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Infection and Tropical Disease

INF-OP-1-3-003

Clinical features of rabies associated with mortality

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INF-OP-1-3-004

Antimicrobial sensitivity of *Salmonella typhi* in Pediatric Ward of Sutomo Hospital

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Abstract

Background Rabies is one of the leading cause of childhood mortality in Manado, North Sulawesi. Clinical features identification to predict the mortality is needed to improve the management.

Objective To identify the clinical features that can predict the mortality in rabies patient.

Methods A 5- year retrospective cohort study was conducted from January 2008 to March 2013. Twenty three children with rabies dog bite were enrolled at the Prof Dr. R.D. Kandou Hospital between the age 1 year to 14 years. We had analyzed clinical feature that predict death.

Results Hypersalivation, excitation, aerophobia, photophobia, hidrofobia, and convulsion showed the highest mortality rate (100%) and statistically significant ($P<0.001$). Dog bite below 30 days had 88.9% mortality rate and statistically significant ($P<0.001$). Sex, age, duration of the fever, location of bite, and the laboratory finding (hemoglobin, leucocyte, hematocrite, and thrombocyte) did not associate with mortality ($P>0.05$).

Conclusion Hypersalivation, excitation, aerophobia, photophobia, hidrofobia, and convulsion are the most important clinical features that can predict the mortality in rabies patient. Dog bites below 30 days are another important factor to predict the mortality in rabies patient.

Keywords: rabies, clinical manifestations

Abstract

Background *Salmonella typhi* infection remains to be a major problem in developing countries and there were report of multi-drug resistant *S.typhi* (MDRST) in other region. There has been no reported data on MDRST in Surabaya.

Objective To describe the antimicrobial sensitivity features to *S.typhi* in Surabaya.

Methods This was a cross sectional study based on medical records of children admitted to the Department of Child Health Soetomo Hospital Surabaya with *S.typhi* infection from January 2009 to December 2012. *S.typhi* infection was defined according to positive blood cultures from typhoid fever patients.

Results During the study period, there were 30 positive *S.typhi* isolates in children aged 1 to 13 years. Sensitivity to the first line antibiotics consisting of chloramphenicol, ampicillin, and cotrimoxazole was 30/30, 25/30, and 27/30, respectively, while sensitivity to the second line antibiotics cefotaxim and ceftriaxone were 26/30 and 20/30 respectively.

Conclusion *S typhi* is highly sensitive to the first line drugs, subsequently reflecting the absence of MDRST.

Keywords: *Salmonella typhi*, antimicrobial sensitivity

ANTIMICROBIAL SENSITIVITY OF *SALMONELLA TYPHI*

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Surabaya, Indonesia

Abstract

Background *Salmonella typhi* infection remains to be a major problem in developing countries and there were report of multi-drug resistant *S.typhi* (MDRST) in ether region. There has been no reported data on MDRST in Surabaya.

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Results During the study period, there were 30 positive *S.typhi* isolates in children aged 1 to 13 years. Sensitivity to the first line antibiotics consisting of chloramphenicol, ampicillin and cotrimoxazole was 100%, 83.33%, and 90%, respectively, while sensitivity to the second line antibiotics cefotaxim and ceftriaxone were 86.66% and 66.66% respectively.

Conclusion *S typhi* was highly sensitive to the first line drugs, subsequently reflecting the absence of MDRST.

Keyword *Salmonella typhi*, antimicrobial sensitivity

1. Latar Belakang

Demam tifoid merupakan infeksi sistemik yang disebabkan oleh *Salmonella enteritica* serotype typhi, famili Enterobacteriaceae.¹⁻⁵ Demam tifoid ini merupakan penyakit endemis di Afrika dan Asia, dan menetap di Timur Tengah, sebagian Negara-negara Eropa selatan dan timur, serta Amerika Serikat dan selatan.⁴ Hingga saat ini demam tifoid masih menjadi penyebab morbiditas dan mortalitas yang cukup tinggi di seluruh dunia, terutama di negara berkembang, bahkan negara maju. Menurut data WHO diperkirakan minimal 12,5 juta kasus terjadi tiap tahunnya di seluruh dunia.² Sedangkan menurut penelitian terbaru yang dilakukan tahun 2004 sedikitnya terdapat 22 juta kasus demam tifoid per tahun dengan angka kematian 200.000 per tahun.⁴ Di Indonesia sendiri terdapat rata-rata 900.000 kasus per tahun, terutama terjadi pada usia antara 3 tahun hingga 19 tahun (91%), dan menyebabkan kematian lebih dari 20000.² Data yang pernah dikumpulkan di bagian anak RSUD Dr Soetomo Surabaya tahun 1987-1992 diperoleh angka 1402 penderita demam tifoid, 434 (31%) diantaranya ditemukan kuman *S.enteritica* serotype typhi dalam darahnya, terutama menyerang anak berusia di atas 3 tahun (64%), tidak ada perbedaan bermakna antara jenis kelamin laki-laki dan perempuan.⁶ Angka pasti demam tifoid sulit dihitung karena gambaran klinisnya sulit dibedakan dengan penyakit yang disertai

panas lainnya. Di sebagian besar daerah mempunyai keterbatasan fasilitas untuk menegakkan diagnosis demam tifoid, maka penentuan diagnosis adalah secara klinis, dan diberikan terapi standart.⁴

Penggunaan antibiotika pada manusia, binatang, baik sebagai terapi penyakit infeksi atau hanya sebagai profilaksis secara sembarangan tanpa seleksi menghasilkan penyebaran secara luas bakteri yang resisten terhadap antimikroba.⁴ Pola resistensi dan sensitifitas *S.enteritica* serotipe typhi terhadap antimikroba berbeda di tiap daerah dan berubah setiap saat.⁷⁻⁸ Ada dua kategori resistensi obat : (i). resisten terhadap kloramfenikol, ampicillin, dan trimetoprim-sulfametoksasol (MDR strains) ; (ii). Resistensi terhadap fluoroquinolon, yang disebut nalidixic-acid-resisteant *S.typhi* (NARST), yang menjadi tanda penurunan sensitifitas terhadap fluoroquinolon, dibandingkan dengan nalidixic-acid-sensitive strains. Resistensi ini dapat total atau parsial. Di India didapatkan sejumlah besar strain MDR, dan beberapa Negara Asia lainnya, namun di Indonesia tidak didapatkan. Nalidixic-acid-resistant strains saat ini endemik di beberapa Negara di Vietnam dan telah dilaporkan dari India dan Tajikistan. Yang lebih meresahkan, diperoleh laporan, walupun masih sedikit, munculnya resistensi kuman terhadap sefalosforin generasi ketiga di Asia. Namun, laporan tersebut

juga disertai bukti munculnya kembali strain yang sensitif terhadap antimikroba lini pertama.²

2. Obyektif

Penelitian ini dilaksanakan untuk mengevaluasi pola sensitivitas antibiotik *S.typhi* di Surabaya.

3. Metode:

Studi *cross sectional* berdasarkan rekam medis pasien di mana didapatkan hasil kultur darah positif *Salmonella typhi* sejak bulan Januari 2011 sampai dengan Desember 2012 dan January 2011 sampai dengan December 2012.

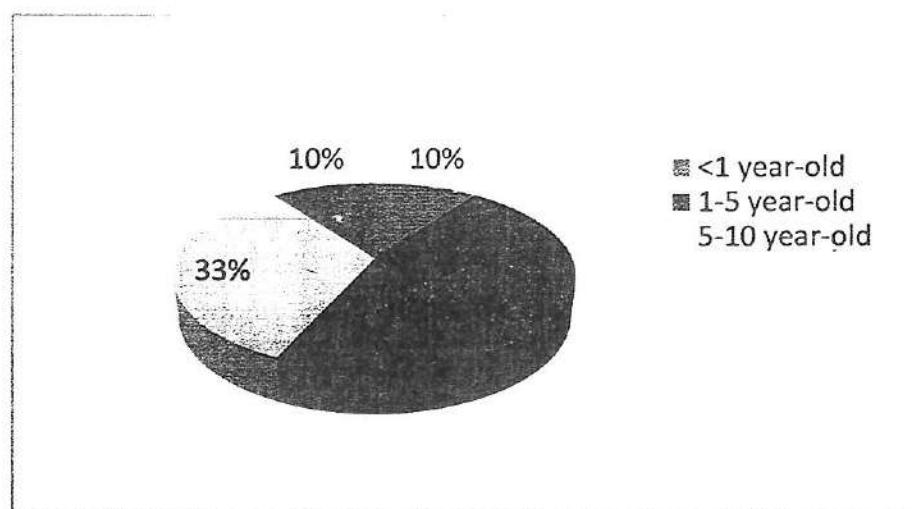
Infeksi *S.typhi* ditegakkan bila didapatkan kultur darah positif *S.typhi* pada pasien demam tifoid. Data kultur darah didapatkan dari Departemen Mikrobiologi, rumah sakit dr. Soetomo Surabaya.

Kriteria inklusi adalah penderita anak di RSU Dr Soetomo Surabaya, baik rawat inap atau rawat jalan, dengan hasil kultur darah *Salmonella typhi*. Pemeriksaan kultur darah dan antibiogram dilakukan dengan teknik Bactec oleh Laboratorium Mikrobiologi RSU Dr Soetomo Surabaya.

4. Hasil:

Selama periode studi, didapatkan 30 sampel positif *S.typhi* pada anak usia 1 sampai 13 tahun. Sensitivitas pada lini pertama antibiotik yang terdiri dari chloramphenicol, ampicillin dan cotrimoxazole berturut-

turut adalah 100%, 83.33%, dan 90%, dimana sensitivitas terhadap lini kedua antibiotik berturut-turut adalah cefotaxim dan ceftriaxone sebesar 86.66% dan 66.66%.

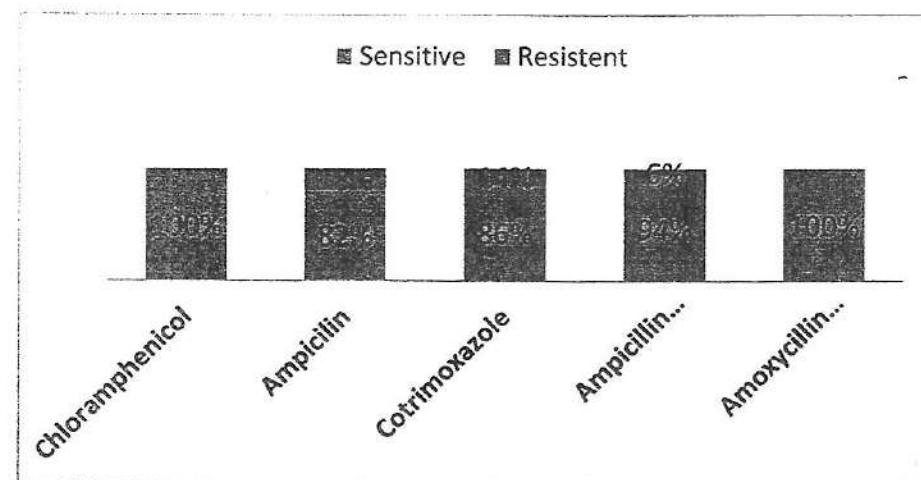


Gambar 1. Usia penderita

Selama Januari 2008 sampai dengan Juli 2009, didapatkan hasil 12 kultur darah positif *Salmonella typhi*. Semua sampel sensitif (100%) terhadap chloramphenicol dan ciprofloxacin. Sensitivitas terhadap ampicillin dan cotrimoxazole adalah 83.3%.

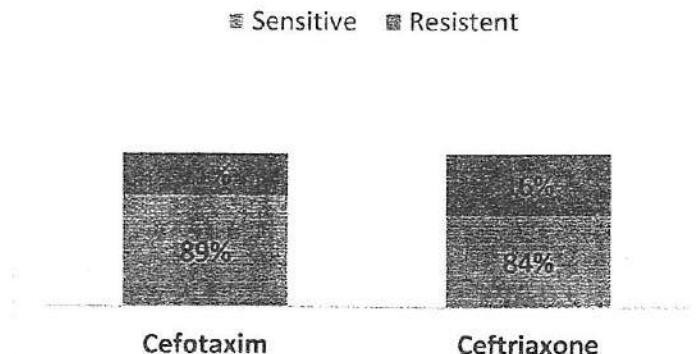
Lima sampel (41,7%) diduga demam tifoid dengan riwayat demam lebih dari 7 hari dan gejala gastrointestinal (CI 95%; 0,13-0,69). Semua pasien dengan keluhan nyeri perut. Gejala gastrointestinal meliputi diare (8,3%), konstipasi (8,3%), meteorismus pada 4 anak (33,3%), dan mual-muntah pada 3 anak (25%). Tujuh anak (58,3%) dengan keluhan demam kurang dari 7 hari dan tanpa gejala gastrointestinal (CI 95%; 0,30-0,86). Empat anak (25%) dengan bronchopneumonia (batuk, dispnu, retraksi dada dan ronki basah

kasar), dua (16,6%) dari empat anak juga didapatkan sepsis. Dua (16,6%) dengan faringitis akut (didapatkan juga penurunan nafsu makan). Satu anak (8,3%) dengan demam subfebris 1 hari sebelum dirawat di rumah sakit dan didiagnosa sebagai Guillan-Barre Syndrome dikarenakan didapatkan gejala *ascending paraplegia*.



Gambar 2. Sensitivitas antimikroba lini pertama

Respon klinis baik dengan penurunan gejala demam setelah terapi mean 3,8 hari (grup dengan sensitivitas antibiotik 100%) dan 4,25 hari (grup). Satu pasien meninggal dengan diagnosis selain demam tifoid (Guillan Barre Syndrome).



Gambar 3. Sensitivitas antimikroba lini kedua

5. Diskusi:

Pada penelitian ini sensitivitas antimikroba chloramphenicole adalah 100%. Menurut Chandra, resistensi terhadap chloramphenicole sudah dilaporkan sejak tahun 1978. Sedangkan menurut Manchanda, resistensi terhadap chloramphenicole dilaporkan sebesar 3%. Sejak ditemukannya chloramphenicole dan terbukti sensitif terhadap *Salmonella typhi*, serta penggunaan antibiotika alternatif lain, ternyata merubah perjalanan klinis demam tifoid. Penggunaan antibiotika pada penderita tifoid diyakini dapat memperpendek perjalanan penyakit, mengurangi komplikasi dan mengurangi angka kematian kasus.

Gejala demam tifoid sangat bervariasi tergantung derajat keparahannya.^{2,4} Manifestasi klinis demam tifoid sangat dipegaruhi umur. Pengamatan klinis di Surabaya yang dilakukan selama 6 tahun (1987-1992) oleh Darmowandowo pada 434 anak dengan demam tifoid atas dasar ditemukannya *S.enteritica* serotype typhi dalam darah dimana 85% penderita sudah mendapat antibiotika sebelum masuk rumah sakit dan tanpa memperhitungkan dimensi waktu sakit dari penderita,

maka didapatkan keluhan dan gejala klinis pada penderita sebagai berikut; anoreksia (88%), nyeri perut (49%), muntah (46%), obstruksi (43%), diare (31%) dan panas (100%). Delirium (16%), apatis (5%), somnolens (5%), sopor (1%), lidah kotor (54%), meteorismus (66%), hepatomegali (67%) dan splenomegalia (7%).⁶

Kelemahan penelitian ini adalah jumlah sampel yang terlalu sedikit. Sehingga tidak dapat digunakan untuk memprediksi kemungkinan suatu demam tifoid pada tahap awal.

Kesimpulan dari penelitian ini adalah tidak ditemukannya gambaran yang khas dan spesifik pada penderita dengan bakteremia *S.typhi*, terutama pada minggu pertama. Pada saat awal bakteremia *S.typhi* dapat menyerupai penyakit lain yang disertai demam.

6. Kesimpulan:

Sensitivitas lini pertama antibiotika terhadap *Salmonella typhi* masih tinggi. Tidak ada gambaran MDRST di RS Dokter Soetomo Surabaya.

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**ANTIMICROBIAL SENSITIVITY OF SALMONELLA TYPHI
IN PEDIATRIC WARD SOETOMO HOSPITAL**

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INTRODUCTION

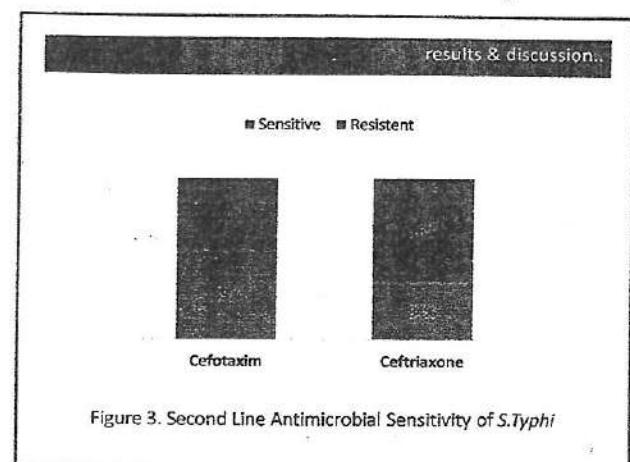
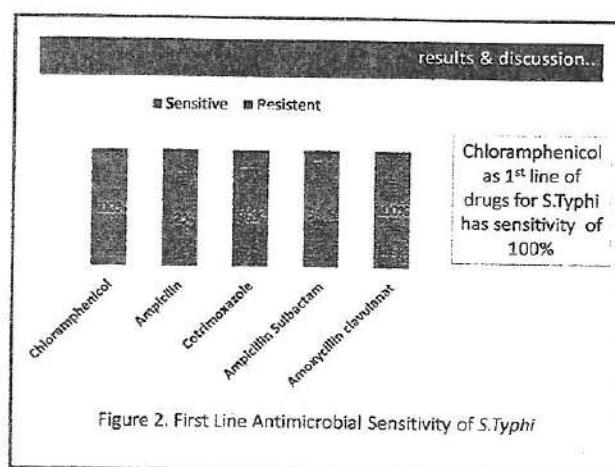
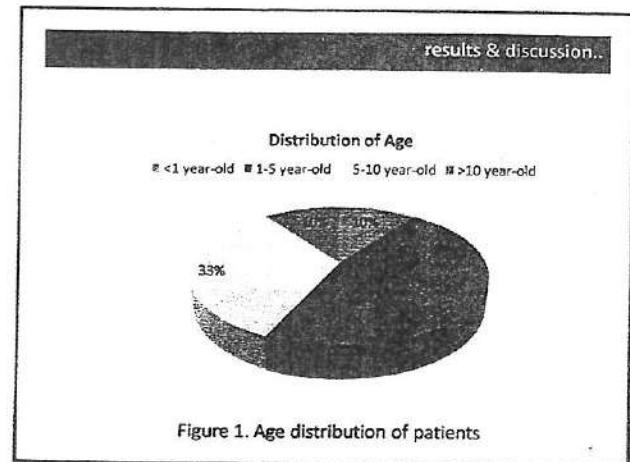
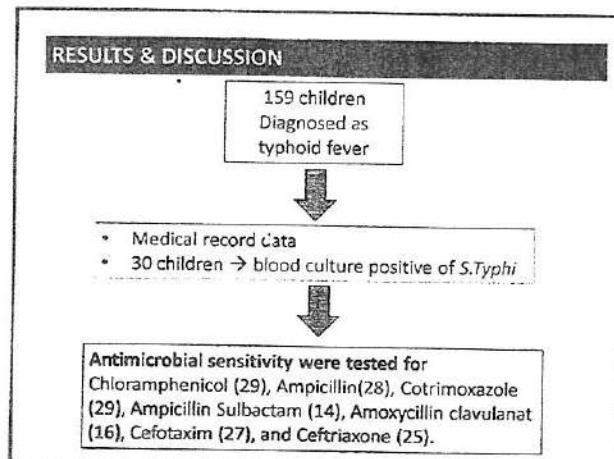
- *Salmonella Typhi* (*S. Typhi*) infection → high morbidity & mortality worldwide in adult and child
(Burton, 1990; Edwards, 2010)
- Emerging resistant strain of *S.Typhi* to 1st line drugs (Chloramphenicol, Cotrimoxazol & Ampicillin) has reported in adult
(Burton, 1990; Edwards, 2010)
- MDRST (multi-drug resistant *S.Typhi*) ↑ & some outbreak reported worldwide
(Vasse, 1971; Ahola, 1978; Liyanage, 2000; Kurniadi, 2001; Indraputra, 2006)
- India: MDRST → 66.6% ↑ morbidity & mortality
(Kumar, 2007)
- MDRST in pediatric typhoid in Surabaya never been reported.
(Prasetyaningsayasa, 2010)

OBJECTIVE

To describe the antimicrobial sensitivity pattern to *S.Typhi* in Surabaya

METHODS

Design : Descriptive study
Subject : Blood culture results recorded from children < 18 years diagnosed as typhoid fever at Soetomo Hospital.
Duration : 2009 to 2012
Outcome : antimicrobial sensitivity to *S.Typhi*, tested for Chloramphenicol , Ampicillin, Cotrimoxazole , Ampicillin Sulbactam, Amoxicillin clavulanat, Cefotaxim, and Ceftriaxone.



results & discussion..

- From 30 children with blood culture positive, 6 (20%) children were having malnutrition.
- One child died due to other disease: Guillain Barre Syndrome.
- One child was a patient of hematologic outpatient clinic, diagnosed as ITP (Idiopathic Thrombocytopenia Purpurae).
- All patients got the first line drugs for typhoid fever intravenously.

DISCUSSION**In our study**

- Sensitivity to chloramphenicol was 100%

Chandra (1984)

-Resistance to chloramphenicol was reported since 1978

Manchanda, 2005

-Chloramphenicol Resistance (3%)

Mamtaz (2002)

-Resistance to Ampicillin, Cotrimoxazole & chloramphenicol was 39%, 36%, 25%, respectively

results & discussion..**In our study**

- No MDRST was reported

Manchanda, 2005

-56 isolates → MDRST 22 cases (39%)

CONCLUSION

Sensitivity to the first line antimicrobial to *S. Typhi* is high

THANK YOU

RESULTS

Table 1. First Line Antimicrobial sensitivity of *S.Typhi*

Antimicrobial	Resistant number (n)	Total number (n)	Percentage (%)
Ampicillin	5	28	17.8
Ampicillin sulbactam	1	15	6.67
Amoxicillin	not tested		
Amoxicillin clavulanat	0	16	0
Cotrimoxazole	4	29	13.8
Chloramphenicol	0	30	0

DISCUSSION

Year	Total number of <i>S.typhi</i> strains isolated	Resistant Number (%)
1978	52	1 (1.92)
1979	89	11 (12.35)
1980	93	2(2.15)
1981	70	5 (7.14)
1982	96	8 (8.33)
1983	144	55 (38.19)
1984	26	6 (23.07)

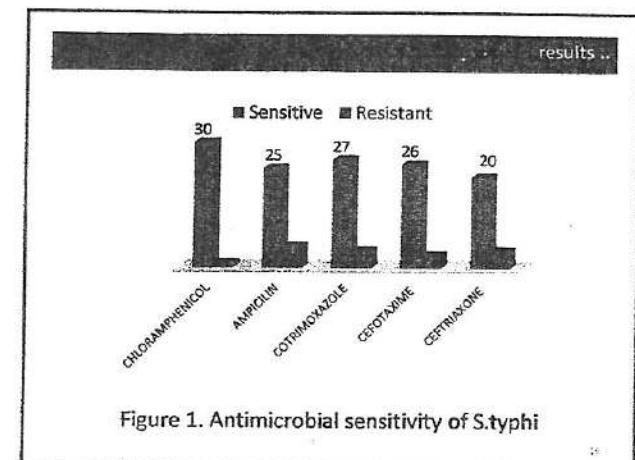


Figure 1. Antimicrobial sensitivity of *S.typhi*

DISCUSSION

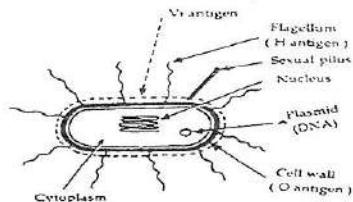
Chandra (1984), Butler (1988)

Chloramphenicol → drug of choice for typhoid fever.

Lampe (1973)

Chloramphenicol-resistant *S. typhi* has recently been reported from Mexico, India and Vietnam.

Penyebab : *S.enteritica* serotype *typhi*
 bakteri gram negatif
 mengandung antigen O, H, Vi.

**METHODS**

Children with typhoid fever

Blood specimen collected → Bactec bottle

Incubated at 37°C → positive bottle were inoculated into blood & Mc Conkey agar

Reading of the antibiotic test were using CLSI standart 2011

Rapid automatic Phoenix system

Tested biochemically

Gambaran klinis demam tifoid di RS Dr.Soetomo :

- ✓ Anoreksia (88%)
- ✓ Nyeri perut (49%)
- ✓ Muntah (46%)
- ✓ Obstipasi (43%)
- ✓ Diare (31%)
- ✓ Panas (100%)
- ✓ Delirium (36%)
- ✓ Apati (5%)
- ✓ Somnolens (5%)
- ✓ Sopo (1%)
- ✓ Lidah kotor (54%)
- ✓ Meteorismus (66%)
- ✓ Hepatomegali (67%)
- ✓ Splenomegali (7%)

Gambutan Miris	Panas < 7 hari (n=7)	Panas > 7 hari (n=6)
Keluhan:		
Panasi Langsung tinggi	2	-
Arah tengggak	5	5
Dare	1	1
Kontaklesi	-	1
Mati	-	3
Membekuk	1	2
Nyeri perut	1	5
Nyeri kepala	-	2
Batuk	4	2
Sekak	4	-
Nyeri telan	2	-
Paraplegi	1	-
Gigik	6	5
Kerasaratan Kompresi intimes	1	-
Apatis	2	-
Faring hipertoni	-	3
Kembung	1	2
Pembengkakan has	4	-
Rokok habus	6	-
Tekukan dinding dada	-	-

(Presbytaryns, 2010)

Terapi demam tifoid dengan komplikasi

Susceptibility	Antibiotic	Optimal parenteral drug		Alternative effective parenteral drug	
		Daily dose mg/kg	Days	Antibiotic	Daily dose mg/kg
High sensitive	Fluoroquinolone e.g. ofloxacin	15	10-14	Chloramphenicol Amoxicillin TMP-SMX	100 100 5-40
Multidrug resistant	Fluoroquinolone	15	10-14	Ceftriaxone or cefotaxime	60 30
Quinolone resistant	Ceftriaxone or cefotaxime	60	10-14	Fluoroquinolone	20
					7-14

An **open-label trial** or **open trial** is a type of **clinical trial** in which both the researchers and participants know which treatment is being administered.

Open-label trials may be appropriate for comparing two very similar treatments to determine which is most effective. An open-label trial may be unavoidable under some circumstances, such as comparing the effectiveness of a medication to intensive physical therapy sessions.



C E R T I F I C A T E

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Dominicus Husada

Has attended in

THE 6th CHILD HEALTH ANNUAL SCIENTIFIC MEETING OF INDONESIAN PEDIATRIC SOCIETY

October 7-9, 2013 in Solo, Central Java, Indonesia

[Handwritten signature]

Badril Hendar, dr., Sp.A(K), PhD

President of Indonesian Pediatric Society

[Handwritten signature]
Prof. Dr. Harsono Salimo, dr., Sp.A(K)
Chairman of the Committee



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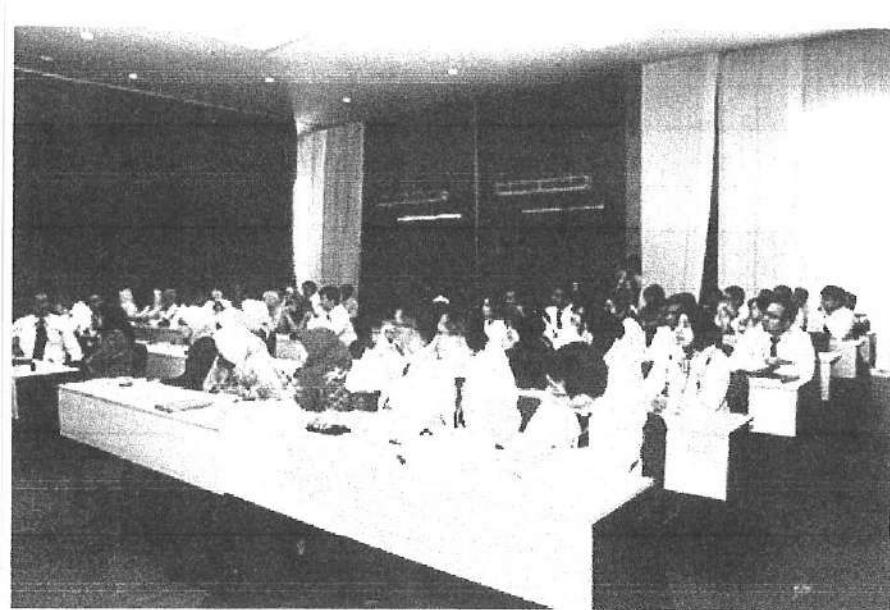
GALERI] PERTEMUAN ILMIAH TAHUNAN ILMU KESEHATAN ANAK KE-6 (PIT VI)

to Kegiatan PIT IKA 6 Solo yang diselenggarakan pada tanggal 5-9 Oktober 2013, dengan topik acara "Acceleration of DGs 2015 Achievement with Comprehensive Management of Pediatric Problems".

orkshop Badan Penerbit "Pemantapan Mutu Publikasi Guna Mencapai Akreditasi Prima"



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Workshop UKK Alergi Imunologi