Typhoid fever in Indonesia clinical picture, treatment and status after therapy

S6-1

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Abstrak

Demam tifoid merupakan penyakit sistemik akut yang disebabkan oleh Salmonella typhi. *Penyakit ini merupakan salah satu penyakit infeksi yang muncul, yang menurut WHO harus diwaspadai secara global. Penyakit ini bersifat endemis hampir di semua kota besar di Indonesia. Sesuai dengan data dari rumah sakit dari kota-kota tersebut, gambaran klinis utama berupa demam, disertai sakit kepala (27-72%), pusing (67-96%), batuk (26-41%), mual (56-61%), muntah (37-41%), tidak nafsu makan (37-97%), konstipasi (27-72%), rasa tidak enak pada perut (6-70%), bradikardia relatif (8-44%), lidah berselaput (41-100%), hepatomegali (58-82%), splenomegali (30-38%), mati rasa (24-43%). Lekopeni dilaporkan antara 16,7-56%. Komplikasi berupa : perdarahan usus (1,5-14%), perforasi usus (2,5-4%), syok septik (5,4-6,9%), bronkopneumonia (2,2-4,6%), miokarditis (2,6-5%), koagulasi intravaskuler (2,2-2,6%), hepatitis (1,8-5%), dan pakreatitis (0,1%). Obat pilihan masih khloramfenikol, tapi karena kekurangannya, seperti relaps (sampai 15%), anemia aplastik (1 dari 100.000 kasus), dan karier kronik/permanen (2-5%), maka kuinolon akan menjadi obat pilihan di kemudian hari. Suatu penelitian yang dilakukan di Surabaya pada pasien tifoid yang diobati dengan khloramfenikol mendapatkan 11,8% karier konvalesen dan 0,97% karier kronik. Pencegahan termasuk perbaikan sanitasi lingkungan (air minum yang aman, WC bersih, pengawasan restoran, pengawasan makanan, industri es dan susu), perbaikan kebersihan pribadi (pendidikan kesehatan masyarakat), kontrol karier dan vaksinasi populasi yang berisiko tinggi.*

Abstract

Typhoid fever is an acute systemic infectious disease caused by Salmonella typhi. *It is one of the emerging infectious disease which WHO has put a global alert warning globally. This disease is endemic in most big cities in Indonesia. According to the data from the hospitals of those cities, the main clinical features are fever, together with : headache (27-72%), dizzines (67-96%), cough (26-41%), nausea (56-61%) vomiting (37-41%), anorexia (37-97%), constipation (27-72%), abdominal discomfort (6-70%), relative bradycardia (8-44%), coated tongue (41-100%), hepatomegaly (58-82%), splenomegaly (30-38%), and loss of sensorium (24-43%). Luecopenia was reported between 16.7%-56%. The complications were: intestinal bleeding (1.5-14%), intestinal perforation (2.5-4%), septic shock (5.4-6.9%), bronchopneumonia (2.2-4.6%), myocarditis (2.6-5%), DIC (2.2-4.6%), hepatitis (1.8-5%), and pancreatitis (0.1%). The drug of choice is still chlorampenicol, but because of its inferiority, i.e relapse (up to 15%), aplastic anemia (1 of 100.000 cases), and chronic/permanent carriers (2-5%). Quinolone will be the drug of choice in the future. An investigation carried out among typhoid patients treated with chloramphenicol in Surabaya yielded 11.8% convalescent carriers and 0.97% chronic carriers. The preventive measures including : improvement of environment sanitation (safe drinking water, hygienic WC, supervision of restaurant, supervision of food, of food ice and milk industries), improvement of personal hygiene (public health education), carriers control and vaccination of high risk group population.*

INTRODUCTION

Typhoid fever (T.F) continues to be global health problem, and will be one of emerging infectious diseases in the era of globalization on 21th century. Problems associated with socioeconomic and ecological changes, which facilitate the transmission of this disease, like population growth, unplanned urbanization, and disturbances in the environmental balance are expected to be on the increase. Extensive travel and trade facilitate the spread of this disease locally, regionally and globally, respectively. It is estimated that the global annual incidence of T.F. is 33 million cases with 1.5 million deaths. This disease is still highly prevalent throughout Indonesia, especially in the urban area. The incidence is estimated between 350-810 cases per 100,000 population per year, with its case fatality rate between 2.8-16%. Household survey in 1986 reported that around 3% of all mortality was caused by T.F., or approximately 50,000 deaths per year. Septic shock, intestinal bleeding or intestinal perforation are the leading cause of death. The clinical picture, diagnosis, treatment, and status after therapy will be illustrated in this article, adding to it an overview of T.F. cases in Dr. Sutomo Hospital Surabaya, during 6 years period (1991-1996/1997).

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DEFINITION

Typhoid fever is an acute systemic illness caused by *Salmonella typhi* infection. Paratyphoid fever (P.T.F.) A, B, C, are those clinically and pathologically similar with T.F. but usually milder illness, caused by *S. paratyphi A, S. schottmulleri, and S. hirschfeldii*. Enteric fever refers to both typhoid and paratyphoid fever, but unless otherwise stated, usually the term typhoid fever will be used to refer either T.F. or P.T.F.

PATHOGENESIS OF TYPHOID FEVER AND ITS COMPLICATIONS

Typhoid fever is caused by *Salmonella typhi (S. typhi)*, infecting men by contaminated water or food. Following ingestion of suitable inoculum, *S. typhi* passes through the gastric barrier reaching the intestines and multiplying there. If there is no influence of humoral mucosal immune response (IgA), the microorganism will adhere to the intestinal wall, invading the epithelial cell especially through the M-cell passing to the lamina propria. In this place the microorganism multiply and phagocytized by the phagocyte cells especially macrophages. *S. typhi* can survive and multiply inside the macrophages, taking it to the Peyer's patches in the distal part of the illeum and then to the mesenteric lymph nodes. Through the ductus thoracicus, the microorganism inside the macrophages (Trojan-horse phenomenon) enter the blood circulation (1st asymptomatic bacteremia), then invading all reticuloendotelial organs of the host, especially the spleen and the liver. Inside those organs, *S. typhi* will leave the phagocyte cells, multiply extracellularly in the organ or sinusoid space, then entering the blood circulation again and causing bacteremia with signs and symptoms of systemic infection (2nd symptomatic bacteremia).

In the liver, the microorganism enter into the gallbladder, multiply there and then be excreted in the faeces, another part will invade the intestinal wall again. The similar process will go on, but the macrophages have been already activated. So the microorganism inside the macrophages make it hyperractive, liberating several mediator substances (cytokines), and causing systemic inflammation reaction, i.e. fever, malaise, headache, myalgia, abdominal discomfort, vascular instability, mental and coagulation disorder. Sepsis and septic shock could occur at this stage.

Hyperactive macrophages in the Peyer's patches induce hyperplastic reaction caused by excessive cytokine (TNF-α) yield local inflammation response : intestinal hemorrhage or perforation. If there is excessive bacterial multiplication and toxins in blood circulation, 2nd symptomatic bacteremia and systemic inflammation could happen, could cause systemic complications: abscess in various organs, neuro psychiatric disorders, sepsis and septic shock.

THE CLINICAL FEATURES

The clinical features of T.F. have not much changed for more than 20 years. Fever is the main sign and symptom of T.F. Patients suffering from fever for 7 days or more in endemic area must be suggested T.F. So any signs and symptoms must be looked for and matched to the clinical appearance of T.F. According to the data collected from studies in several hospitals in Indonesia (1976 - 1995), the signs and symptoms of T.F. were as seen in Table 1 and Table 2.

Table 1. Symptoms of Typhoid Fever Patients in some Hospitals in Indonesia

Investigators Symptoms (%)	Juwono 1976 Surabaya	Zulkarnain 1978 Jakarta	Hendarwanto 1979 Jakarta	Hadi Halim 1981 Medan	Damanik 1994 Palembang
Fever	100	100	100	100	100
Headache	72	–	27.1	53	–
Dizziness	67	96	27.1	–	–
Chills	–	75	44.6	38	38
Loss of Sensorium	21	43	15.2	40	30
Cough	41	26	26.1	57	43.4
Nausea	56	61	57	57	43.4
Vomiting	41	–	52	37	44.2
Anorexia	97	–	37	57	–
Constipation	44	56	27.1	33	27
Diarrhea	36	47	21.7	38	44.2
Abdominal Discomfort	15	70	6.5	–	23.9
Hematoschezia	–	–	8.7	8	–

Table 2. Signs of Typhoid Fever Patients in Some Hospitals in Indonesia

Investigators Signs (%)	Juwono 1976 Surabaya	Zulkarnain 1978 Jakarta	Hendarwanto 1979 Jakarta	Hadi Halim 1981 Palembang	Damanik 1984 Medan
Fever	100	92	86.9	100	100
Relative Bradicardy	49	22	7.6	45	48.7
Coated Tongue	92	100	41.3	72	–
Hepatomegaly	82	74	43	35	1.8
Splenomegaly	36	30	23.9	23	6.2
Loss Of Sensorium	21	43	23.9	50	–
Rose Spot	–	3	1.1	–	–
Abdominal Distention	–	6	–	15	1.8
Rales / Ronchi	18	7	–	–	–

Table 3. Leucocyte Count of Typhoid Fever Patients in Some Hospitals in Indonesia

Investigators Number Of Leukocytes (per Cmm)	Zulkarnain 1978 Jakarta	Soenarto 1978 Semarang	Juwono 1979 Surabaya	Hendarwanto 1979 Jakarta	Rivai In Children Jakarta	Rivai In Adults Jakarta
<5.000 (%)	30	56	16.7	28.3	54	51.4
5.000-10.000 (%)	62	36	68.7	66.3	40.5	44.1
>10.000 (%)	8	8	14.6	5.4	5.5	4.5

SEX AND AGE DISTRIBUTION

There was no difference in sex distribution of T.F. in some hospitals in endemic area in Indonesia. Most cases (± 80%) are adolescents and young adults (12-30 years of age). Only ± 6% of cases are >40 years of age. So in endemic area, we must suspected T.F. for adolescence or adults cases suffering from fever for 7 days or more.

LABORATORY FINDINGS

Blood

According to the literature, leukopenia was always found in T.F. But it is not always true, especially in endemic area. Leukopenia and neutropenia are present in around 25% of patients. Normal white blood count is present in almost patients, albeit low in relation to the degree of fever. In Indonesia, the most prevalence was normal leukocyte count up to 68% (see Table 3).

Leukocytosis develops in the event of intestinal perforation or pyogenic complications. Rarely anemia can occur, caused by blood loss and chronic infection.

Bacteriology Isolation

a. Blood culture is the most frequent laboratoric examination, definition the diagnoses of typhoid fever. If it is done in the first week of illness, the positive probability is up to 80%. But it is less sensitive. Studies in Dr. Sutomo Hospital, Surabaya reported its sensitivity was 47.65% (bile culture), and 43.3% (trypticase phosphate broth), respectively.
b. Bone marrow aspiration culture, is the most sensitive culture of *S.typhi* (80-90%).
c. Faecal culture is mostly become positive in the 2nd or 3rd week of illness. Its sensitivity is about 26-43%.
d. Urine culture, is also mostly become positive in the 2nd or 3rd week of illness. Its sensitivity is around 25%.

Urine culture and faecal culture (especially faecal culture) are always positive in carrier.

Table 4 visualized comparative results of blood, faeces, urine, and bone marrow aspirate, reported by some researchers from some hospitals.

Table 4. Result of Positive Cultures in Typhoid Fever Patients in Some Hospitals

Investigators		Percentage of (+) Cultures			
		Blood (%)	Faeces (%)	Urine (%)	Bone Marrows
Stuart	(1946)	72	25	23	–
Soriano	(1963)	20	0.7	0	–
Gilman	(1975)	40	37	7	–
Sunotoredjo	(1976)	53	5	2	–
Tehupeiory	(1978)	62.5	43	2.8	–
Soetjitro	(1978)	40	6.5	13	70
Panggabean MP	(1979)	50	44	–	78

Serology Test

a. The Widal test (detection of antibody or O and H agglutinin H titer) is still widely used. In endemic area, detector of H antibody is not recommended. Four fold rising titer of O antibody of plain samples taking for at least one week interval, most suggestive typhoid fever. The sensitivity of the Widal slide test is equal with the Widal tube test, but more rapid (5-30 minutes v/s one-day). The specificity of this test depends on the antigen type. Local antigen is more specific than imported one. Studies reported from Dr.Sutomo Hospital, Surabaya have proved it. It is important to confirm the cut off value of this test in local population.
b. ELISA test, especially indirect ELISA test to detect antibody, recently are widely used. Studies reported from Dr.Sutomo Hospital Surabaya using local antigen O have proved its sensitivity and specificity up to 90%, for both IgM and IgG. Using specific outer membrane protein (OMP) increase the accuracy of this test. For community practical diagnostic purpose, Dot Enzyme Immunoassay (Typhi dot) tests have been developed recently. Serological and ELISA tests to detect antigen of *S.typhi* are more specific than the former serological tests and can be used as early diagnostic tool accurately.

Polymerase chain reaction (PCR) test

This new test can detect specific DNA of *S.typhi*. It is more sensitive and specific than the other tests according to the specific primers used in this test, and can't be used routinely. Study reported from Surabaya has proved it.

TREATMENT

Patients care

Patients must be cared cautiously. Usually absolute bed rest designed for acute T.F., to prevent serious complication i.e. intestinal bleeding or perforation. This procedure is performed for at least 7 days afebrile. Some authors advocated this procedure be performed until the 2nd or 3rd week of illness.

Diet

Safe and optimal diet must be given during acute phase of this disease (1st - 2nd week of illness). Liquid or soft diet with high calorie (3000-5000 calorie/day) and high protein (100 grams/day) is usually performed during this phase, besides minimally 2-3 liters/day solution. This form of diet is changed to solid diet gradually, to prevent intestinal complications. Studies of solid diet (consists of made boil-rice, meat, fish, egg, and low cellulose vegetables), given earlier during acute phase, appeared safe. This form of diet is more pleasant than liquid or soft diet.

Drugs

Specific therapy

Chloramphenicol is still the drug of choice against T.F. It is cheaper than other alternative antibiotics and easy to find in our country. But the disadvantage of chloramphenicol is its high rate of relapse (up to 15%), irreversible aplastic anemia, and does not prevent chronic carriers (2-5%). There are various dosages and schedule of this antibiotic, but usually 50 mg/kg Body weight/day every 6-8 hours for 2 week or 3-4 x 500 mg/day orally for 7 days afebrile.
Some chloraphenicol resistance cases have been reported from Semarang and Jakarta (1.8 - 16.7%).

The alternative drugs

1. Ampicillin
   Dosage: 60-80 mg/kg BW/day in four devided dose for children; or 500-1000 mg/dose for adults, four doses/day.
2. Cotrimoxazole/Trimethoprime Sulphamethaxazole 80/400 mg
   Dosage : 2 tablets twice daily, orally for 7 days after the temperature becomes normal or for 14 days.
3. Thiamphenicol
   Dosage : 500 mg/day in four-devided dose, orally for 7 days after temperature becomes normal or for 14 days

4. Amoxicillin
   Dosage: 50 mg/kg BW/day in three-devided dose for children; or 500-1000 mg/dose for adults, three doses/day.
5. Third generation cephalosporin
   Ceftriaxone is very effective antibiotic against TF, especially for children
   Dosage : 3-4 gram iv (50-80 mg/kg BW), once daily, for 7 days.
6. Quinolone (4-Fluoro-quinolone)
   Ciprofloxacin
   Dosage: 100 - 250 mg orally, twice daily for 7 days
   Ofloxacin
   Dosage: 200 - 400 mg orally, twice daily for 7 days
   Pefloxacin
   Dosage: 200 - 400 mg orally, twice daily for 7 days

   NB:– Quinolone is very potent and effective against TF especially in adult and reducing the incidence of convalescence carriers. But this antibiotic is expensive and not recommended for children <18 years of age.

Supportive therapy

Supportive therapy could accelerate recovery.
High dose of vitamin B and C.

Symptomatic therapy

Acute febrile cases (over 40°C) should be given cold compress or paracetamol. Salicylates are not recommended because salicysilates should be avoided to diminish the danger of intestinal hemorrhage.
Obstipation must be treated with paraffine liquidum. Purgative is contraindicated.
Severe meteorismus is decompressed by nasogastric tube, oral diet is not recommended, parenteral diet is preferred.
Tranquilizer should be given to the delirium cases.

Treatment of pregnant woman cases

Chloramphenicol is contraindicated especially during 3rd trimester. It is the same for cotrimoxazole.
Ampicillin, amoxycillin and cephalosporine are the safe antibiotics for pregnant women with TF.

TREATMENT OF TYPHOID FEVER WITH COMPLICATIONS

Typhoid fever with complications is a serious problem, so it must be kept under special attention. If necessary the patients must be managed in the intensive care unit (ICU).

Specific therapy

High dose antibiotics specific for *S.typhi*, parenterally.

1. Chloramphenicol (the drug of choice)
   Doses: 2-4 grams/day, i.v. In adult (50-100 mg/kg/day), in four divided doses
2. Ampicillin
   Doses: 100-150 mg/kg, i.v. every 4-6 hours
3. Amoxicillin
   Doses: 500-1000 mg i.v. every 6-8 hours
4. Cotrimoxazole (trimethoprim/sulfamethoxazole 80/400 mg = 1 ampule @ 5 cc)
   Doses: 2 ampules (10 cc), i.v. infusion in 250 ml fluid infusion over 1 hour, twice daily
5. Third generation cephalosporins :
   Cefotaxime
   Doses: 2x (1-2) gram/day i.v. max. 12 gram/day, in 3-4 doses (50-100 mg/kg/day in 3-4 doses, max 200 mg/kg/day in 3-4 doses
   Ceftriaxone
   Doses: 3-4 gram iv (80 mg/kg), once daily
6. Quinolone (4-fluoroquinolones)
   Ciprofloxacin : 100-200 mg i.v. infusion, twice daily
   Ofloxacin : 200-400 mg i.v. infusion, twice daily
   Pefloxacin : 400 mg, twice daily by slow i.v. infusion in 200 ml 5% glucose infusion, over 1 hour
   Don't administer with salt solution (NaCl) or any other solution containing chloride, because of the risk of precipitation.

   NB: Quinolones are not recommended for children under 13 years of age.

Individual management of complications

Intestinal hemorrhage

Prompt fluid resuscitation or blood transfusion should be given if blood loss is greater than 2 ml/minute. **Vasopressin infusion** should be tried or surgical intervention must be done if the bleeding is profuse (>2 ml/minute) or intractable.
After confirming the site of bleeding with a selective superior mesenteric angiogram, a vasopressin infusion should be given at the rate of 0.2-0.4 unit/min initially, followed by tapering doses over 36 hours. **Surgical management**. Selective angiography, radio isotopic scanning methods, or sometimes endoscopy must be taken preoperatively to localize the bleeding site.

Intestinal perforation

Surgery is the treatment of choice. The standard

method for the treatment of typhoid enteric perforations is still presently trimming and primary suturing of the perforated viscous and peritoneal drainage. Bowel perforation should be closed into layers for best result. Supportive treatments with fluids or blood transfusions are always needed. Antibiotics should be selected to treat not only *S.typhi* but also facultative and anaerobic bowel flora.
In general, a broad-spectrum antibiotic regimen should be used consisting of a combination of chloramphenicol, gentamycin (1.5 mg/kg i.v. every 8 hours) and metronidazole (500 mg i.v. every 6 hours)

Sepsis with septic shock

Sepsis with septic shock is a very critical situation with high mortality. Patients can die quickly. Successful management requires early diagnosis, prompt high doses of specific antibiotics intravenously (see.ad.I), and concurrent with hemodynamic and respiratory support. If there is a focal source of infection (abscess) it should be removed or drained quickly. Intravenous fluid typically 1-2 of normal saline should be initiated to hypotensive patients over 1-2 hours. Large volumes of fluid may be needed according to the volume deficit. Monitoring of central venous pressure (normally 10-12 cmH_2O) or pulmonary capillary wedge pressure (normally 12-15 mmHg), should be done for in-patient with refractory shock. The urine production should be kept >30 ml/h, and mean arterial blood pressure of >60 mmHg (systolic pressure >90 mmHg). If patients are still hypotensive, vasoactive amines should be given (low doses Dopamine 5-10 µg/kg/min). Ventilatory therapy with intubation should be given to ensure adequate oxygenation, especially for patients with hypoxemia, hypercapnea, neurologic deterioration or respiratory failure. Blood transfusion is indicated for anemic patient. Hydrocortisone (50 mg i.v. every 6 hours) should be given to in-patient with adrenal insufficiency. High dose steroid iv. should be given in the seriously ill patients, i.e. : Dexamethasone 3 mg/kg i.v. or methylprednisolon 30 mg/kg iv. Over 30 min. for 48 to 72 hours. Bicarbonate should be given to patient with severe metabolic acidosis (arterial pH 7.2). The roles of antiendotoxin and antimediator agents are still under investigation.

Abscess

Internal abscesses (spleen, ovarium etc.) should be drained accurately besides being treated with high dose of specific antimicrobial iv.

Disseminated intravascular coagulation (DIC)

Patients with bleeding as a major symptom should be given fresh frozen plasma to replace depleted clotting factors and platelet concentrates to correct thrombocytopenia. Although it is still controversial, heparin (300-600 IU/kg/24 h.i.v) could be given in severe DIC with acrocyanosis.

Neuropsychiatric complications

High dose steroid and specific antimicrobials iv. should be given concurrently.
Patients with severe illness, who present with central nervous system manifestation and for evidence of disseminated intravenous coagulation should be given dexamethazone 3 mg/kg BW as a loading dose over 30 minutes, followed by 1 mg/kg BW every 6 hours for 24 to 48 hours in addition to parenteral anti microbial i.e.: cefriaxone 3 to 4 grams once daily iv. in adults or 80 mg/kg BW i.v. once daily in children for 3 to 7 days.

STATUS POST TREATMENT

The Relapse

The early use of effective spesific antibiotics is associated with a relatively high rate of relapse. Compared with untreated patients, the relapse rate is 20 % compared with 5-10%. Maybe prompt therapy inhibits the development of an adequate immune response. Usually relapses are milder than initial attack, and will respond to the same antibiotics used initially.

The Carriers

Choramphenicol appears to have little or no effect on the carier state. There was evidence that 10% of T.F. patients discharge typhoid bacilli in their faeces (faecal carriers) for 3 months after the onset of infection (Convalescence carrier), while 2-5% of these patients become persistent carriers (chronic carriers). Soewandojo, E. (in Surabaya) have reported 18% convalescence carriers from Dr.Sutomo Hospital , Surabaya, and Sabdoadi, et al (in Surabaya) reported 11.8% convalescence carriers, and 0.97% chronic carriers respectively.
Carriers are more common in women over the age of 40 years, no doubt due to the higher incidence of cholecystitis and gall stones.
Eradication of the chronic carrier state is very difficult, especially in the presence of gall stones. Commonly used regimens are 100 mg/Kg BW/day of ampicillin or amoxicillin plus probenecid (30 mg/Kg BW/day), or cotrimoxazole (trimethoprim-sulpha-

methaxazole 160/800 mg) twice daily plus probenecid 600 mg once daily for at least 6 weeks. Recent studies suggested that a 4-fluroquinolone should be the drug of choice against chronic carriers cases, with or without gall stones.

PREVENTION AND CONTROL

Usually improvement of environmental sanitation's including sewage disposal and water supplies, will sharply reduce the incidence of T.F. Supervision of restaurants, ice factories, food industries, against food handling (Chronic carriers), and the quality of water and raw materials, is very important. Special attention must be given to the ice vendors in the urban or rural areas in Indonesia. Immunization has been used to protect high-risk persons, where those approaches are not yet possible, and for travelers. There are 3 kinds of vaccine :

1. Tradional heat-killed phenol extracted whole typhoid vaccine
   The protective efficacy of multiple doses are 65% and last just a few months
   Side effect : local pain on injection side, fever post vaccination
2. First generation live oral vaccine (Ty-21a)
   Three doses, orally, will produce the protective efficacy equivalent to the killed vaccine, but last for at least several years
3. Purified Vi polysaccharide vaccine
   One dose has been proven as effective and long lasting as multiple doses of Ty-21a vaccine
4. Genetically engineered live vaccines and Vi-protein conjugates vaccine
   The vaccines are still actively being developed

A short overview of typhoid fever in Dr. Sutomo Hospital, Surabaya.

Department of Paediatric

During the period of 1991-1996 (6 years), there were 147 hospitalized typhoid fever patients, with 3 cases (0.26%) deaths (Table 5). All of them with sepsis and septic shock complication (Table 6).

Table 5. Incidence of typhoid and its mortality in Department of Paediatric Dr.Sutomo Hospital Surabaya (1991-1996).

Year	Male	Female	Numbers	Deaths
1991	122	111	233	– (0 %)
1992	126	109	235	1 (0.42 %)
1993	112	98	210	2 (0.95 %)
1994	98	71	169	– (0 %)
1995	87	83	170	– (0 %)
1996	75	55	130	– (0 %)
Total	620	527	1147	3 (0.26 %)

Table 6. Type of complications and its mortality in Department of Paediatric Dr.Sutomo Hospital Surabaya (1991-1996)

Complications	1991	1992	1993	1994	1995	1996	Numbers	Deaths
Intestinal hemorrhage	–	–	–	2	–	–	2	–
Febrile convulsion	–	–	–	–	1	–	1	–
Sepsis + Septic shock	7	2	2	3	2	1	17	3 (17.65 %)
Perforation & peritonitis	–	–	–	–	–	1	1	–
Encephalopathy	–	–	–	–	–	3	3	–
Total	7	2	2	5	3	5	24	3 (12.5 %)

Table 7. Incidence of typhoid fever and its mortality in Department of Internal Medicine Dr.Sutomo Hospital Surabaya (1991-1997)

Year	*Male*	*Female*	*Numbers*	*Deaths*
1991	156	177	333	8 (2.40 %)
1992	146	187	333	6 (1.80 %)
1993	161	221	382	5 (1.30 %)
1994	123	172	295	9 (3.05 %)
1995	133	158	291	6 (2.06 %)
1996	144	190	334	6 (1.79 %)
1997*	102	86	188	0 (0 %)
Total	965	1191	2156	40 (1.85 %)

* *Until: October 1997*

Table 8. Type of complications and its mortality in Department of Internal Medicine Dr.Sutomo Hospital Surabaya (1991-1997)

Complications	1991	1992	1993	1994	1995	1996	1997	Numbers	Deaths
Sepsis + Septic shock	10	10	4	13	8	10	6	61	38 (62.30 %)
Intestinal hemorrhage	16	15	15	16	5	4	4	75	2 (2.67 %)
Cerebral organic syndrome	2	10	12	17	12	8	5	66	
Perforation	-	-	-	-	1	-	-	1	
Reactive Hepatitis	5	2	-	4	4	2	1	18	
Acute renal failure	1	-	-	-	1	-	1	3	
Total	34	37	31	50	31	24	17	224	40 (17.85 %)

Department of Internal Medicine

During the period of 1991-1997 (October 1997), there were 2156 typhoid fever patients hospitalized, with 40 cases (1.85%) deaths (Table 7). It's caused by: sepsis and septic shock (38 cases = 62.3%), and intestinal hemorrhage (2 cases = 2.67%), (Table 8).

Department of Surgery

During period of 1991-1997 (until October 1997), there were 57 patients hospitalized with intestinal perforation, and only one case (1.7%) death (Table 9).

Table 9. Incidence of typhoid fever with intestinal perforation and its mortality in Department of Surgery, Dr. Sutomo Hospital Surabaya (1991-1997)

Year	Male	Female	Numbers	Deaths
1991	4	1	5	–
1992	1	1	2	–
1993	6	1	7	–
1994	10	–	10	1 (sepsis)
1995	7	2	9	–
1996	11	3	14	–
1997*	9	1	10	–
Total	48	9	57	1 (1.75%)

* *Until: October 1997*

Table 10. The Cases Fatality Rate (CFR) of septic shock, Intestinal Hemorrhage and Perforation in Dr. Sutomo Hospital Surabaya (1991-1997).

Complications	Septic shock			Intestinal Hemorrhage			Intestinal Perforation		
Department	N	Fatality		N	Fatality		N	Fatality	
		N	%		N	%		N	%
Paediatric	17	3	17.65	2	-	-	1	-	-
Internal Medicine	61	38	62.30	75	2	2.67	1	-	-
Surgery	57	1	1.75	-	-	-	57	1	1.75
Total	135	42	31.11	77	2	2.59	59	1	1.69

Total cases fatality rate (CFR) of septic shock, intestinal hemorrhage and perforation in Dr.Sutomo Hospital Surabaya (1991-1997), were 31.11%, 1.69%, and 2.59%, respectively (Table 10).

SUMMARY

Typhoid fever is endemic in Indonesia. The incidence is 350-810 cases per 100,000 population, annually, with CFR 2-8%. The main causes of death are septic shock, intestinal bleeding and intestinal perforation. The clinical pictures are not significantly change during 20 years. Prolong fever is the main sign and symptom. Normal leukocyte count is usually found, and blood culture is the standard diagnostic of TF. Bone marrow culture is more sensitive than blood culture but because it is invasive, it's not done routinely. Widal test is still widely used but its interpretation must be taken carefully. Recently, Typhi-dot is used as screening test in the community, and PCR is used, as academic not routinely tests. Chloramphenicol is still the drug of choice, and the alternative drugs are: ampicillin/amoxicillin, co-trimoxazole, thiamphenicol, 3rd generation cephalosforin, and 4-fluoro-quinolone. High dose dexametasone should be given for severe cases. Approximately 20% of the patients treated with chloramphenicol become relapse, 10% become convalescence, and 3-5% become chronic carrier. Improvements of environmental sanitation; management of chronic carriers, and immunization are the main prevention and control of TF. In Dr.Sutomo Hospital, Surabaya, during 5 years period (1991-1996) in the pediatric department 1147 cases were hospitalized, with 3 (0.26%) death caused by sepsis and septic shock. In The Department of Internal Medicine, during 6 years period (1991- October 1997), 2156 cases were hospitalized, with 40 (1.85%) death, caused by sepsis + septis shock (38 cases), and intestinal haemorrhage (2 cases). In The Department of Surgery, during the same period, 57 cases of TF perforation were hospitalized, with one (1.75%) death.

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