sulfamethoxazole, ciprofloxacin and 3rd generation cephalosporins, and sensitive to – carbapenems and azithromycin[35].

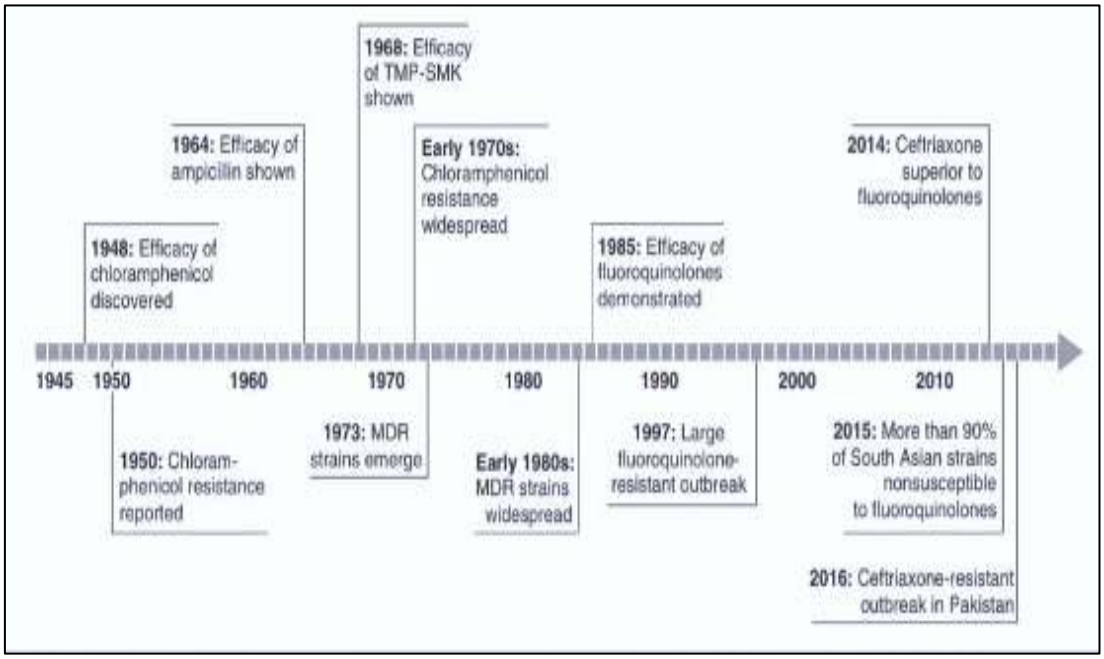


Figure 5: Antibiotic Resistance

Treatment:

Patient should be empirically started on injection ceftriaxone 2 g/day IV for 10-14 days, or tablet azithromycin 1 g/day orally for 5 days. Azithromycin is an excellent drug to treat MDR and fluoroquinolone resistant strains[37], there is very little evidence of resistance against it. In patients from Pakistan / Iraq where XDR strains are seen, one can start empirical therapy with meropenem, and deescalate once blood culture and sensitivity profile is available. It is essential to change the antibiotic of choice according to the drug sensitivity pattern, as soon as it is available, in order to

prevent further induction of antibiotic resistance[38]. If the strain is fully susceptible, the first line antibiotics include ciprofloxacin 500 mg twice a day orally or 400 mg 12th hourly IV for 5-7 days or azithromycin 1 g/day orally for 5 days. Alternatives that can be used are amoxicillin 1 g three times a day orally or 2 g 6th hourly IV for 14 days or chloramphenicol 25 mg/kg three times a day orally or IV for 14-21 days or trimethoprim – sulfamethoxazole 160/800 mg twice a day orally for 7-14 days. First line drugs like ceftriaxone 2 g/day IV for 10-14 days or tab azithromycin 1 g/day orally for 5 days can be given for multidrug resistant strains. Alternative drugs include ciprofloxacin 500 mg twice a day orally or 400 mg 12th hourly IV for 5-14 days. Quinolone resistant isolates should be treated with ceftriaxone 2 g/day IV for 10-14 days or azithromycin 1 g/day orally for 5 days. Other options for XDR strains include high dose ciprofloxacin – 750 mg twice a day orally or 400 mg 8th hourly IV for 10-14 days. In case of severe infections adjunctive steroids can be added – injection dexamethasone initial dose of 3 mg/kg IV followed by 8 doses of 1 mg/kg IV 6th hourly[39]. Chronic carriers must be treated with 4 weeks of ciprofloxacin or other fluoroquinolones[40]. Usually in relapse case, infection is by the same strain with usually the same susceptibility pattern, therefore, the same treatment should be initiated. In cases of gastrointestinal bleed or perforation, patient should be started on antibiotics, and appropriate surgical intervention should be planned[41].

Prevention:

Prevention, as with any type of disease, is always better than cure. The prevention of enteric fever is easy and serves the purpose of not only eliminating this food and water-borne disease, it also helps in tackling various others like viral hepatitis: A and E, infections by E. Coli, non-typhoidal Salmonella, Shigella, Entamoeba histolytica, Giardia, and many viruses. At a household level, simple

measures like avoiding contaminated food and water, practicing hygienic toilet practices, filtration or boiling of water before consumption, washing raw and uncooked fruits and vegetables well before using and hand washing before touching food can help in prevention of enteric fever as the main route of spread if faeco-oral[41]. It is important to avoid consumption of food prepared by street vendors, especially when signs of unhygienic practices are present like lack of handwashing, lack of using disposable gloves, abundance of houseflies near the food preparation and consumption area. School going children are very susceptible to this infection, their risk of exposure increases with more interaction with other children, especially practices like sharing tiffin boxes, water bottles, etc. Therefore, the goal should be to educate children and adolescents in order to combat this disease. Basic hygienic practices can be taught in school like handwashing before meals and after using toilets. At the community level, good sewage treatment and waste disposal facilities can help. It is important for the local government to invest in as well as maintain these, so as to provide mass protection against all diseases transmitted via food and water. Specific protection against enteric fever is via immunization. Vaccines available for use are Ty21a and ViCPS vaccine[42]. Ty21a is a live attenuated, oral vaccine with doses given on the following days: day 1, day 2, day 5 and day 7; revaccination with full 4 doses to be done every 5 years. The minimum age requirement for vaccination is 6 years. ViCPS is a Vi polysaccharide vaccine, in which the Vi antigen has been purified, in which only one dose is given. Booster is given every 2 years. Minimum age requirement for vaccination is 2 years. The indication for vaccination is travel to endemic areas, ideally the vaccination regimen should be completed 7 days before the date of travel[43]. Vaccination is not recommended for adults living in endemic areas or after being exposed in a common

source outbreak[44]. Some other licensed vaccines are Vi-TT typhoid conjugate vaccines (TCV). These are vaccines that have linkage between tetanus toxoid (TT) and Vi polysaccharide antigen. Examples of these vaccines are Typbar-TCV, Typhibev, PedaTyph and ZyVac-TCV. Another vaccine, a parenteral heat-inactivated vaccine called Typhoid vaccine was used in the United States but was discontinued after 2001[43]. Vi-antigen based vaccines are effective against S. typhi, which contains the Vi antigen while they are not effective against S. paratyphi, which lack this antigen. However, live attenuated vaccines like Ty21a show some cross-reactivity with S. paratyphi due to cross reaction with O12 antigen as well as cell-mediated immunity.

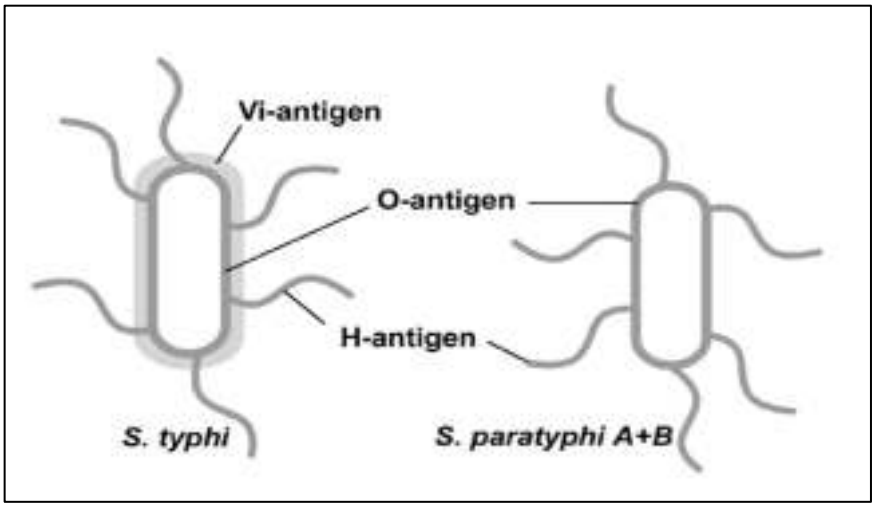


Figure 6: Morphology of Salmonella typhi and paratyphi

Relevant studies:

In the study done by Khosla SN et al, 'haematological profile in typhoid fever', published in 1995 in the Tropical Doctrine - 20 culture positive patients with typhoid fever were studied. Changes seen were anaemia, leukopenia, eosinopenia, thrombocytopenia and sub-clinical disseminated intravascular coagulation. The bone marrow was also studied. It showed arrest in myeloid maturation, decrease in the

number of erythroblasts and megakaryocytes with increased phagocytosis by histiocytes[5].

In the study conducted by S. Jog et al, published in the 'Journal of association of Physicians of India: Volume 56', in Mumbai, from the period of January 2003 to September 2005, the laboratory and clinical profile of culture proven enteric fever cases was studied. Out of 119 culture proven enteric fever cases, absolute eosinopenia was observed in 76.9% patients. It was deduced that an absolute eosinophil count of 0 % could possibly be a feasible and significant marker of enteric fever[45].

In the retrospective study done by Ramaswamy Ganesh et al, published in the Indian journal of Paediatrics, in Chennai, from July 2005 to June 2008, 316 total children diagnosed with typhoid fever (culture positive) were analysed, out of which eosinopenia was seen in 72 % of the culture proven enteric cases, which was statistically significant[46].

In the study done by Aliasgar Lokhandwala et al**,** published in the Ibnosina Journal of Medicine and Biomedical Sciences, a retrospective study was done on a total of 51 patients with confirmed diagnosis of enteric fever in a tertiary care hospital in UAE, from the period of July 2002 to April 2010. Out of these, 29 had positive blood culture while the remaining 22 patients had a significant positive Widal test. Thirty-seven patients out of 51 had an absolute eosinophil count of zero (73%). The result established that significant eosinopenia was present in all enteric fever patients and eosinophil count of zero was almost diagnostic of enteric fever in the right clinical setting. Hence, it was proved that absolute eosinopenia is an important finding that should help timely diagnosis and early treatment initiation of enteric fever[6].

The API recommendations for the management of typhoid fever, published in the 'Journal of association of physicians of India, Volume 63', November 2015,

written by Rajesh Upadhyay et al states that eosinopenia is an important and consistent finding seen in typhoid fever, especially in the first week of illness[47].

In the study done by Hetal N Jeeyani et al, 'Enteric Fever in Children - Clinical Profile, Sensitivity Patterns and Response to Antimicrobials' in 2015, published in the GCSMC Journal of Medical Sciences, absolute eosinopenia was seen in 72.5 % patients included in the study, which can be used as a pointer towards diagnosis of enteric fever[48].

In the study done by Matono et al in South Asia, between 2006 to 2015, 'Role of classic signs as diagnostic predictors for enteric fever among returned travellers: Relative bradycardia and eosinopenia', published in 'PLOS one journal', 63% of cases of enteric fever had absolute eosinopenia, case definition being culture proven enteric fever while only 38% of the controls had eosinopenia[49].

In the study done by Ghosh T et al, 'A Hospital Based Cross-Sectional Study on Enteric Fever – Evolving Clinical Features, Basic Laboratory Parameters and Serological Profiles' published in the IOSR 'Journal of Dental and Medical Sciences (IOSR-JDMS)' in December 2016, 170 patients of enteric fever were examined. The case definition was either culture positive or serology. 71.76% of the patients had absolute eosinopenia on admission[50]

In the study done by Farmakiotis et al, 'Typhoid Fever in an Inner City Hospital: A 5-Year Retrospective Review' published in the Journal of Travel Medicine, studied febrile travellers over a 5 year period, ie from 2006-2010. They observed that a febrile traveller returning from the Indian subcontinent, is more likely to have enteric fever if he has absolute eosinopenia and elevated liver enzymes, provided malaria has been ruled out[51].

In the study done by Malik et al in Pakistan, 'Eosinopenia in Patients With Typhoid Fever: A Case-Control Study' published in the Cureus Journal in September 2020, they inferred that out of 100 patients of enteric fever, 59 had eosinopenia while 41 did not[7].

In the study by Suwarto et al, 'Laboratory parameters for predicting Salmonella bacteraemia: a prospective cohort study' published in the Sage Journal, examined patients in Indonesia between 2014-2016. They found a high percentage of absolute eosinopenia, ie 82.1% in culture positive enteric fever patients[52].

In the study done by Kontoni VS et al 'Paediatric Enteric Fever in Brussels: a case series over 16 years' in July 2021, absolute eosinopenia was observed in 69% of the patients[53].

In the study by Chhabra R et al, 'Enteric Fever In India–Clinico-hematological Profile, Antimicrobial Sensitivity And Response' publish in the British Medical Journal, patients were observed in Gurgaon, India from 2010-2013, and 154 patients with positive culture for Salmonella typhi or paratyphi were included in the study. Absolute eosinopenia was observed in 81.8% of these cases[54].

In the study done by Behera JR et al, 'Clinical and Laboratory Profile of Enteric Fever in Children From a Tertiary Care Centre in Odisha, Eastern India' published in Cureus Journal in 2021, eosinopenia was a finding in 58.93% of the patients[55]

METHODOLOGY

Study design:

A one year hospital based cross-sectional study.

Period of study:

1st January 2020 to 31st December 2020

Source of the data:

Patients admitted in the wards and visiting the OPD of KLES Dr. Prabhakar Kore Hospital, Belagavi, a tertiary care hospital in Karnataka, India, satisfying the inclusion criteria.

Sample size: 45

This was calculated by –

The minimum sample size formula based on prevalence is

$$n = \frac{z_\alpha{}^2 P(1-P)}{d^2}$$

where P is taken as the percentage of prevalence and d is taken as the percentage likely difference in the prevalence.

z_α is linked with the level of significance. For 5% level of the significance $z_\alpha = 1.96$.

Ref:

With P = 58% and d = 25% of P = 14.5%, the sample size is 45.

Inclusion criteria:

Patients diagnosed as enteric fever by a positive blood culture for S. typhi/paratyphi or showing rising Widal titres.

Exclusion criteria:

Clinically suspected enteric fever with no laboratory evidence

Immunocompromised individuals

Co-existing infections

Bacteremia due to other causes

Ethical Consideration:

Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants who signed the informed consent were included in the study. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of study participants was maintained.

Data collection tool:

All the relevant parameters were documented in a structured study proforma.

Material and methods:

All patients with suspected enteric fever, willing to participate in the study were included.

Their detailed history and complete examination was done according to the proforma attached. Their written informed consent was taken in their vernacular language.

The following investigations were sent for the patient included in the study:

1. Complete blood count including differential blood count and absolute eosinophil count
2. Blood cultures
3. Widal tests at 1 week and after 10 days, if necessary.

The blood investigations were collected from the patient via venepuncture. The diagnosis of enteric fever was done based on the laboratory investigations i.e a positive blood culture for Salmonella typhi or paratyphi A/B/C OR a widal test showing rising titres when done at 1 week and thereafter repeated after 10 days.

The blood culture was done using automated blood culture technique with BACTEC method. Widal test was performed using latex / tube agglutination method. Data was analysed and tabulated. Eosinophil count was correlated with a diagnosed enteric fever case.

Statistical analysis:

Since the study is of observational study the plan of analysis was as follows.

For the continuous quantitative variables mean and standard deviation were calculated. For the purpose of comparison if the data is divided into two groups with respect to certain qualitative characteristic, the continuous variables were compared using suitable tools of statistics like student's unpaired t test. The pre and post treatment measures were compared using student's paired t test.

Discrete variables were represented by median.

The categorical data was expressed in terms of rates, ratios and percentages. The association between the outcome, clinical and demographic characteristics was tested using Chi-square test, test of proportion or Fisher's exact test.

For discrete variables nonparametric tests were used.

Apart from the above suitable tools like ANOVA, correlation, regression etc., were used according to the need.

Suitable graphs were used to depict the comparison.

For all the tests the value of p less than 5% (0.05) was considered significant.

RESULTS

This study was done on 45 patients, in KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, Karnataka, India.

Figure 7: Age Distribution

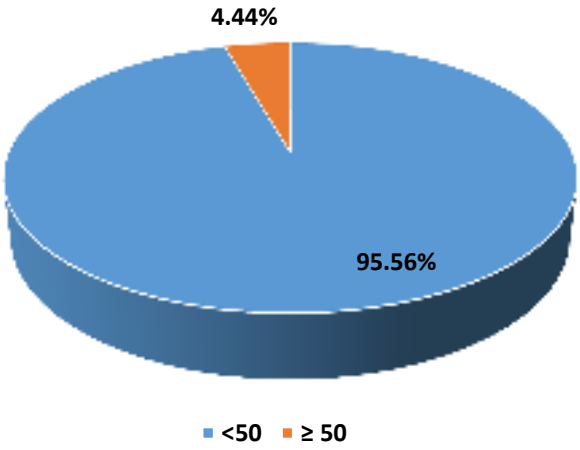


Table 1: Mean, Standard Deviation, Maximum and Minimum Ages of the patients

	MEAN	S.D.	MINIMUM	MAXIMUM
AGE	25.47	10.22	15	65

Table 2: Age Distribution of the patients

AGE (YEARS)	NUMBER	PERCENTAGE
<50	43	95.56%
≥ 50	2	4.44%
TOTAL	45	100.00%

Out of the 45 patients, the mean age of distribution was 25.47, with a standard deviation of 10.22. The minimum age was 15 years and maximum age was 65 years. The age distribution of the study is depicted in the above figure. Thus, majority of the subjects (95.56%) were below the age of 50 years.

Figure 8: Gender Distribution

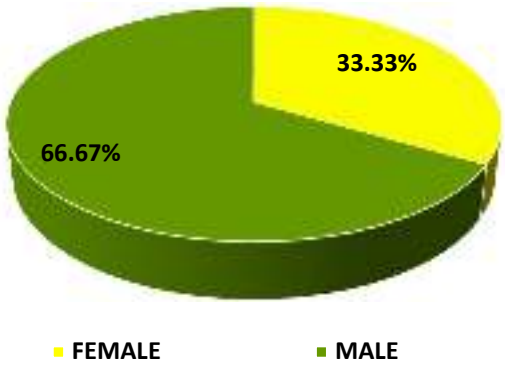


Table 3: Gender distribution of the patients

GENDER	NUMBER	PERCENTAGE
MALE	30	66.67%
FEMALE	15	33.33%
TOTAL	45	100.00%

In the total number of subjects studied, males made up the majority. As shown in the figure, the gender distribution of the study was 66.67% males and 33.33% females.

Table 4: Clinical presentation of the patients: Fever

FEVER	NUMBER	PERCENTAGE
YES	45	100.00%
NO	0	0.00%
TOTAL	45	100.00%

Out of all the subjects analyzed, 100% had complaints of fever on admission.

Figure 9: Distribution of Abdominal Pain

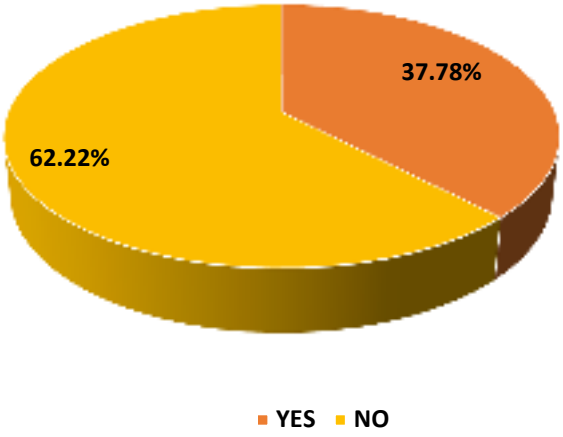


Table 5: Clinical presentation of the patients: Abdominal pain

ABDOMINAL PAIN	NUMBER	PERCENTAGE
YES	17	37.78%
NO	28	62.22%
TOTAL	45	100.00%

However, in contrast to fever, abdominal pain was present in 37.78% of the patients, and absent in 62.22% of the patients, as summarized above.

Table 6: Clinical presentation of the patients: Other complaints

OTHER COMPLAINTS	NUMBER	PERCENTAGE
HEADACHE	10	22.22%
NAUSEA / VOMITING	8	17.77%
LOOSE STOOLS	7	15.55%
COUGH	6	13.33%
CONSTIPATION	5	11.11%
BODYACHE	5	11.11%
GENERALISED WEAKNESS / FATIGUE	4	8.88%
MALENA	2	4.44%
GIDDINESS	1	2.22%
JAUNDICE	1	2.22%
COLD	1	2.22%
ALTERED SENSORIUM	1	2.22%

Headache was one of the complaints in 22.22% patients, while nausea and vomiting was present in 17.77% patients. Loose stools occurred in 15.55% patients, cough in 13.33%, constipation in 11.11% and bodyache in 11.11%. Generalised weakness and fatigue occurred in 8.88% of the patients, while malena was a complaint in 4.44% patients. The complaints of giddiness, jaundice, cold and altered sensorium occurred in 1 patient each, ie 2.22%.

Table 7: Clinical presentation of the patients: Pulse Rate

PULSE RATE	NUMBER	PERCENTAGE
RELATIVE BRADYCARDIA	10	22.22%
BRADYCARDIA	0	0.00%
TACHYCARDIA	4	8.88%
NORMAL PULSE RATE	31	68.88%
TOTAL	45	100.00%

Out of the 45 patients, 22.22% (n=10) had relative bradycardia, ie, temperature-pulse dissociation while 8.88% had tachycardia. None of the patients had bradycardia. The rest of the patients had normal pulse rate, ie between 60-100 beats per minute.

Table 8: Clinical presentation of the patients: Organomegaly

ORGANOMEGALY	NUMBER	PERCENTAGE
HEPATOMEGALY	6	13.33%
SPLENOMEGALY	0	0.00%
HEPATOSPLENOMEGALY	10	22.22%
ORGANOMEGALY	6+0+10=16	35.55%
NO ORGANOMEGALY	29	64.44%
TOTAL	45	100.00%

13.33% patients had hepatomegaly, none had isolated splenomegaly and both hepatosplenomegaly were present in 22.22% patients. So, a total of 16 patients, ie 35.55% showcased organomegaly. 29 patients, ie 64.44% did not show evidence of organomegaly on examination.

Figure 10: Hemoglobin (g/dl)

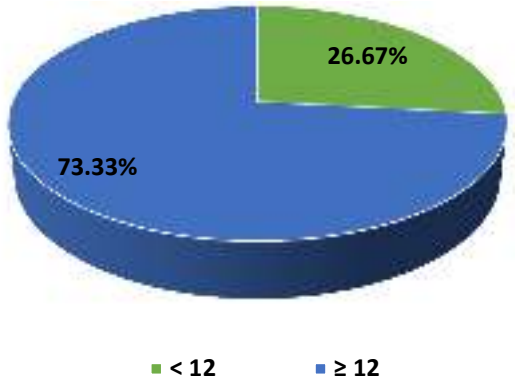


Table 9: Mean, Standard deviation, Minimum and Maximum hemoglobin levels in g/dl among the patients.

	MEAN	S.D.	MINIMUM	MAXIMUM
HEMOGLOBIN	13.52	1.66	9.5	17

Table 10: Presence of Anemia among the patients.

HEMOGLOBIN	NUMBER	PERCENTAGE
< 12	12	26.67%
≥ 12	33	73.33%
TOTAL	45	100.00%

The statistical analysis of the laboratory investigations revealed the following. The mean hemoglobin (in g/dl) was 13.52 with a standard deviation of 1.66. The minimum hemoglobin was 9.5 g/dl and maximum was 17 g/dl. Anemia, ie Hb < 12 g/dl was present in only 26.67% of the participants, while the rest 73.33% had normal Hb, as depicted in the above figure.

Figure 11: Total Leukocyte Count (cells/mm3)

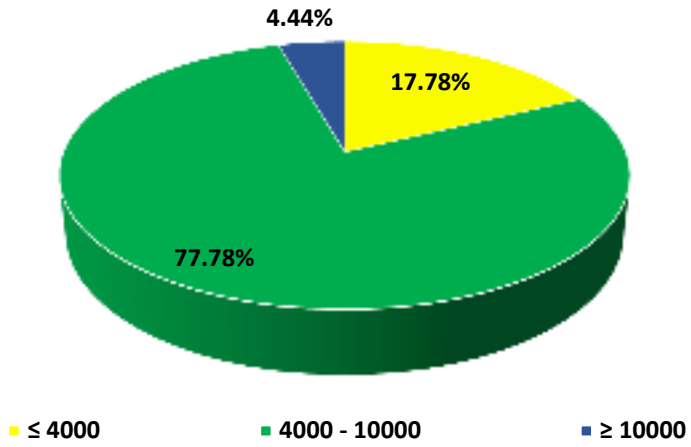


Table 11: Mean, Standard Deviation, Minimum and Maximum Total Count in /mm^3 among the patients

	MEAN	S.D.	MINIMUM	MAXIMUM
TOTAL COUNT	6021.56	2195.85	2200	11200

Table 12: Leukopenia, Leukocytosis and Normal Leukocyte Count among the patients.

TOTAL COUNT	NUMBER	PERCENTAGE
≤ 4000	8	17.78%
4000 – 10000	35	77.78%
≥ 10000	2	4.44%
TOTAL	45	100.00

The total leukocyte count, normal values being 4000-10000 cells/mm3, was performed for every sample. The mean total leukocyte count was 6021.56 cells/mm3, with a standard deviation of 2195.85 cells/mm3. The minimum total leukocyte count was 2200 cells/mm3 while maximum was 11200 cells/mm3 among the 45 participants. The results were in the normal range for 77.78% of the patients, while

17.78% and 4.44% showed leukopenia and leukocytosis respectively, as shown in the figure.

Figure 12: Eosinophil Count (cells/mm3)

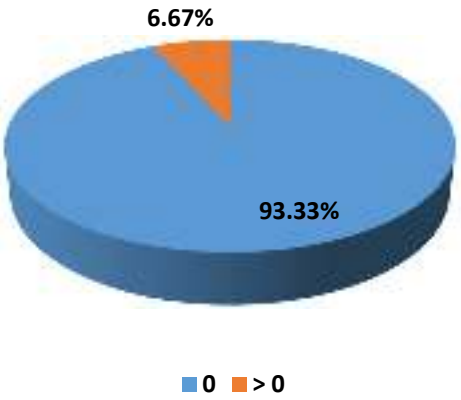


Table 13: Presence of Eosinopenia in the patients

EOSINOPHILS (%)	NUMBER	PERCENTAGE
0	42	93.33%
> 0	3	6.67%
TOTAL	45	100.00%

The absolute eosinophil count was obtained for all the samples. Absolute eosinopenia, ie an absolute eosinophil count of 0 cells/mm3 or an eosinophil percentage of 0 was seen in 42 (93.33%) of the total 45 patients. Only 3 (6.67%) of the patients showed a normal eosinophil count. This is depicted in the figure above.

Figure 13: Platelet count (cells/mm3)

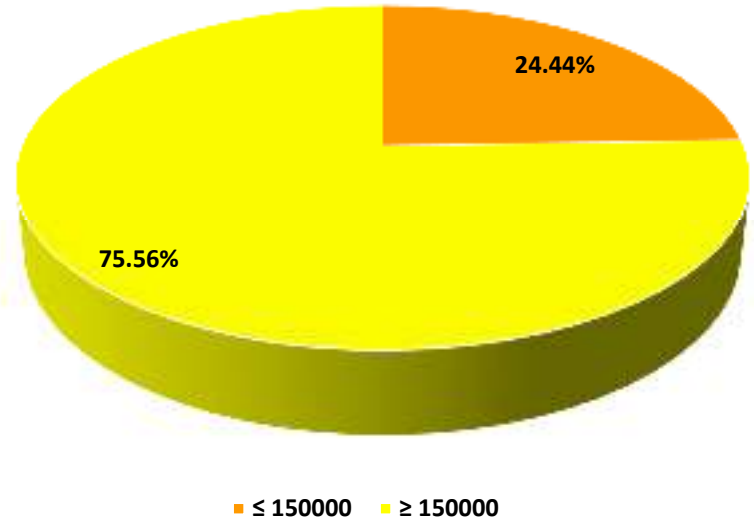


Table 14: Thrombocytopenia and Normal Platelet Count among the patients.

PLATELET COUNT	NUMBER	PERCENTAGE
≤ 150000	11	24.44%
≥ 150000	34	75.56%
TOTAL	45	100.00%

Platelet count, normal being 1,50,000 – 4,50,000 cells/mm3, was done for all 45 of the patients, revealing the following results during analysis. 75.56% of the patients had a normal platelet count, ie, within the range mentioned above. 24.44% patients revealed thrombocytopenia, ie a platelet count of less than 1,50,000 cells/mm3.

Figure 14: Growth in blood culture

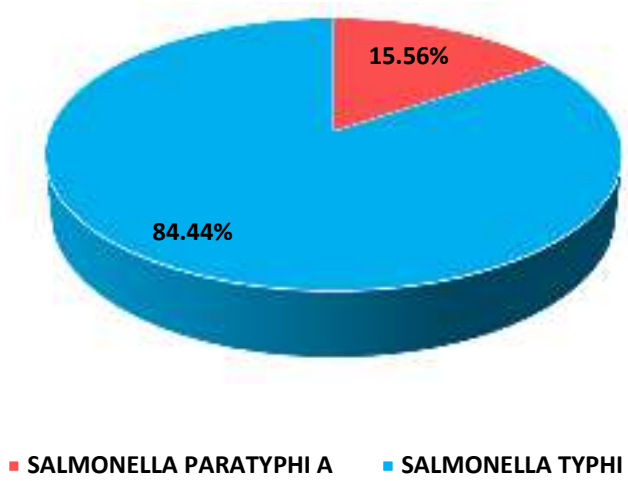


Table 15: Growth in blood culture

GROWTH IN BLOOD CULTURE	NUMBER	PERCENTAGE
SALMONELLA PARATYPHI A	7	15.56%
SALMONELLA TYPHI	38	84.44%
TOTAL	45	100.00%

All the subjects selected for the study had blood culture positive for enteric fever. Growth on blood culture was Salmonella typhi for 38, ie 84.44% patients which the rest 7, ie 15.56% grew Salmonella paratyphi A as summarized in figure above.

Figure 15: Antibiotic sensitivity pattern

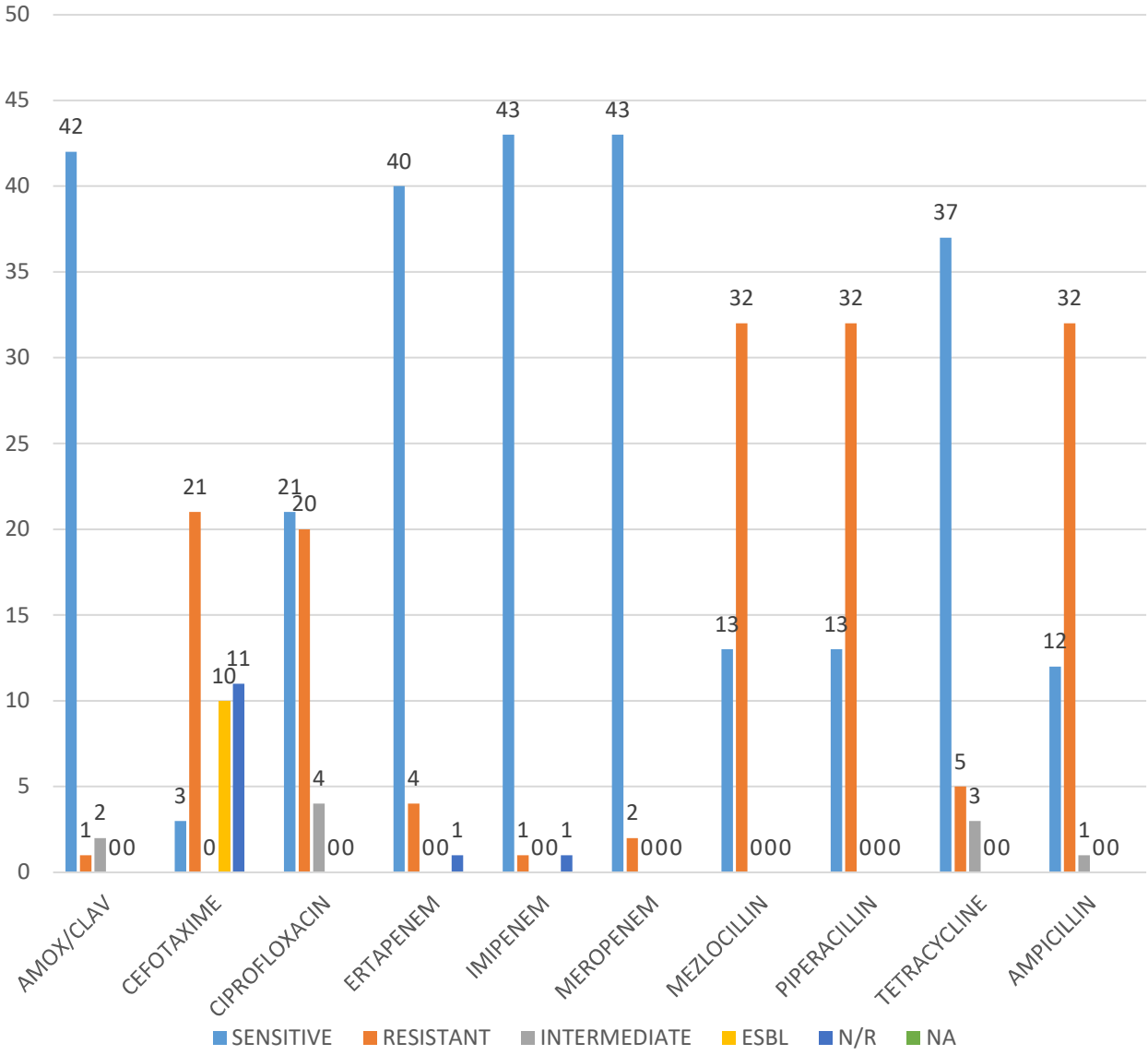
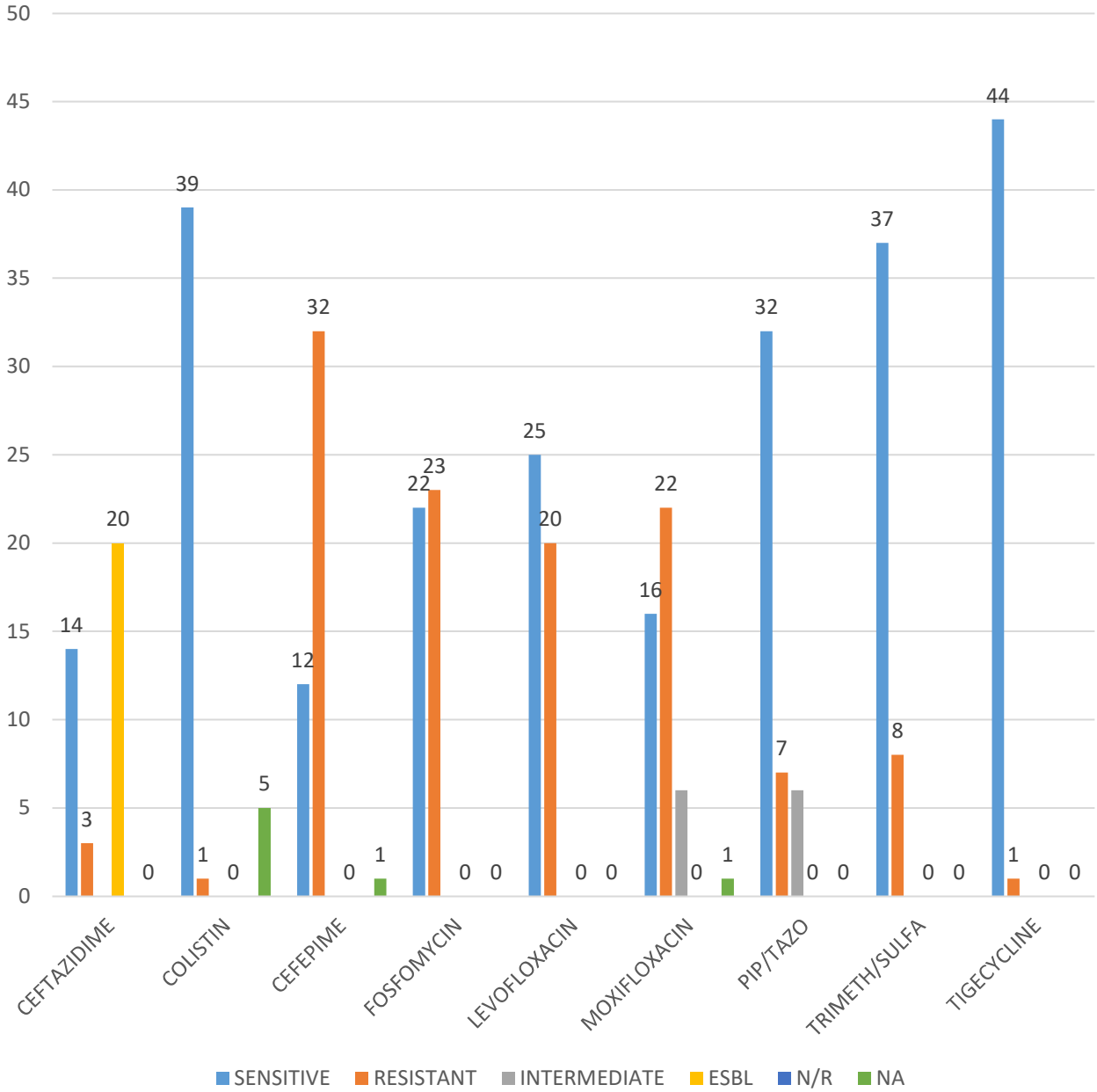


Figure 16: Antibiotic sensitivity pattern (2)



Along with the growth of Salmonella species on blood culture, the laboratory provided us with information about various antibiotics and their sensitivity patterns. It revealed the following results.

Table 16: Sensitivity pattern of antibiotics: Amoxicillin-Clavulanic acid

AMOXICILLIN/CLAVULANIC ACID	NUMBER	PERCENTAGE
SENSITIVE	42	93.33%
RESISTANT	1	2.22%
INTERMEDIATE	2	4.44%
TOTAL	45	100.00%

Out of the samples analyzed, 42 (93.33%) were sensitive to Amoxicillin-Clavulanic acid, while 1 (2.22%) was completely resistant and 2 (4.44%) showed intermediate resistance.

Table 17: Sensitivity pattern of antibiotics: Cefotaxime

CEFOTAXIME	NUMBER	PERCENTAGE
SENSITIVE	3	6.67%
RESISTANT	21	46.67%
ESBL	10	22.22%
N/R	11	24.44%
TOTAL	45	100.00%

3 (6.67%) of the samples were sensitive while 21 (46.67%) were resistant to cefotaxime, while 10 (22.22%) showcased extended spectrum beta lactamases against cefotaxime. Data was not available for 11 (24.44%) of the samples.

Table 18: Sensitivity pattern of antibiotics: Ciprofloxacin

CIPROFLOXACIN	NUMBER	PERCENTAGE
SENSITIVE	21	46.67%
RESISTANT	20	44.44%
INTERMEDIATE	4	8.89%
TOTAL	45	100.00%

21 (46.67%) samples out of the total 45 analyzed were sensitive to ciprofloxacin, while 20 (44.44%) were resistant. 4 (8.89%) showed intermediate resistance to the same.

Table 19: Sensitivity pattern of antibiotics: Ertrapenem

ERTAPENEM	NUMBER	PERCENTAGE
SENSITIVE	40	88.89%
RESISTANT	4	8.89%
N/R	1	2.22%
TOTAL	45	100.00%

The organisms were highly sensitive to the antibiotic ertrapenem, 40 (88.89%) were deemed sensitive while only 4 (8.89%) were resistant to the same. Data was not available for 1 (2.22%) sample.

Table 20: Sensitivity pattern of antibiotics: Imipenem

IMIPENEM	NUMBER	PERCENTAGE
SENSITIVE	43	95.56%
RESISTANT	1	2.22%
N/R	1	2.22%
TOTAL	45	100.00%

Out of the 45 cultures, 43 (95.56%) were sensitive to Imipenem, while only 1 (2.22%) was resistant. Data was not available for 1 (2.22%) sample.

Table 21: Sensitivity pattern of antibiotics: Meropenem

MEROPENEM	NUMBER	PERCENTAGE
SENSITIVE	43	95.56%
RESISTANT	2	4.44%
TOTAL	45	100.00%

Culture sensitivity pattern data showcased sensitivity to meropenem, as high as 43 (95.56%) were sensitive, while only 2 (4.44%) were resistant.

Table 22: Sensitivity pattern of antibiotics: Mezlocillin

MEZLOCILLIN	NUMBER	PERCENTAGE
SENSITIVE	13	28.89%
RESISTANT	32	71.11%
TOTAL	45	100.00%

The antibiotic Mezlocillin was also analyzed, only 13 (28.89%) samples were sensitive whereas 32 (71.11%) were resistant.

Table 23: Sensitivity pattern of antibiotics: Piperacillin

PIPERACILLIN	NUMBER	PERCENTAGE
SENSITIVE	13	28.89%
RESISTANT	32	71.11%
TOTAL	45	100.00%

The antibiotic piperacillin had 13 (28.89%) samples which were sensitive, while 32 (71.11%) were resistant.

Table 24: Sensitivity pattern of antibiotics: Tetracycline

TETRACYCLINE	NUMBER	PERCENTAGE
SENSITIVE	37	82.22%
RESISTANT	5	11.11%
INTERMEDIATE	3	6.67%
TOTAL	45	100.00%

37 (82.22%) samples were sensitive to tetracycline, while 5 (11.11%) were resistant. 3 (6.67%) showed intermediate resistance.

Table 25: Sensitivity pattern of antibiotics: Ampicillin

AMPICILLIN	NUMBER	PERCENTAGE
SENSITIVE	12	26.67%
RESISTANT	32	71.11%
INTERMEDIATE	1	2.22%
TOTAL	45	100.00%

Out of the 45 culture samples analyzed, 12 (26.67%) showed sensitivity towards ampicillin, while 32 (71.11%) were completely resistant. 1 (2.22%) showed intermediate resistance towards the same.

Table 26: Sensitivity pattern of antibiotics: Ceftazidime

CEFTZIDIME	NUMBER	PERCENTAGE
SENSITIVE	14	31.11%
RESISTANT	3	6.67%
ESBL	28	62.22%
TOTAL	45	100.00%

14 (31.11%) of the S. typhi and paratyphi organisms were sensitive to ceftazidime, while 3 (6.67%) were resistant. 28 (62.22%) showcased the presence of extended spectrum beta lactamases, out of the total 45 culture samples.

Table 27: Sensitivity pattern of antibiotics: Colistin

COLISTIN	NUMBER	PERCENTAGE
SENSITIVE	39	86.67%
RESISTANT	1	2.22%
NA	5	11.11%
TOTAL	45	100.00%

39 (86.67%) of the samples were sensitive to colistin, while only 1 (2.22%) was resistant. Data was not available for 5 (11.11%) of the samples.

Table 28: Sensitivity pattern of antibiotics: Cefipime

CEFEPIME	NUMBER	PERCENTAGE
SENSITIVE	12	26.67%
RESISTANT	32	71.11%
NA	1	2.22%
TOTAL	45	100.00%

12 (26.67%) samples were found to be sensitive to cefepime, while 32 (71.11%) were found to be resistant. Data was unavailable for 1 (2.22%) of them.

Table 29: Sensitivity pattern of antibiotics: Fosfomycin

FOSFOMYCIN	NUMBER	PERCENTAGE
SENSITIVE	22	48.89%
RESISTANT	23	51.11%
TOTAL	45	100.00%

22 (48.89%) samples were sensitive to fosfomycin while 23 (51.11%) were resistant, out of the total 45 samples analyzed.

Table 30: Sensitivity pattern of antibiotics: Levofloxacin

LEVOFLOXACIN	NUMBER	PERCENTAGE
SENSITIVE	25	55.56%
RESISTANT	20	44.44%
TOTAL	45	100.00%

25 (55.56%) samples were found to be sensitive to levofloxacin, while 20 (44.44%) were found to be resistant.

Table 31: Sensitivity pattern of antibiotics: Moxifloxacin

MOXIFLOXACIN	NUMBER	PERCENTAGE
SENSITIVE	16	35.56%
RESISTANT	22	48.89%
INTERMEDIATE	6	13.33%
NA	1	2.22%
TOTAL	45	100.00%

Out of the 45 culture samples analyzed, 16 (35.56%) showed sensitivity towards moxifloxacin, while 22 (48.89%) were completely resistant. 6 (13.33%) showed intermediate resistance towards the same. Data was not available for 1 (2.22%) sample.

Table 32: Sensitivity pattern of antibiotics: Piperacillin / Tazobactam

PIPERACILLIN / TAZOBACTAM	NUMBER	PERCENTAGE
SENSITIVE	32	71.11%
RESISTANT	7	15.56%
INTERMEDIATE	6	13.33%
TOTAL	45	100.00%

32 (71.11%) showed sensitivity towards piperacillin / tazobactam, while 7 (15.56%) were completely resistant. 6 (13.33%) showed intermediate resistance towards the same.

Table 33: Sensitivity pattern of antibiotics: Trimethoprim / Sulfamethoxazole

TRIMETHOPRIM / SULFAMETHOXAZOLE	NUMBER	PERCENTAGE
SENSITIVE	37	82.22%
RESISTANT	8	17.78%
TOTAL	45	100.00%

37 (82.22%) samples were found to be sensitive to trimethoprim / sulfamethoxazole, while 8 (17.78%) were found to be resistant.

Table 34: Sensitivity pattern of antibiotics: Tigecycline

TIGECYCLINE	NUMBER	PERCENTAGE
SENSITIVE	44	97.78%
RESISTANT	1	2.22%
TOTAL	45	100.00%

44 (97.78%) of the patients showed sensitivity to tigecycline while 1 (2.22%) showed resistance to the same.

Figure 17: Widal test results

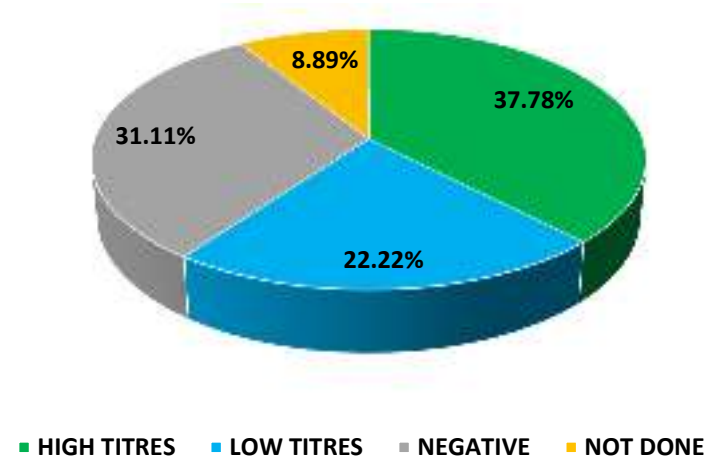


Table 35: Widal Test Results

WIDAL TEST RESULTS	NUMBER	PERCENTAGE
HIGH TITRES (AT LEAST 1 TITRE =/> 1:160)	17	37.78%
LOW TITRES (ALL BELOW 1:160)	10	22.22%
NEGATIVE (ALL 3 NEGATIVE)	14	31.11%
NOT DONE	4	8.89%
TOTAL	45	100.00%

Widal test was performed for 41 out of the 45 patients. It revealed the antibody titres for Salmonella typhi O antigen, Salmonella typhi H antigen and for Salmonella paratyphi AH antigen. High titres (ie at least 1 titre =/> 1:160) were present in 37.78% of the patients, while low titres (ie all below 1:160) were seen in 22.22% of the patients. Widal test was negative for 31.11% of the patients.

Figure 18: Treatment received

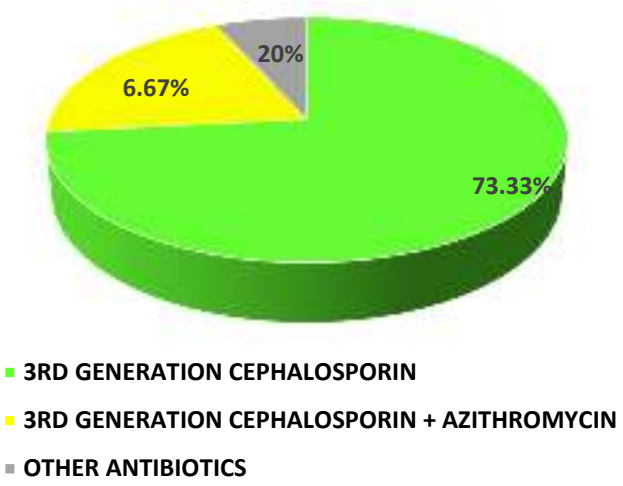


Table 36: Treatment received by the patients.

TREATMENT RECEIVED	NUMBER	PERCENTAGE
3RD GENERATION CEPHALOSPORIN	33	73.33%
3RD GENERATION CEPHALOSPORIN + AZITHROMYCIN	9	20.00%
OTHER ANTIBIOTICS	3	6.67%
TOTAL	45	100.00%

Based on the clinical pattern and laboratory investigations, patients included in this study were started on the required antibiotics. 73.33% received only 3rd generation cephalosporin, which 20% received 3rd generation cephalosporin along with azithromycin. Only 6.67% of the patients received other antibiotics like fluoroquinolones, amoxicillin-clavulanic acid, piperacillin-tazobactam, doxycycline, meropenem, etc.

Based on the above results, there was a significant positive correlation between eosinopenia and enteric fever.

DISCUSSION

This study was a hospital based cross sectional study done in KLES Dr. Prabhakar Kore Hospital and Medical Research Centre in Belagavi, Karnataka. 45 patients with culture proven enteric fever, either admitted in the hospital or on out-patient basis, were studied for a one year period, ie from 1st January 2020 to 31st December 2020. The objective of the study was to prove that eosinopenia is a diagnostic marker of enteric fever.

In our study, 95.56% of the patients were under the age of 50 years, with the mean age being 25.47 years. The youngest patient was 15 years old and the oldest patient was 65 years old. In the study done by S. Jog et al, the mean age was 21.7 years[45]. In the study done by Ishaq U et al, the mean age of the participants in the study was 32.04±16.30 years[7]. The median age was 31 years, ranging from 4 to 56 years in the study done by Matono et al[49]. This reinforces the fact that enteric fever is a disease that affects the younger age group, usually adolescents and children. It is very rare after the age of 50 due to development of antibodies that are bactericidal to Salmonella typhi as well as Vi anticapsular antibodies.

66.67%, ie 30 patients in our study were males while 33.33%, ie 15 patients were females. Males were more commonly affected compared to females in our study. Our findings are keeping up with the various publications in the past, all having male: female ratio of >1. S. Jog et al, in their study, analyzed a total of 119 patients out of which 74 were male and 45 were female[45]. Ganesh et al, in their study of 316 children, found that majority were males, ie 178 while females were 138. The male to female ratio was 1.29:1[46]. The study done by Hetal N. Jeeyani et al, described enteric fever in 62 patients in a tertiary care hospital in India. Out of the 62 subjects, 34 were male and 28 were female[48]. The study by Matono et al, showed that 68% of the

patients were males while the rest were females[49]. In the study by Behera et al, 62.5% of the patients were males and 37.5% were females, male: female ratio being 1.66:1[55].

Fever was a consistent complaint, present in all of our patients. Other varied symptoms displayed by our patients included abdominal pain, which was seen in 37.78% of the patients. Fever was a finding that was present in all the patients on admission in the study done by S. Jog et al. In the same study, abdominal pain was present in 33.6% patients[45]. Fever was present in 100% of the patients while abdominal pain was present in 45.2% patients in the study done by Hetal N. Jeeyani et al[48]. The study by Ghosh et al, where 98 culture positive enteric fever cases were studied, all had a presenting complaint of fever, and the symptom of abdominal pain was present in 68.23% of the patients[50]. The study by Kontoni et al also had fever as a presenting complaint in all the subjects included in the study. In the same study, abdominal pain was a feature seen in 75% of the subjects[53]. In the study by Behara et al, 98.21% of the 112 patients presented with the chief complaint of fever, and 21.43% of these also had abdominal pain as a presenting complaint[55]. The other complaints seen in our study were headache, which was present in 22.22% patients. Nausea and vomiting was present in 17.77% patients. Loose stools were present in 15.55% patients. Cough, constipation and bodyache were present in 13.33%, 11.11% and 11.11% patients respectively. Generalized weakness and fatigue were seen in 8.88% patients. Giddiness, cold, jaundice and altered sensorium were the complaints in 1 patient each, ie 2.22%.

Relative bradycardia, which was once considered a hallmark sign of enteric fever, was seen in about 10 patients, ie 22.22% in our study population. 8.88% had tachycardia. None of the patients had bradycardia. The rest of the patients had normal pulse rate, ie between 60-100 beats per minute. In the study by S. Jog et al, none of

the patients had relative bradycardia[45]. In our study, 13.33% patients had hepatomegaly, while 22.22% had hepatosplenomegaly. None of the patients in our study had isolated splenomegaly. Therefore, organomegaly was present in 35.55% of our patients, while 64.44% did not have evidence of organomegaly. The study by S Jog et al showed hepatosplenomegaly in 12.6% patients. Only hepatomegaly was seen in 15.9% while only splenomegaly was seen in 7.5% patients[45]. In the study by Hetal N. Jeeyani et al, hepatosplenomegaly was present in 22.5% patients, only hepatomegaly was seen in 35.4% patients while only splenomegaly was a finding in 33.8%[48]. The study by Kontoni et al, showed hepatosplenomegaly in 9% of the patients[53]. The study by Behera et al, showed the presence of hepatomegaly in 16.07% of the subjects, and splenomegaly in 8.93% of them[55].

It was interesting to note that the rate of complications was very low in our study group, which throws light on the overall global complication rate. In the study done by Ganesh et al, the rate of complication was 4%[46]. With the advent of antibiotics, the once feared and fatal disease has now become very easy to treat, with very less rate of severity and complications due to prompt treatment with empirical antibiotics as soon as the patient is diagnosed, and then switching to the given specific antibiotic once detailed evaluation of the sensitivity pattern of the organism is available.

Anemia was found on performing a complete hemogram blood test in 26.67% of the patients, while the rest of the study participants had normal hemoglobin levels. Anemia was present in 42.86% of the patients in the study by Behera et al[55]. The total leukocyte count was normal in majority of patients, ie 77.78%, while 17.78% patients had leukopenia and 4.44% had leukocytosis. In the study done by S Jog et al, 85% of the samples analyzed had a normal total leukocyte count. 11.4% of the patients had

leukopenia while leukocytosis was seen in only 4 patients[45]. Hetal N. Jeeyani et al in their study found that a total leukocyte count was seen in 74% patients while 9.6 % patients had leukopenia. Leukocytosis was seen in 16.2 % patients[48]. In the study by Ganesh et al, leukopenia was seen in 8% and leukocytosis in 12%[46]. The study by Suwarto et al showed the presence of leukopenia in 30.8% of the patients[52]. In the study by Kontoni et al, leukopenia was present in 9% patients, leukocytosis in 12% while 79% had a normal leukocyte count[53]. The study by Behera et al showed the presence of leukopenia in 10.71% patients and leukocytosis in 19.64% patients[55]. In our study, we found that thrombocytopenia was seen in 11 patients, ie 24.44% patients. In the study done by S. Jog et al, 25.9% patients had thrombocytopenia[45]. Thrombocytopenia was seen in 11.2 % of the patients in the study by Hetal N. Jeeyani et al. The study by Suwarto et al showed the presence of thrombocytopenia in 35.9% of the patients[52]. In the study by Kontoni et al, 9% of the patients had thrombocytopenia[53]. 14.29% of the patients in the study by Behera et al showed the presence of thrombocytopenia[55].

Absolute eosinopenia, ie an absolute eosinophil count of 0 was seen in 42 out of the total 45 patients studied, ie 93.33% of the total study population. This is in accordance with the study done by Khosla et al, which states that the findings seen on blood picture are anemia, leukopenia, eosinopenia, thrombocytopenia and sub-clinical disseminated intravascular coagulation [5]. Anemia, leukopenia, eosinopenia and thrombocytopenia were also seen in the study done by S Jog et al[45]. Absolute eosinopenia was also observed in the studies done by Rajesh Upadhyay et al[47]. These findings are postulated to be caused by arrest of myeloid maturation, reduced levels of erythroblasts and megakaryocytes as well as increased phagocytosis in the bone marrow. Eosinophils get rapidly sequestered in the spleen in response to C5a and

fibrin, resulting in low levels of eosinophils in the peripheral circulation. In the study conducted by S. Jog et al, the laboratory and clinical profile of culture proven enteric fever cases was studied. Absolute eosinopenia was observed in 76.9% of the patients participating in their study. It was deduced that an absolute eosinophil count of 0 % could possibly be a feasible and significant marker of enteric fever[45]. In the retrospective study done by Ramaswamy Ganesh et al, eosinopenia was seen in 72% of the culture proven enteric cases in children, which was statistically significant[46]. Aliasgar Lokhandwala et al deduced in their study**,** a retrospective study, 73% had an eosinophil count of 0. The result established that significant eosinopenia was present in all enteric fever patients and eosinophil count of zero was almost diagnostic of enteric fever in the right clinical setting. Hence, it was proved that absolute eosinopenia is an important finding that should help timely diagnosis and early treatment initiation of enteric fever[6]. In the study done by Hetal N Jeeyani et al, absolute eosinopenia was seen in 72.5 % patients included in the study[48]. In the study done by Matono et al in South Asia, 63% of cases of enteric fever had absolute eosinopenia, case definition being culture proven enteric fever while only 38% of the controls had eosinopenia[49]. Ghosh T et al performed a study in which 170 patients of enteric fever were examined. The case definition was either culture positive for S. typhi or paratyphi or serology. 71.76% of the patients had absolute eosinopenia on admission[50]. In the study done by Farmakiotis et al, febrile travellers were studied over a 5 year period, ie from 2006-2010. They observed that a febrile traveller returning from the Indian subcontinent, is more likely to have enteric fever if he has absolute eosinopenia and elevated liver enzymes, provided malaria had been ruled out[51]. A Pakistani study, done by Malik et al, the inference made was that out of 100 patients of enteric fever, 59 had eosinopenia while 41 did not[7]. Suwarto et al

published findings of a high percentage of absolute eosinopenia, ie 82.1% in culture positive enteric fever patients[52]. In the study done by Kontoni VS et al in pediatric patients, absolute eosinopenia was observed in 69% of the patients[53]. An Indian study performed by Chhabra R et al from 2010-2013 enrolled 154 patients with positive culture for Salmonella typhi or paratyphi. Absolute eosinopenia was observed in 81.8% of these cases[54]. In the study done by Behera JR et al, eosinopenia was a finding in 58.93% of the patients[55]. The findings in our study are consistent with all the other studies mentioned above, hence proving the eosinopenia is an indispensable tool in order to diagnose this easily treatable acute febrile illness.

All the samples taken in our study were blood culture positive. 84.44 % patients were infected with Salmonella typhi organism while 15.56% were infected with Salmonella paratyphi A. This is keeping in consistency with the 4:1 ratio described in literature regarding the incidence of both the organisms. In the study by S. Jog et al, 61% patients were positive for Salmonella typhi while 39% of the cultures grew Salmonella paratyphi[45]. Hetal N. Jeeyani et al, found in their study that 89.5% of the samples grew Salmonella typhi on blood culture while only 10.5% grew Salmonella paratyphi[48]. In the study by Walia et al, 80.6% cultures were positive for Salmonella typhi and 19.4% for Salmonella paratyphi A[14]. In the study by Suwarto et al, 69.23% of the cultures grew S. typhi organism while 30.77% grew S. paratyphi[52]. In the study by Chhabra et al, 78% of the cultures were positive for Salmonella typhi while 22% were positive for Salmonella paratyphi[54].

Apart from the type of organism grown, culture reports from our microbiology laboratory also provided us with antibiotic sensitivity patterns. In this era of fluoroquinolone resistance, where fluoroquinolones are no longer the preferred choice of therapy for enteric fever, our study found that 21 (46.67%) samples out of

the total 45 analyzed were sensitive to ciprofloxacin, while 20 (44.44%) were resistant. 4 (8.89%) showed intermediate resistance to the same. Walia et al performed a study from 2001 to 2003 in New Delhi, India where they observed a rise in nalidixic acid resistant strains from 56.9% in 2001 to 88.9% in 2003[14]. Rodrigues et al noted that the incidence of nalidixic acid resistant strains has increased from 82% in 2000 to 88% in 2002[15]. In the study by Farmakiotis et al, 76% of the cultures were resistant to nalidixic acid, while all the samples were sensitive to third generation cephalosporins[51]. The drug of choice for MDR strains is 3rd generation cephalosporin in India. Our laboratory provided sensitivity pattern with respect to ceftazidime. It was surprising to note that only 14 out of 45 samples, ie 31.11% were sensitive to ceftazidime, while 3, ie 6.67% were completely resistant. 28 samples, ie 62.22% showed evidence of production of ESBL (Extended Spectrum Beta Lactamase). All the patients with positive blood culture for Salmonella in the study by Behera et al were sensitive to ceftriaxone. In the same study, 80% and 66.66% of the samples were resistant to ciprofloxacin and levofloxacin respectively. Nalidixic acid resistance was showed by all the samples. The samples were 100% sensitive to cotrimoxazole, piperacillin-tazobactam and meropenem[55].

These findings throw light over the fact that, we may be heading towards an era of XDR strains in India, which until now were only reported in Pakistan and Iraq, where the suggested empirical regimen in suspected enteric fever is not 3rd generation cephalosporin, but instead is meropenem. Our laboratory did not provide information about azithromycin, another important antibiotic used to treat MDR strains. Sensitivity to meropenem, imipenem and ertrapenem was 95.56%, 95.56% and 88.89% respectively.

The Widal test was performed for a total of 41 out of 45 samples. It is important to note that Widal test is neither a sensitive nor a specific test. Out of the 41 patients who underwent this serological test, which consisted of 3 components: Salmonella typhi O antigen, Salmonella typhi H antigen and Salmonella paratyphi AH antigen. Only 17 patients, ie 37.78% had a positive Widal test with high titres, ie at least 1 antibody titre was equal to or more than 1:160, 10 patients, ie 22.22% had a positive Widal test but low titres, which means that none of the antibody titres were more than 1:160, and 14 patients, ie 31.11% had a negative Widal test, inspite having positive blood culture for S.typhi or paratyphi. In the study by Suwarto et al, 39 blood Salmonella positive samples were analyzed, out of these, Widal test was positive for 53.1% of the patients while it was negative for 46.9%[52]. This reinforces the fact that the Widal test should not be used for diagnosis of enteric fever, especially in an endemic country like India, because results can be obscure. Evidence based medicine suggests that one must trust reliable tests like blood culture for the diagnosis, while eosinopenia can help guide the physician to order the right test, especially when the clinical scenario suggests the same.

In our study, out of the 45 patients, 73.33% patients received 3rd generation cephalosporin, while 20% received both 3rd generation cephalosporin and azithromycin. 6.67% patients received other antibiotics like co-amoxiclav, piperacillin-tazobactam, meropenem, etc. The findings are similar to what was found in the study by S. Jog et al, ceftriaxone was the commonest antibiotic used to treat these patients, ie 62.1% patients. 13.4% patients received a combination of ceftriaxone and azithromycin. 25% patients received other antibiotics[45]. 86% of the patients received ceftriaxone in the study done by Ganesh et al[46]. In the study by

Behera et al, 94.6% of the patients were treated with 3rd generation cephalosporin, 1.79% were treated with piperacillin-tazobactam and 3.57% with meropenem[55].

All the patients in our study had a favourable outcome, with no mortality. This proves that correct and rapid diagnosis along with the appropriate treatment, with the judicious use of empirical antibiotics in settings where the differential diagnosis of acute febrile illness is enteric fever, will help in prompt recovery of the patient without complications or death. Hence, it is very important to suspect enteric fever in the right setting, and if suspected, laboratory guided diagnosis can be done by simple tests like eosinopenia and specific tests like cultures, and the most appropriate drug should be started without delay for the same. If the above is followed, there is no doubt that a patient of enteric fever will be correctly diagnosed as well as cured.

CONCLUSION

This study suggests that the diagnosis of enteric fever based on clinical features may overlap with other acute febrile illnesses, and the laboratory investigations to confirm the same may be tedious and in resource-less settings may not be feasible. Therefore, eosinopenia is a simple, rapid, inexpensive test, which can be and is usually performed for every patient of enteric fever, irrespective of the setting. The correlation in this study proves that this is a very effective marker to diagnose enteric fever, and the absence of eosinopenia may essentially rule out the same. As members of the health care system, it is our responsibility to ensure that each and every patient diagnosed with enteric fever receives the best diagnosis and treatment in accordance to the resources available to us, keeping in mind the discrepancies in health care system in a developing country like ours.

SUMMARY

Enteric fever, caused by Salmonella typhi or paratyphi is a disease which spreads by the faeco-oral route. It mimics other conditions that present like acute febrile illness, therefore, one cannot solely rely on signs and symptoms to diagnose the same. A positive culture obtained from blood or any other body fluid is the gold standard laboratory test to diagnose enteric fever. However, due to lack of resources, it may not be performed everytime. Even when it is performed, it is time consuming and expensive. A simple test, which is usually done on every patient with fever, is a complete blood count. A finding obtained on the complete blood count is absolute eosinopenia, ie an eosinophil count of 0, consistent with enteric fever. Our study found that 93.33% of patients had absolute eosinopenia, hence proving the importance of this simple yet indispensable investigation. Our study also reinforced the unreliability of the Widal test, a test which is used so frequently but should not be done so, as it misdiagnoses enteric fever. The drug of choice for enteric fever in India is 3rd generation cephalosporin, to which our study showed an alarming amount of resistance. Hence, our study throws light towards the future of antibiotic resistance, where higher antibiotics may be required to combat this disease.

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ANNEXURE I - ETHICAL CLEARANCE.

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed - to - be - University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (India)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 228.

Date: 24/12/2019

To,

REGISTRATION NO: BG0119002
PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"EOSINOPENIA AS A DIAGNOSTIC MARKER FOR ENTERIC FEVER: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY "**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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ANNEXURE II

INFORMED CONSENT

TITLE OF THE RESEARCH STUDY: EOSINOPENIA AS A DIAGNOSTIC MARKER FOR ENTERIC FEVER: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

Principal Investigator:

REGISTRATION NO: BG0119002

Post Graduate Student,

Department of General Medicine,

JNMC, Belgaum.

Guide:

Dr. _____

Professor & Head

Department of General Medicine,

JNMC, Belgaum.

Introduction and Purpose:

Enteric fever is a disease that is endemic to the Indian population and amounts to a significant national and global burden. Enteric fever is caused by Salmonella typhi / paratyphi A,B,C and transmitted via contaminated food and water. It is an easily recognizable and treatable disease, but it is often misdiagnosed. The only way to confirm the diagnosis of enteric fever is via isolation of the organism, most commonly blood, but unfortunately this may require sophisticated resources as well as technical superiority. Serological tests like widal test which are often used to diagnose

enteric fever have a lot of fallacies, especially in an endemic area like ours, with high false positivity rate. Hence, the use of a simple test like eosinophil count, although not specific, is an excellent guide towards diagnosis of enteric fever.

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn.

You may not be benefited by these investigations but you will be part of this study which is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study. If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts / incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

1. Dr. Roopa Bellad, Chairman, J.N.M.C Ethical Committee for Human Research 9480275601	2. Dr. _____ Professor & Head Dept of General Medicine, JNMC, Belgaum. 9448845883

3. REG. NO: BG0119002
Investigator,
PG in General Medicine,
JNMC, Belgaum.
9870018310

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has Been read to me, this consent form and have had all the questions answered.

Participant's name: ……...

Signature / Left thumb impression of the participant:

……...

Name of the legally authorized representative / guardian:

……...

Signature / Left thumb impression: ……...

Name of the Witness: ……...

Signature / Left thumb impression: ……...

Investigator's name and signature: ……...

Date:

Place:

ತಿಳುವಳಿಕೆಯ ಸಮ್ಮತಿ

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಎಂಟ್ರಿಕ್ ಜ್ವರಕ್ಕೆ ಡಯಾಗ್ನೋಸ್ಟಿಕ್ ಮಾರ್ಕರ್ ಆಗಿ ಇಯೊಸಿನೊ ಪೆನಿಯಾ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: –

REGISTRATION NO: BG0119002

ಸ್ನಾತಕೊತ್ತರ ವಿದ್ಯಾರ್ಥಿ,

ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,

ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಮಾರ್ಗದರ್ಶಿ: -

ಡಾ. _____

ಪ್ರೊಫೆಸರ್ ಮತ್ತು ಮುಖ್ಯಸ್ಥ

ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,

ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಪರಿಚಯ ಮತ್ತು ಉದ್ದೇಶ:

ಎಂಟರಿಕ್ ಜ್ವರವು ಭಾರತೀಯ ಜನಸಂಖ್ಯೆಗೆ ಸ್ಥಳೀಯವಾಗಿದೆ ಮತ್ತು ಇದು ಗಮನಾರ್ಹ ರಾಷ್ಟ್ರೀಯ ಮತ್ತು ಜಾಗತಿಕ ಹೊರೆಯಾಗಿದೆ. ಎಂಟರಿಕ್ ಜ್ವರವು ಸಾಲ್ಮೊನೆಲ್ಲಾ ಟೈಫಿ / ಪ್ಯಾರಾಟಿಫಿ ಎ, ಬಿ, ಸಿ ಯಿಂದ ಉಂಟಾಗುತ್ತದೆ ಮತ್ತು ಕಲುಷಿತ ಆಹಾರ ಮತ್ತು ನೀರಿನ ಮೂಲಕ ಹರಡುತ್ತದೆ. ಇದು ಸುಲಭವಾಗಿ ಗುರುತಿಸಬಹುದಾದ ಮತ್ತು ಚಿಕಿತ್ಸೆ ನೀಡಬಹುದಾದ ಕಾಯಿಲೆಯಾಗಿದೆ, ಆದರೆ ಇದನ್ನು ಹೆಚ್ಚಾಗಿ ತಪ್ಪಾಗಿ ನಿರ್ಣಯಿಸಲಾಗುತ್ತದೆ. ಎಂಟರಿಕ್ ಜ್ವರ ರೋಗನಿರ್ಣಯವನ್ನು ದೃಶ್ಚಿಕರಿಸುವ್ ಏಕೈಕ ಮಾರ್ಗವೆಂದರೆ ಜೀವಿಯ ಪ್ರತ್ಯೇಕತೆಯ ಮೂಲಕ, ಸಾಮಾನ್ಯವಾಗಿ ರಕ್ತ, ಆದರೆ ದುರದೃಷ್ಟವಶಾತ್ ಇದಕ್ಕೆ ಅತ್ಯಾಧುನಿಕ ಸಂಪನ್ಮೂಲಗಳು ಮತ್ತು ತಾಂತ್ರಿಕ ಶ್ರೇಷ್ಠತೆಯ ಅಗತ್ಯವಿರುತ್ತದೆ. ಎಂಡರಿಕ್ ಜ್ವರವನ್ನು ಪತ್ತೆಹಚ್ಚಲು ಹೆಚ್ಚಾಗಿ ಬಳಸಲಾಗುವ ಅಗಲ ಪರೀಕ್ಷೆಯಂತಹ ಸೆರೋಲಾಜಿಕಲ್ ಪರೀಕ್ಷೆಗಳು ಬಹಳಷ್ಟು ತಪ್ಪುಗಳನ್ನು ಹೊಂದಿವೆ, ವಿಶೇಷವಾಗಿ ನಮ್ಮಂತಹ ಸ್ಥಳೀಯ ಪ್ರದೇಶದಲ್ಲಿ, ಹೆಚ್ಚಿನ ಸುಳ್ಳು ಸಕಾರಾತ್ಮಕತೆಯೊಂದಿಗೆ. ಆದ್ದರಿಂದ, ಇಯೊಸಿನೊಫಿಲ್ ಎಣಿಕೆಯಂತಹ ಸರಳ ಪರೀಕ್ಷೆಯ ಬಳಕೆಯು ನಿರ್ದಿಷ್ಟವಾಗಿಲ್ಲದಿದ್ದರೂ, ಎಂಟರಿಕ್ ಜ್ವರ ರೋಗನಿರ್ಣಯದ ಅತ್ಯುತ್ತಮ ಮಾರ್ಗದರ್ಶಿಯಾಗಿದೆ.

ವಿಧಾನ:

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ನೀವು ಒಪ್ಪಿದರೆ, ನಿಮಗೆ ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ಕೇಳಲಾಗುತ್ತದೆ ಮತ್ತು ಸಂಬಂಧಿತ ಕ್ಲಿನಿಕಲ್ ಪರೀಕ್ಷೆ ಮತ್ತು ತನಿಖೆಗೆ ಒಳಪಡಿಸಲಾಗುತ್ತದೆ. ಅಗತ್ಯ ತನಿಖೆಗಾಗಿ ನೀವು ರಕ್ತದ ಮಾದರಿಗಳನ್ನು ಸಹ ನೀಡಬೇಕಾಗುತ್ತದೆ.

ಅಪಾಯ ಮತ್ತು ಪ್ರಯೋಜನಗಳು:

ತನಿಖೆಗಾಗಿ ನಿಮ್ಮ ತೋಳಿನಿಂದ ರಕ್ತವನ್ನು ತೆಗೆದುಕೊಳ್ಳುವಾಗ ನೀವು ಪಡೆಯುವ ಏಕೈಕ ಅಪಾಯ ಮತ್ತು ಸಂಭವನೀಯ ಅಸ್ವಸ್ಥತೆ. ಇದು ರಕ್ತವನ್ನು ಸೆಳೆಯುವ ಸ್ಥಳದಲ್ಲಿ ಸ್ವೀಲಿಂಗ್, ನೋವು, ಕೆಂಪು (ವಿರಳವಾಗಿ ಸಂಭವಿಸುತ್ತದೆ) ಗೆ ಕಾರಣವಾಗಬಹುದು.

ಈ ತನಿಖೆಯಿಂದ ನಿಮಗೆ ಯಾವುದೇ ಪ್ರಯೋಜನವಾಗದಿರಬಹುದು ಆದರೆ ಭವಿಷ್ಯದಲ್ಲಿ ಇತರರಿಗೆ ಉಪಯುಕ್ತವಾಗಲಿರುವ ಈ ಅಧ್ಯಯನದ ಭಾಗವಾಗುತ್ತೀರಿ.

ಪರ್ಯಾಯಗಳು:

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆಯ್ಕೆ ಮಾಡಬಹುದು.

ನೀವು ಭಾಗವಹಿಸಲು ನಿರ್ಧರಿಸಿದರೆ ನೀವು ನಂತರ ನಿಮ್ಮ ಮನಸ್ಸನ್ನು ಬದಲಾಯಿಸಬಹುದು ಮತ್ತು ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು. ನಿಮ್ಮ ನಿರ್ಧಾರವು ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೋಗ್ಯ ರಕ್ಷಣೆ ಅಥವಾ ನೀವು ಸ್ವೀಕರಿಸುವ ಇತರ ಸೇವೆಗಳನ್ನು ಬದಲಾಯಿಸುವುದಿಲ್ಲ. ಅಧ್ಯಯನ ವೈದ್ಯರು ಅಥವಾ ಪ್ರಾಯೋಜಕರು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಿಲ್ಲಿಸಬಹುದು. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆರಿಸಿದರೆ, ನಿಮ್ಮ ಸ್ಥಿತಿಯ ರೋಗಿಗಳಿಗೆ ನೀವು ಪ್ರಮಾಣಿತ ಚಿಕಿತ್ಸೆಯನ್ನು ಸ್ವೀಕರಿಸುತ್ತೀರಿ.

ಗೌಪ್ಯತೆ ಮತ್ತು ಗೌಪ್ಯತೆ:

ಈ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಬಗ್ಗೆ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಕಾನೂನಿನಿಂದ ಅನುಮತಿಸುವ ಮಟ್ಟಿಗೆ ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ದಾಖಲೆಯಲ್ಲಿ ಕೋಡ್ ಸಂಖ್ಯೆಗಳು ನಿಮ್ಮನ್ನು ಗುರುತಿಸುತ್ತವೆ. ಈ ಅಧ್ಯಯನದ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಆದರೆ ಯಾವುದೇ ಪ್ರಕಟಣೆಯಲ್ಲಿ ನಿಮ್ಮ ಗುರುತು ಗೌಪ್ಯವಾಗಿರುತ್ತದೆ.

ಸಂಸ್ಥೆ / ಪ್ರಾಯೋಜಕರ ನೀತಿ:

ಈ ಸಂಶೋಧನೆಗೆ ಅನ್ವಯಿಸುವುದಿಲ್ಲ

ಭಾಗವಹಿಸುವಿಕೆಗೆ ಆರ್ಥಿಕ ಪ್ರೋತ್ಸಾಹ:

ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮಗೆ ಯಾವುದೇ ಉಡುಗೊರೆಗಳನ್ನು / ಪ್ರೋತ್ಸಾಹಕಗಳನ್ನು ನೀಡಲಾಗುವುದಿಲ್ಲ / ನೀಡಲಾಗುವುದಿಲ್ಲ.

ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಕಟಿಸಲು ಅಧಿಕಾರ:
ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳನ್ನು ಎಂಡಿ ಪದವಿ, ವಿಮರ್ಶೆ ಮತ್ತು ಪ್ರಕಟಣೆಯ ಪೂರ್ಣಗೊಳಿಸುವ ಅಗತ್ಯತೆಯ ಭಾಗವಾಗಿ ಬೆಳಗಾವಿ ಕೆಎಲ್ಇ ವಿಶ್ವವಿದ್ಯಾಲಯಕ್ಕೆ ರವಾನಿಸಲಾಗುತ್ತದೆ.

ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಅಥವಾ ಭವಿಷ್ಯದಲ್ಲಿ ನೀವು ಈ ಕೆಳಗಿನ ವ್ಯಕ್ತಿಗಳನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು,

ಡಾ.ರೂಪಾ ಬೆಲ್ಲಾದ, ಅಧ್ಯಕ್ಷರು,
ಮಾನವ ಸಂಶೋಧನೆ ನೈತಿಕ ಸಮಿತಿ,
ಜೆಎನ್ಎಂಸಿ 9480275601

ಡಾ._____
ಪ್ರೊಫೆಸರ್ ಮತ್ತು ಮುಖ್ಯಸ್ಥ
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಡಾ. _____
ಸ್ನಾತಕೊತ್ತರ ವಿದ್ಯಾರ್ಥಿ,
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಒಪ್ಪಿಗೆ ಪತ್ರ

ಕೆಳಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪುತ್ತೇನೆ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು. ಈ ಫಾರ್ಮ್ಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ನಾನು ನನ್ನ ಯಾವುದೇ ಕಾನೂನು ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಡುತ್ತಿಲ್ಲ. ಕೆಳಗಿನ ನನ್ನ ಸಹಿ ನಾನು ಈ ಒಪ್ಪಿಗೆಯ ಫಾರ್ಮ್ ಅನ್ನು ಓದಿದ್ದೇನೆ ಅಥವಾ ಈ ಸಮ್ಮತಿಯ ಫಾರ್ಮ್ ಅನ್ನು ನನಗೆ ಓದಿದ್ದೇನೆ ಮತ್ತು ಎಲ್ಲಾ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿದೆ ಎಂದು ಸೂಚಿಸುತ್ತದೆ

ಭಾಗವಹಿಸುವವರ ಹೆಸರು: …… ...

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: …… ...

ಭಾಗವಹಿಸುವವರ

ಕಾನೂನುಬದ್ಧವಾಗಿ ಅಧಿಕಾರ ಪಡೆದವರ ಹೆಸರು: …… ...

ಪ್ರತಿನಿಧಿ / ರಕ್ಷಕ

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: …… ...

ಸಾಕ್ಷಿ ಹೆಸರು: …… ...

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: …… ...

ತನಿಖಾಧಿಕಾರಿ ಹೆಸರು ಮತ್ತು ಸಹಿ: …… ...

ದಿನಾಂಕ:

ಸ್ಥಳ:

माहितीपूर्ण संमती

संशोधन अभ्यासाचे शीर्षकः एटोरिक फिव्हरचे निदान चिन्ह म्हणून ईओसिनोपेनिया.

प्रधान अन्वेषक: -

REGISTRATION NO: BG0119002

पदव्युत्तर विद्यार्थी,
सामान्य औषध विभाग,
जेएनएमसी, बेलागावी.

मार्गदर्शनः-

डॉ. _____

प्राध्यापक आणि प्रमुख
सामान्य औषध विभाग,
जेएनएमसी, बेलागावी.

परिचय आणि उद्देश: –

एन्टरिक फीव्हर हा एक आजार आहे जो भारतीय लोकसंख्येसाठी एक सामान्य रोग आहे आणि तो राष्ट्रीय आणि जागतिक दरावर महत्त्वपूर्ण आहे. एंटरिक ताप साल्मोनेला टायफी / पाराटीफि ए, बी, सी द्वारे होतो आणि दूषित अन्न आणि पाण्याद्वारे संक्रमित होतो. हा एक सहज ओळखता येण्यासारखा आणि उपचार करण्यायोग्य आजार आहे, परंतु बऱ्याचदा चुकीचे निदान केले जाते. आतड्यांसंबंधी तापाच्या निदानाची पुष्टी करण्याचा एकमेव मार्ग म्हणजे जीव वेगळे करणे, बहुतेक सामान्यतः रक्त, परंतु दुर्दैवाने यासाठी परिष्कृत संसाधने तसेच तांत्रिक श्रेष्ठता देखील आवश्यक असू शकते.

विध्वंसक चाचणीसारख्या सेरोलॉजिकल चाचण्या ज्यात बहुतेक वेळा आतड्यांसंबंधी तापाचे निदान करण्यासाठी वापरले जाते त्यामध्ये बरेच खोटे असतात, विशेषतः आपल्यासारख्या स्थानिक भागात, उच्च खोट्या पॉझिटिव्हिटी रेटसह. म्हणूनच, ईओसिनोफिल गणना सारख्या साध्या चाचणीचा वापर विशिष्ट नसला तरी, आतड्यांसंबंधी तापाचे निदान करण्यासाठी एक उत्कृष्ट मार्गदर्शक आहे.

क्रियाः

आपण संशोधन अभ्यासाचा भाग होण्यासाठी सहमत असल्यास, आपणास संबंधित इतिहास विचारला जाईल आणि संबंधित क्लिनिकल परीक्षा आणि तपासणीस पात्र केले जाईल. आवश्यक तपासणीसाठी आपल्याला रक्ताचे नमुने देखील द्यावे लागतील.

जोखीम आणि फायदे:

तपासणीसाठी आपल्या बाहेरून रक्त घेत असताना आपल्याला फक्त धोका आणि संभाव्य असुविधाची समस्या उद्भवू शकते. ज्या स्थानावरून रक्त ओढले आहे त्या जागेवर सूज, वेदना, लालसरपणा (क्वचितच घडते) होऊ शकते.
या तपासणीमुळे आपल्याला फायदा होणार नाही परंतु भविष्यात इतरांसाठी उपयुक्त ठरणाऱ्या या अभ्यासाचा आपण भाग व्हाल.

विकल्पः
या अभ्यासामध्ये भाग घेणे ऐच्छिक आहे. आपण या अभ्यासामध्ये भाग न घेणे निवडू शकता.
आपण भाग घेण्याचा निर्णय घेतल्यास आपण नंतर आपले मत बदलू आणि अभ्यासापासून दूर जाऊ शकता. आपल्या निर्णयामुळे आपल्याला प्राप्त झालेल्या वर्तमान किंवा भविष्यातील आरोग्य सेवा किंवा इतर सेवा बदलणार नाहीत. अभ्यास डॉक्टर किंवा प्रायोजक या अभ्यासात आपला सहभाग कधीही थांबवू शकतात. आपण अभ्यासामध्ये भाग न घेणे निवडल्यास, आपल्या स्थितीतील रूग्णांसाठी आपल्याला प्रमाणित उपचार मिळेल.

गोपनीयता आणि गोपनीयता:
या अभ्यासाच्या दरम्यान आपल्याबद्दल संकलित केलेली सर्व माहिती कायद्याद्वारे परवानगी असलेल्या मर्यादेपर्यंत गोपनीय ठेवली जाईल. कोड नंबर आपल्याला या संशोधन रेकॉर्डमध्ये ओळखतील. या अभ्यासाची माहिती प्रकाशित केली जाऊ शकते परंतु आपली ओळख कोणत्याही प्रकाशनात गोपनीय असेल.

संस्था / प्रायोजक यांचे धोरणः
या संशोधनास लागू होत नाही

सहभागासाठी आर्थिक प्रोत्साहनः
अभ्यासामध्ये भाग घेण्यासाठी आपल्याला कोणत्याही भेटवस्तू / प्रोत्साहन दिले जाणार नाहीत.

परिणाम प्रकाशित करण्यासाठी अधिकृतताः
अभ्यासाचे निकाल एमडी पदवी, आढावा आणि प्रकाशन पूर्ण करण्याच्या आवश्यकतेनुसार केएलई विद्यापीठ, बेळगाव येथे पाठविले जातील.

अभ्यासाच्या वेळी किंवा भविष्यातील प्रश्नांच्या बाबतीत आपण खालील व्यक्तींशी संपर्क साधू शकता,

डॉ. रूपा बेलाड, अध्यक्ष,

नैतिक समिती मानव संशोधन जे.एन.एम.सी,

9480275601

डॉ. _____

प्राध्यापक आणि प्रमुख

सामान्य औषध विभाग,

जेएनएमसी, बेलागावी.

REGISTRATION NO: BG0119002

पदव्युत्तर विद्यार्थी,

सामान्य औषध विभाग,

जेएनएमसी, बेलागावी.

संमती फॉर्म

मी खाली स्वाक्षरी करून या अभ्यासात भाग घेण्यास स्वेच्छेने सहमत आहे. मी कधीही माघार घेऊ शकतो. या फॉर्मवर सही करून मी माझा कोणताही कायदेशीर हक्क सोडत नाही. खाली माझी स्वाक्षरी सूचित करते की मी हा संमती फॉर्म वाचला आहे किंवा हा संमती फॉर्म मला वाचला आहे आणि मला सर्व प्रश्नांची उत्तरे दिली आहेत

सहभागीचे नाव: ....

स्वाक्षरी / डावा अंगठा ठसा: ....

सहभागीचा

कायदेशीररीत्या अधिकृत नाव: ....

प्रतिनिधी / पालक

स्वाक्षरी / डावा अंगठा ठसा: ....

साक्षीचे नाव: ....

स्वाक्षरी / डावा अंगठा ठसा: ....

अन्वेषकांचे नाव आणि स्वाक्षरीः ....

तारीख:

ठिकाणः

ANNEXURE III

PROFORMA

INTRODUCTION:

Case No:

Name:

Age/sex:

IP No.:

Address:

Occupation:

HISTORY:

Chief complaints:

History of presenting illness:

Past history:

Personal history:

Family history:

GENERAL EXAMINATION:

General condition:

Temperature:

Pulse:

Blood pressure:

Respiratory rate:

Pallor: yes / no

Icterus: yes / no

Cyanosis: yes / no

Clubbing: yes / no

Lymphadenopathy: yes / no

Edema: yes / no

Any other features on general examination:

SYSTEMIC EXAMINATION:

Per Abdomen:

Respiratory system:

Cardiovascular system:

Central nervous system:

INVESTIGATIONS:

1. Complete hemogram including differential white blood cell count and absolute eosinophil count
2. Blood cultures
3. Widal test:
    a. At the end of first week
    b. Repeat test after 10 days from first test

NO	AGE	SEX	IP NO/ OP NO	FEVER	ABDOMINAL PAIN	OTHER COMPLAINTS	PAST HISTORY	PERSONAL HISTORY	FAMILY HISTORY	PULSE	BLOOD PRESSURE	GENERAL EXAMINATION	PER ABDOMEN	ANY OTHER SIGNIFICANT FINDING	HEMOGLOBIN (g/dl)	TOTAL COUNT (/mm3)	NEUTROPHILS (%)	LYMPHOCYTES (%)
1	23	F	885930	YES	NO	HEADACHE, CONSTIPATION	HYPOTHYROIDISM	NS	NS	76	120/80	NAD	NAD	NAD	9.5	3400	48	46
2	25	M	904658	YES	YES	LOOSE STOOLS	NS	NS	NS	88	120/80	NAD	RIGHT ILIAC FOSSA TENDERNESS, HEPATOSPLENOMEGALY	NAD	14.5	9900	78	18
3	22	M	905543	YES	YES	LOOSE STOOLS	NS	NS	NS	80	120/80	FEBRILE	SUPRAPUBIC TENDERNESS	NAD	13.4	2200	58	37
4	21	F	912010	YES	YES	NAUSEA, VOMITING, LOOSE STOOLS	NS	3 MONTHS AMENORRHEA	NS	70	90/60	NAD	RIGHT HYPOCHONDRIAC TENDERNESS	B/L BASAL AIR ENTRY REDUCED	11	6500	76	18
5	18	M	912628	YES	YES	HEADACHE	NS	CHRONIC TOBACCO CHEWER, CONSTIPATION	NS	80	110/70	FEBRILE	EPIGASTRIC TENDERNESS	NAD	14.8	5400	64	26
6	16	M	913180	YES	NO	-	NS	NS	NS	80	120/80	NAD	NAD	NAD	13.4	4800	67	29
7	23	F	931161	YES	NO	BODYACHE	NS	NS	NS	78	110/70	NAD	NAD	NAD	11.5	5400	71	22
8	18	M	936493	YES	NO	COUGH	NS	CHRONIC SMOKER	NS	80	110/70	NAD	NAD	LEFT SIDE AIR ENTRY REDUCED	15.6	4800	62	31
9	27	M	946540	YES	YES	-	HYPERTENSION	NS	NS	82	130/80	NAD	EPIGASTRIC TENDERNESS, HEPATOSPLENOMEGALY	NAD	15.1	5900	67	27
10	20	F	946564	YES	NO	HEADACHE	NS	REDUCED APPETITE	NS	108	120/70	FEBRILE	NAD	NAD	10.1	2200	77	21
11	23	M	950125	YES	NO	GENERALISED WEAKNESS, CONSTIPATION	HYPERTENSION	REDUCED APPETITE	NS	70	110/70	NAD	NAD	NAD	14.2	8500	72	21
12	20	M	951486	YES	NO	BODYACHE	NS	INCREASED FREQUENCY OF STOOLS	NS	76	120/80	NAD	NAD	NAD	16	8300	72	23
13	17	M	952149	YES	NO	-	NS	NS	NS	70	110/70	NAD	HEPATOMEGALY	NAD	15.3	5900	76	15
14	48	F	952193	YES	YES	VOMITING	HYPOTHYROIDISM, HYPERTENSION, IHD	NS	NS	80	120/80	FEBRILE	EPIGASTRIC TENDERNESS	NAD	13.8	6800	72	22
15	33	M	953113	YES	YES	CONSTIPATION	HYPERTENSION	NS	NS	94	120/80	NAD	NAD	NAD	17	6400	78	19
16	30	F	953845	YES	YES	-	HYPERTENSION	REDUCED APPETITE, CONSTIPATION	NS	78	120/70	FEBRILE	RIGHT ILIAC FOSSA TENDERNESS	NAD	11.5	4600	65	27
17	53	F	954461	YES	NO	HEADACHE, BODYACHE	DIABETES	NS	NS	82	100/70	NAD	RIGHT HYPOCHONDRIAC TENDERNESS	NAD	14.1	9200	71	21
18	24	M	955460	YES	NO	COUGH , CONSTIPATION	NS	NS	NS	70	110/70	NAD	NAD	NAD	13	3500	57	34
19	22	F	955951	YES	NO	NAUSEA, VOMITING	NS	NS	NS	100	100/70	NAD	NAD	NAD	11.6	3500	57	37
20	18	M	955722	YES	NO	HEADACHE	NS	LOOSE STOOLS	NS	70	90/60	NAD	NAD	NAD	14.8	5300	69	27
21	22	M	956674	YES	NO	HEADACHE	NS	REDUCED APPETITE	NS	78	110/70	NAD	HEPATOMEGALY	NAD	14.1	7800	64	32
22	21	M	959233	YES	NO	LOOSE STOOLS	NS	CHRONIC TOBACCO CHEWER	NS	81	120/80	NAD	NAD	NAD	14.9	6000	72	19
23	19	F	962097	YES	NO	COUGH, COLD, VOMITING	HYPOTHYROIDISM	NS	NS	84	90/60	NAD	DIFFUSE TENDERNESS	NAD	11.9	2700	70	26
24	15	M	961946	YES	NO	HEADACHE, FATIGUE	NS	NS	NS	80	100/60	NAD	DIFFUSE TENDERNESS	NAD	13.5	7000	74	16
25	26	M	962350	YES	NO	GIDDINESS, MALENA	NS	NS	NS	98	140/90	FEBRILE	TENDER HEPATOMEGALY	NAD	14.5	10000	82	9
26	15	M	5371930	YES	YES	LOOSE STOOLS	NS	NS	NS	82	120/80	NAD	TENDERNESS IN SUPRAPUBIC AND RIGHT ILIAC REGION	NAD	13.4	5800	66	27
27	40	M	965240	YES	NO	COUGH	HYPERTENSION	NS	NS	100	130/80	NAD	NAD	NAD	13.9	4900	63	32
28	39	M	5376782	YES	YES	VOMITING	NS	CONSTIPATION	NS	110	120/70	FEBRILE	HEPATOSPLENOMEGALY, DIFFUSE TENDERNESS	NAD	15.8	8100	64	26
29	15	M	967340	YES	YES	CONSTIPATION	NS	NS	NS	70	110/70	NAD	NAD	NAD	14.2	8300	82	16
30	25	M	972276	YES	NO	HEADACHE	NS	CHRONIC SMOKER	NS	70	120/80	NAD	NAD	NAD	12.8	5300	58	33
31	20	M	976771	YES	NO	BODYACHE	NS	NS	NS	76	110/70	NAD	TENDER HEPATOMEGALY	RIGHT SIDE AIR ENTRY REDUCED	13.4	4000	82	13
32	28	F	978634	YES	YES	NAUSEA, VOMITING, LOOSE STOOLS	NS	NS	NS	88	110/80	FEBRILE	TENDER HEPATOMEGALY, SPLENOMEGALY	NAD	11.7	8800	70	25
33	19	M	983458	YES	YES	-	NS	REDUCED APPETITE	NS	70	120/80	FEBRILE	TENDER HEPATOMEGALY, SUPRAPUBIC TENDERNESS	B/L BASAL AIR ENTRY REDUCED	14.3	3100	69	27
34	65	F	984118	YES	NO	GENERALISED WEAKNESS, NAUSEA	DIABETES, HYPERTENSION	REDUCED APPETITE, CONSTIPATION	NS	76	140/90	NAD	NAD	NAD	13.6	8000	84	12
35	32	F	987668	YES	NO	HEADACHE, VOMITING	HYPERTENSION	REDUCED APPETITE	NS	88	130/80	NAD	DIFFUSE TENDERNESS	NAD	11.8	6000	76	20
36	38	M	991001	YES	NO	JAUNDICE, MALENA	HYPERTENSION	NS	NS	68	110/70	NAD	TENDER HEPATOMEGALY	NAD	13.7	11200	64	30
37	17	M	1001533	YES	NO	BODYACHE, HEADACHE, COUGH	BRONCHIAL ASTHMA	REDUCED APPETITE	NS	82	110/60	NAD	HEPATOMEGALY	NAD	15	4400	84	13
38	26	M	1006402	YES	NO	COUGH, GENERALISED WEAKNESS	NS	NS	NS	84	100/70	FEBRILE	NAD	NAD	14.5	4300	62	28
39	23	M	1008218	YES	NO	-	NS	REDUCED APPETITE	NS	68	120/70	FEBRILE	HEPATOSPLENOMEGALY	B/L BASAL AIR ENTRY REDUCED	14.4	7670	69	28
40	20	M	1019734	YES	NO	ALTERED SENSORIUM	NS	NS	NS	124	90/60	FEBRILE, RASH OVER ABDOMEN	HEPATOSPLENOMEGALY	B/L BASAL AIR ENTRY REDUCED	11.6	4200	78	17
41	19	F	1036030	YES	YES	LOOSE STOOLS, VOMITING	NS	REDUCED APPETITE	NS	120	90/60	FEBRILE	TENDERNESS IN RIGHT ILIAC FOSSA	NAD	12.3	5500	60	28
42	23	F	1038332	YES	YES	-	NS	REDUCED APPETITE	NS	78	120/70	NAD	RIGHT HYPOCHONDRIAC TENDERNESS	NAD	11.1	3800	57	34
43	26	M	5604153	YES	YES	-	NS	REDUCED APPETITE	NS	70	120/80	NAD	TENDER HEPATOMEGALY	NAD	14.9	6700	72	18
44	25	M	1047101	YES	NO	-	HYPERTENSION	NS	NS	70	140/80	FEBRILE	NAD	NAD	15.2	5900	72	24
45	27	F	1047256	YES	YES	-	NS	NS	NS	70	110/70	NAD	DIFFUSE TENDERNESS	NAD	11.9	9000	72	21

EOSINOPHILS (%)	MONOCYTES (%)	BASOPHILS (%)	ABSOLUTE EOSINOPHIL COUNT	PLATELET COUNT (/mm3)	PERIPHERAL SMEAR	GROWTH IN BLOOD CULTURE	AMOX/CLAV	CEFOTAXIME	CIPROFLOXACIN	ERTAPENEM	IMIPENEM	MEROPENEM	MEZLOCILLIN	PIPERACILLIN	TETRACYCLINE	AMPICILLIN	CEFTZIDIME	COLISTIN
0	6	0	0	137000	NA	SALMONELLA PARATYPHI A	SENSITIVE	ESBL	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	NA
0	4	0	0	247000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH NEUTROPHILIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	RESISTANT
0	5	0	0	84000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH LEUCOPENIA AND THROMBOCYTOPENIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	6	0	0	257000	NA	SALMONELLA TYPHI	SENSITIVE	N/R	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	10	0	0	153000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	N/R	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	4	0	0	114000	NA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	7	0	0	202000	NORMOCYTIC NORMOCHROMIC ANEMIA	SALMONELLA TYPHI	SENSITIVE	ESBL	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	RESISTANT	RESISTANT	ESBL	NA
0	7	0	0	178000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	N/R	N/R	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	NA
0	6	0	0	119000	NA	SALMONELLA PARATYPHI A	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	2	0	0	60000	NA	SALMONELLA TYPHI	SENSITIVE	ESBL	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	NA
0	7	0	0	207000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	5	0	0	215000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	N/R	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	9	0	0	257000	NA	SALMONELLA PARATYPHI A	SENSITIVE	N/R	NTERMEDIATI	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	NTERMEDIATI	RESISTANT	SENSITIVE	SENSITIVE
0	6	0	0	250000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	3	0	0	180000	NA	SALMONELLA TYPHI	SENSITIVE	N/R	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	8	0	0	159000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	RESISTANT	ESBL	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	8	0	0	272000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	N/R	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	9	0	0	96000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH LEUCOPENIA AND THROMBOCYTOPENIA	SALMONELLA TYPHI	SENSITIVE	N/R	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	6	0	0	191000	NORMOCYTIC NORMOCHROMIC ANEMIA WITH LEUCOPENIA	SALMONELLA PARATYPHI A	SENSITIVE	N/R	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	4	0	0	134000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH MILD THROMBOCYTOPENIA	SALMONELLA PARATYPHI A	SENSITIVE	ESBL	NTERMEDIATI	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	4	0	0	262000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	9	0	0	242000	NA	SALMONELLA TYPHI	SENSITIVE	ESBL	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	4	0	0	95000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH LEUCOPENIA AND THROMBOCYTOPENIA	SALMONELLA TYPHI	SENSITIVE	ESBL	NTERMEDIATI	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE
0	10	0	0	201000	NORMOCYTIC HYPOCHROMIC BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	N/R	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	9	0	0	206000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH NEUTROPHILIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	7	0	0	186000	NA	SALMONELLA TYPHI	NTERMEDIATI	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE
2	3	0	100	133000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH MILD THROMBOCYTOPENIA	SALMONELLA PARATYPHI A	SENSITIVE	RESISTANT	NTERMEDIATI	RESISTANT	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	NTERMEDIATI	RESISTANT	ESBL	SENSITIVE
0	10	0	0	239000	NA	SALMONELLA TYPHI	SENSITIVE	N/R	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	2	0	0	123000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH MILD THROMBOCYTOPENIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	9	0	0	170000	NORMOCYTIC HYPOCHROMIC BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	ESBL	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	5	0	0	165000	NORMOCYTIC HYPOCHROMIC BLOOD PICTURE WITH NEUTROPHILIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	5	0	0	295000	NA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	4	0	0	60000	MACROCYTOSIS WITH LEUCOPENIA AND THROMBOCYTOPENIA	SALMONELLA TYPHI	SENSITIVE	ESBL	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	4	0	0	232000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH NEUTROPHILIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	4	0	0	214000	NORMOCYTIC NORMOCHROMIC ANEMIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	RESISTANT	RESISTANT	ESBL	SENSITIVE
0	6	0	0	230000	NORMOCYTIC NORMOCHROMIC BLOOD PICTURE WITH MILD NEUTROPHILIC LEUCOCYTOSIS	SALMONELLA PARATYPHI A	SENSITIVE	N/R	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE
0	3	0	0	171000	NA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	10	0	0	150000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	NTERMEDIATI	SENSITIVE	SENSITIVE	SENSITIVE
1	2	0	75	237000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	5	0	0	155000	NORMOCYTIC NORMOCHROMIC ANEMIA WITH NEUTROPHILIA	SALMONELLA TYPHI	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
2	10	0	100	267000	MICROCYTIC HYPOCHROMIC ANEMIA	SALMONELLA TYPHI	NTERMEDIATI	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	RESISTANT	NTERMEDIATI	RESISTANT	SENSITIVE
0	9	0	0	192000	NORMOCYTIC NORMOCHROMIC ANEMIA WITH LEUCOPENIA	SALMONELLA TYPHI	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE
0	10	0	0	172000	NA	SALMONELLA TYPHI	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE
0	4	0	0	208000	NORMAL BLOOD PICTURE	SALMONELLA TYPHI	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	NA
0	7	0	0	248000	NORMOCYTIC NORMOCHROMIC ANEMIA	SALMONELLA TYPHI	SENSITIVE	ESBL	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	ESBL	SENSITIVE

CEFEPIME	FOSFOMYCIN	LEVOFLOXACIN	MOXIFLOXACIN	PIP/TAZO	TRIMETH/SULFA	TIGECYCLINE	WIDAL: BASELINE: S. TYPHI O; S. TYPHI H; S. PARATYPHI AH	REPEAT WIDAL: S. TYPHI O; S. TYPHI H; S. PARATYPHI AH	TREATMENT RECEIVED: 3RD GENERATION CEPHALOSPORIN	TREATMENT RECEIVED: 3RD GENERATION CEPHALOSPORIN + AZITHROMYCIN	TREATMENT RECEIVED: OTHER ANTIBIOTICS	OUTCOME	OTHER REMARKS
RESISTANT	RESISTANT	SENSITIVE	INTERMEDIATE	RESISTANT	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	1:160; 1:160, NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	1:80; 1:160; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:160; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	INTERMEDIATE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	NO	NO	YES	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	INTERMEDIATE	RESISTANT	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	SENSITIVE	1:160; 1:320; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	RESISTANT	SENSITIVE	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	RESISTANT	RESISTANT	NTERMEDIATI	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; 1:320; 1:160	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	RESISTANT	SENSITIVE	INTERMEDIATE	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	NO	NO	YES	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	NA	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NTERMEDIATI	SENSITIVE	SENSITIVE	1:160; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NTERMEDIATI	SENSITIVE	SENSITIVE	1:160; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	NA	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NTERMEDIATI	SENSITIVE	SENSITIVE	1:160; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NA	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:160; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NTERMEDIATI	SENSITIVE	SENSITIVE	1:80; 1:160; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	1:160; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	RESISTANT	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	NA	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NTERMEDIATI	SENSITIVE	SENSITIVE	1:80; 1:160; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:160; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:160; 1:320; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	NTERMEDIATI	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	NO	NO	YES	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	RESISTANT	SENSITIVE	INTERMEDIATE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; 1:160	NA	NO	YES	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	RESISTANT	INTERMEDIATE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:160; 1:160, NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	RESISTANT	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
SENSITIVE	SENSITIVE	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:160; 1:160, NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
RESISTANT	SENSITIVE	RESISTANT	RESISTANT	NTERMEDIATI	SENSITIVE	SENSITIVE	NEGATIVE; NEGATIVE; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE
NA	SENSITIVE	RESISTANT	NA	SENSITIVE	RESISTANT	SENSITIVE	1:80; 1:160; NEGATIVE	NA	NO	YES	NO	IMPROVED	NONE
RESISTANT	RESISTANT	RESISTANT	RESISTANT	SENSITIVE	SENSITIVE	SENSITIVE	1:80; 1:80; NEGATIVE	NA	YES	NO	NO	IMPROVED	NONE