- **ENTERIC FEVER & BRUCELLOSIS**

- **Objectives**
- Causative agents.
- Clinical features and epidemiology.
- Complications.
- Management.
- Prevention .

- ***Enteric* fever**
- Typhoid fever (more commonly termed typhoid fever) is caused by *Salmonella* Typhi a gram-negative bacterium.
- A very similar but often less severe disease is caused by *S.* Paratyphi A and rarely by *S.* Paratyphi B (Schotmulleri) and *S.* Paratyphi C (Hirschfeldii).
- In developing countries S. typhi is often the most common salmonella isolate.
- Human is the only natural reservoir, so direct or indirect contact with infected person , ingestion of foods or water contaminated with human feces is the most common mode of transmission ,a variety of sources of fecal contamination have been reported, including street foods and contamination of water reservoirs.
- Congenital transmission can occur by trans placental infection from a bacteremic mother to her fetus.Intra partum transmission is also possible, occurring by a fecal-oral route from a carrier mother.

PATHOGENESIS OF TYPHOID FEVER: The bacteria invade through the pyres patches producing hyperplasia, necrosis, and sloughing of the overlying epithelium which produce ulcer that may bleed , Ulcers heal without scarring.then the organism are transport to the intestinal LN, to the blood stream `bacteremia``, then seeded in the RES and may seeds the other organs.

CLINICAL MANIFESTATION OF TYPHOID FEVER

- Incubation period is usually 7-14 days but may range 3-30 days .
- **In School aged and adolescent**:-the onset of symptom is insidious, starting as fever, malaise, anorexia, myalgia, headache, &abdominal pain over 2-3 days, although diarrhea having ***pea-soap*** consistency may be present at early stage, constipation later become more prominent symptom. The temperature increase in stepwise fashion, becomes an unremitting and high fever within a week often reaching 40 C, and persist during the second wk with fatigue, anorexia, cough, and abdominal symptoms increases in severity, the pt look ill, disoriented, lethargic, delirium and stupor may be observed
- **On examination:** relative bradycardia , hepatomegaly, splenomegaly, distended abdomen with diffuse tenderness.In about 25% of cases, a macular or maculopapular rash (rose spots) may be visible around the 7th-10th day of the illness, and lesions may appear in crops of 10-15 on the lower chest and abdomen and last 2-3 days ..
- ***In infant &young children<5 yr:***
- Enteric fever is relatively rare in this age group in endemic area, the disease is mild on presentation although clinical sepsis can occur.

- Typhoid fever in **young children** commonly presented with diarrhea leading to a diagnosis of acute gastroenteritis. **Non typhoidal** *Sal.* milder, with a shorter duration of fever and a lower rate of complications.
- If no complications occur, the symptoms and signs gradually resolve within 2-4 wk, but malaise and lethargy may persist for 1-2 mo. however, the illness may be associated with malnutrition in a number of affected children.
- **Neonates**: The neonatal disease usually begins within 3 d of delivery. Vomiting, diarrhea, and abdominal distention are common. Temp. is variable but may be as high as 40.5°C, Seizures may occur, hepatomegaly, jaundice, anorexia, and weight loss can be marked.

COMPLICATION OF TYPHOID FEVER:-

- Sever GIT hemorrhage(<1%)& perforation(0.5-1%) both occur after the 1st wk
- Hepatitis, cholecystitis & Toxic myocarditis, Pneumonia or bronchitis (by other organism)
- Neurological complication are relatively uncommon include delirium, psychosis, increased ICP, acute cerebellar ataxia, chorea, deafness, and Guillain-Barré syndrome.
- Others: fatal B.M. necrosis, pyelonephritis, DIC, nephritic syndrome, hemolytic-uremic syndrome and orchitis.

DIAGNOSIS OF TYPHOID FEVER

- ***LAB. FINDING:***

1- CBC show: normochromic normocytic anemia
2- Leucopenia, usually not < 2,500 cells/mm^3, in younger children leukocytosis is common and may reach 20,000-25,000 cells/mm^3 .
3- Thrombocytopenia may be striking and persist for as long as 1 wk and may be a marker of severe illness or may accompany DIC
4- Proteinuria is common. Fecal leukocytes and fecal blood are very common.
5- Serological test(widal test)is less helpful (high false positive and false negative)

- **CONFIRMING DIAGNOSIS OF ENTERIC FEVER**:

1- Blood culture in the 1st week repeated sample may be needed, positive in 40-60%.
2- Stool and urine culture in 2nd wk and in carriers.
3- Bone marrow culture the most sensitive (positive in 85-90%),less influenced by prior anti-microbial therapy.
4- Culture of aspirated duodenal fluid may be helpful in confirming infection.
5- PCR: sensitive, specific, noninvasive.

TREATMENT OF TYPHOID FEVER:

- The vast majority of patients can be managed at home with oral antibiotics and close medical follow-up for complications or failure of response to therapy. Hospitalization are needed for Patients with persistent vomiting, severe diarrhea, and abdominal distention .

1– Supportive treatment: There are general principles of management of typhoid fever. Adequate rest, hydration, and correct fluid and electrolyte imbalance. A soft, easily digestible diet should be continued unless the patient has abdominal distention or ileus

- Antipyretic therapy (acetaminophen 10-15 mg/kg / 4-6 hr PO) should be provided as required

2-Antimicrobial Therapy

- Antibiotic therapy is critical to minimize complications ,Choosing the appropriate empirical therapy may be problematic, It has been suggested that traditional therapy with either

chloramphenicol or amoxicillin is associated with relapse rates of 5-15% and 4-8%, respectively, whereas use of the quinolones and third-generation cephalosporins is associated with higher cure rates.

- ***Treatment of Uncomplicated Typhoid Fever:-*** By using either of:
  - ***Chloramphenicol*** 50-75 mg/kg/day for 14-21days
  - ***Amoxicillin: 75-***100mg/kg/day tid Po for 14 days.
  - **Ceftriaxone** 75 mg/kg/day for 10-14 days.
  - **Cefixim:15-** 20 mg/kg/day for 7-14 days
  - ***Ofloxacin*** 15mg/kg/day for 10-14 days
  - ***Azithromycin:*** 8-10 mg/kg/day for 7 days.
- ***Treatment of sever Typhoid Fever*** **Fully sensitive:**
  - Chloramphenicol
  - or Ceftriaxone .
- **Multidrug-resistant cases**: Fluoroquinolone, e.g., ofloxacin or ciprofloxacin.

- 3rd G cephalosporin(Cefixim, Ceftriaxone *or* Cefotaxime
- **Quinolone-resistant cases:** Ceftriaxone., ***Azithromycin***

3-<u>Dexamethason</u>: short course of dexamethason starting with 3 mg/kg for initial dose then 1 mg/kg/6hr for 48 hr improve survival rate of pt with shock, obtundation, stupor or coma

4-<u>Treatment of complication:</u>

- Blood transfusion for sever hemorrhage.
- Surgical intervention for perforation.
- Platlete transfusion for sever thrombocytopenia.
- Broad spectrum antibiotic for pt with perforation

THE PROGNOSIS :

depends on the rapidity of diagnosis and institution of appropriate antibiotic therapy. Other factors are the patient's, age, general state of health, and nutrition, the causative *Salmonella* serotype, and the appearance of complications.

- Despite appropriate therapy, 2-4% of infected children may experience relapse after initial clinical response to treatment. Individuals who excrete *S.* Typhi for ≥3 mo after infection are regarded as chronic carriers**.** The risk for becoming a carrier is low in children (<2% for all infected children) and increases with age.

PREVENTION OF TYPHOID FEVER

1. Safe water supply and improve sanitation.
2. Hand washing& good personal hygiene (specially in food handler)
3. Vaccination:2 type of vaccine are available:
   - Oral live attenuated vaccine have good efficacy (67-82%) for up to 5 y.
   - vi capsular polysaccharide as single i.m injection for >2 yrs. with a booster every 2 yr. and has a protective efficacy of 70-80%.

- The recent Vi-conjugate vaccine has a protective efficacy exceeding 90% in younger children

- ***Brucellosis,*** ***Undulent Fever, Malta Fever, Mediteranian Fever***
- Human brucellosis is a zoonotic infection caused by organism of the genus Brucella, a small aerobic, non spore forming, non motile G -ve cocco bacilli.
- The humans are accidental hosts acquire the infection from direct contact with infected animal or consumption of product from infected animal.

AETIOLOGY OF BRUCELLA

the most common species causing brucellosis are:

- *B. abortus* (cattle)
- *B. melitenses* (goats /sheep).
- *B. suis* (swine =pig).
- *B. canis* (dogs).

- These organisms are fastidious in their growth but can be grown on various laboratory media including blood and chocolate agars.

EPIDEMIOLOGY OF BRUCELLA:-

- Brucellosis exist world wide but specially prevalent in the Mediterranean basin, Arabian gulf, Mexico, central & south America.
- Occupational exposure to infected animal is the major risk factor for the development of the disease.
- in children consumption of un pasteurized milk or other dairy products from cows, goats or camels may be an important risk factor.

PATHOGENESIS OF BRUCELLA :-

- The pt gets the infection by inoculation through a cut or skin abrasion, inhalation of infectious aerosols, or by ingestion of contaminated meat or dairy products.
- Trans placental passage ….. congenital infection.
- The risk for infection depends on the nutritional and immune status of the host, the route of inoculum, and the species of *Brucella.*
- The brucella are facultative intracellular pathogens that can survive and replicate inside the phagocytes of RES system.

CLINICAL MANIFESTATION OF BRUCELLA:-

- Brucellosis is a systemic illness started as acute or insidious onset 2-4 week after inoculation with classical ***triad of fever, arthralgia /arthritis*** , ***and hepatosplenomegally***,
- Monoarticular arthritis of the knees and hips in children and of the sacroiliac joint in adolescents and adults can be found. other features include abdominal pain, headache, night sweats, fatigue, cough, pharyngitis, refusal to eat, refusal to bear weight, and failure to thrive.

DIAGNOSIS OF BRUCELLA:-

- Brucellosis is very difficult to diagnose without history of animal or food exposure , routine laboratory examinations of the blood are not helpful, pancytopenia may occur.
- A **Definitive Diagnosis** is established by recovering the organisms in the blood, bone marrow, or other tissues.
- Automated culture systems and the use of the lysis-centrifugation method have shortened the isolation time from weeks to days.

- In the absence of positive culture results, various serologic tests have been applied to the diagnosis of brucellosis. **The serum agglutination test** (SAT most patients with acute infections have titers of ≥1 : 160)
- Recently: enzyme immunoassay and PCR

TREATMENT OF BRUCELLA:-

- **For pt ≥ 8 yr either of**:
  - ***Doxycyclin*** 2-4 mg/kg/day; maximum 200 mg/day PO for 6 weeks.
  - + ***Rifampin*** 15-20 mg/kg/day; maximum 600-900 mg/day PO for 6 wks

  Or ***Doxycycline*** 2-4 mg/kg/day; maximum 200 mg/day PO for 6 wks
  - + ***Streptomycin*** 15-30 mg/kg/day; maximum 1 g/day1 g/ 24 hr IM for **2-3 Week**s
  - Or ***gentamicin*** 3-5 mg/kg/day IV,IM for **1-2wk**
- ***pt < 8 years are treated with***:
- ***Trimethoprim-sulfamethoxazole TMP-SMX:***10mg TMP**, 50**mg SMX PO for **4-8 wk.**
  + *Rifampin:* 15-20 mg/kg/ day PO for 6 weeks.

TREATMENT OF BRUCELLA COMPLIACTIONS

- ***Meningitis, Osteomylitis, Or Endocarditis:***
- ***Doxycyclin*** 2-4 mg/kg/day; maximum 200 mg/day PO **for 4-6 mo**.
  +gentamicin 3-5 mg/kg/day IV for **2 wk.**
  +/- Rifampin 15-20 mg/kg/day PO for **4-6 mo**.

THE PROGNOSIS: prognosis after specific therapy is excellent if patients are compliant with the prolonged therapy

PREVENTION OF BRUCELLA

1-Effective eradication of the organism from cattle, goats, & sheep.
2-Pasteurization of milk and dairy products.
No vaccine available.

References:

- Nelson Textbook of Pediatrics , 20 edition .
- Nelson essentials Textbook of Pediatrics , 7th edition.
- Illustrated textbook of pediatrics.