

International Journal of Innovative Pharmaceutical Sciences and Research

www.ijipSR.com

STUDY ON THE MEDICINE USE OF SCRUB TYPHUS IN COMPARISON WITH DHR-ICMR GUIDELINES

¹Prathyusha Mandala *, ¹N Ganesh Rajan**, ¹P.Mahendrarvarman, ²S.Chidambarnathan

¹Department of Pharmacy Practice, Annamalai University, Tamil Nadu, INDIA

²Department of Paediatrics, RMMCH, Annamalai University, Tamil Nadu, INDIA

Abstract

Observational prospective study on the medicine management of scrub typhus in paediatric unit. The objective of the study is to observe prescription pattern for the management of scrub typhus in comparison with DHR-ICMR guidelines and adverse drug reactions (if present any) in the Department of paediatrics at Rajah Muthiah Medical College & Hospital (RMMCH). The study was conducted by collecting data from the patients who were referred to or admitted in the department of paediatrics at the tertiary care teaching hospital. The study was conducted among the patients admitted in paediatrics with scrub typhus (November 2016 – April 2017). The pattern of medication use was obtained from the case sheets and patient interview. A total of 47 patients were included in this study and the patients were selected based on the inclusion & exclusion criteria. Out of total population of 47 enrolled in this study, mostly prescribed with Ceftriaxone and Azithromycin as the primary therapy & others as adjuvant therapy. Antibiotic therapies of Ceftriaxone, Amikacin, Ampicillin, Amoxicillin+ Clavulanic acid, Gentamycin are given as empirical therapy before confirmation of diagnosis. Later changed to Doxycycline or Azithromycin as primary therapy. Thus the given treatment regimen in our hospital completely complies with the standard DHR-ICMR treatment guidelines of Scrub Typhus.

Keywords: Scrub Typhus, DHR-ICMR, antibiotics, doxycycline, azithromycin, paediatrics.

Corresponding Author:

Prathyusha Mandala & N Ganesh Rajan

Department of Pharmacy Practice,

Annamalai University,

Tamil Nadu, INDIA

E-mail: prathyushamandala025@gmail.com / ganeshpharma01@gmail.com

Phone: +91-9514677736 / +91-7418312295

INTRODUCTION

In India, many cases of scrub typhus were reported and recently the numbers of cases are increasing in southern region. The reported variety of cases of scrub typhus from totally different components of the country notably from giant tertiary care hospitals don't provides a true image of prevalence of scrub typhus within the country. Thus far there don't seem to be several community primarily based studies in our country. One such community primarily based study involving many districts in state showed that rickettsial disease and bacterium diseases were cosmopolitan within the state [1-4]. Scrub Typhus is an acute, febrile, infectious illness that is caused by *Orientia* family *Rickettsia tsutsugamushi*. It is also known as *tsutsugamushi* disease. Humans are accidental hosts in this zoonotic disease [5]. These are the diseases caused by *rickettsiae*, which are small, gram-negative bacilli adapted to obligate intracellular parasitism and transmitted by arthropod vectors.

DHR-ICMR GUIDELINES

There is paucity of evidence based on randomized controlled trials for the management of *rickettsial* diseases including Scrub Typhus [6]. These guidelines for treatment cover the most common infection, the Scrub Typhus, Murine Typhus and Indian Tick typhus and do not cover acute Q fever though treatment of Q fever is on similar lines. Without waiting for laboratory confirmation of the *Rickettsial* infection, antibiotic therapy should be instituted when *rickettsial* disease is suspected.

STANDARD TREATMENT:

At Primary level:

The Health Care provider needs to do the following:

- a) Recognition of disease severity, if the patients come with complications to primary health facility and treating physician considers it as rickettsial infection, treatment with *Doxycycline* should be initiated before referring the patient.
- b) Referral to secondary or tertiary centre in case of complications like ARDS, acute renal failure, meningo-encephalitis, multi-organ dysfunction. In addition to recommended management of community acquired pneumonia, *Doxycycline* is to be initiated when scrub typhus is considered likely.
- c) In fever cases of duration of 5 days or more where malaria, dengue and typhoid have been ruled out; following drugs should be administered when scrub typhus is considered likely –

Doxycycline in the dose of 4.5 mg/kg body weight/day in two divided doses for children below 45 kg

Or

Azithromycin in the single dose of 10mg/kg body weight for 5 days.

At secondary and tertiary care:

The treatment as specified above in uncomplicated cases.

b) In complicated cases the following treatment is to be initiated –

i) Intravenous *Doxycycline* (wherever available) 100mg twice daily in 100 ml normal saline to be administered as infusion over half an hour initially followed by oral therapy to complete 7-15 days of therapy.

Or

ii) Intravenous *Azithromycin* in the dose of 500mg IV in 250 ml normal saline over 1 hour once daily for 1-2 days followed by oral therapy to complete 5 days of therapy [8].

Or

iii) Intravenous *Chloramphenicol* 50-100 mg/kg/d 6 hourly doses to be administered as infusion over 1 hour initially followed by oral therapy to complete 7-15 days of therapy.

iv) Management of the individual complications should be done as per the existing practices.

Doxycycline and/or *Chloramphenicol* resistant strains have been seen in South-East Asia. These strains are sensitive to *Azithromycin* [6, 7, 9].

MATERIALS & METHODS

This was a prospective, observational Study carried out over a 6 month period from NOVEMBER 2016- APRIL 2017 at Rajah Muthiah Medical College & Hospital, Annamalai Nagar-608002, Tamilnadu, India. The study was conducted among the patients admitted in paediatrics with scrub typhus (November 2016 – April 2017). The pattern of medication use was obtained from the case sheets and by patient interview. A total of 47 patients were included in this study and the patients were selected based on the inclusion & exclusion criteria.

Inclusion Criteria:

Patients admitted in paediatrics wards for the diagnosis of Scrub Typhus.

Patients above 1 year of age.

Exclusion Criteria:

Patients above 12 years of age.

Patients who are not willing to participate.

RESULTS AND DISCUSSION

Table 1: Antibiotic Therapies

DRUG	NO.OF PATIENTS
CEFTRIAZONE	21
AZITHROMYCIN	20
DOXYCYCLINE	19
CEFOTAXIME	15
AMIKACIN	16
AMOXICILLIN + CLAVULANIC ACID	7
GENTAMYCIN	2

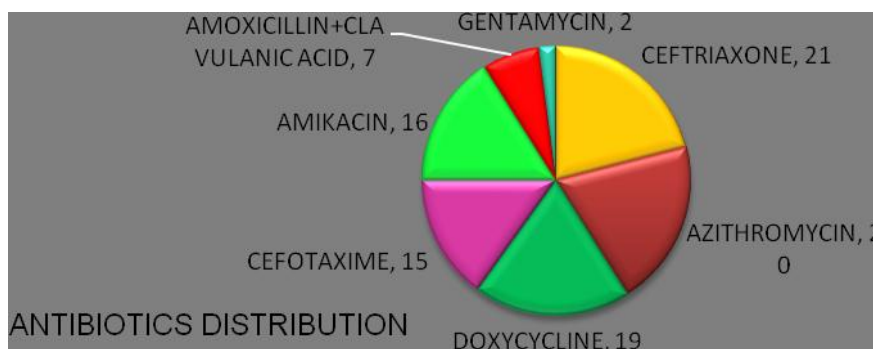


Fig. 1: Antibiotic Distribution

Out of 47 patients enrolled in our study, most of the patients are prescribed with Ceftriaxone and Azithromycin as primary therapy and other antibiotics are used as adjuvant therapy.

Table 2: Symptomatic Relieving Drugs

DRUGS	NO. OF PATIENTS	PERCENTAGE
Anti-tussive agents	24	51.06%
Tab.Clonazepam	4	8.51%
IV Fluid therapy	38	80.85%
Paracetamol Suppository	7	14.89%
Syp.Paracetamol	29	61.70%
Syp.Bifilac	2	4.25%
Syp.Chloroquine	5	10.63%
Tab. Mefenamic acid	1	2.12%
Tab. Paracetamol	14	29.78%
Inj. Ondansetron	13	27.65%
Inj. Ranitidine	12	25.53%
Inj. Vitamin A	3	6.38%
Tab. MVT	13	27.65%
Syp.Thrombobliss	4	8.51%
Syp.Choline salicylate +benzakonium chloride	1	2.12%
Tab. Albendazole	2	4.25%
Tab.chlorphenramine maleate	2	4.25%

ORS	3	6.38%
Syp.Terbutaline	2	4.25%
Tab.B complex	6	12.75%
Tab.Metronidazole	1	2.12%
Inj.Dopamine	3	6.38%
Tab Lansoprazole	11	23.40%
Inj Vitamin k	1	2.12%
Inj. Furosemide	1	2.12%

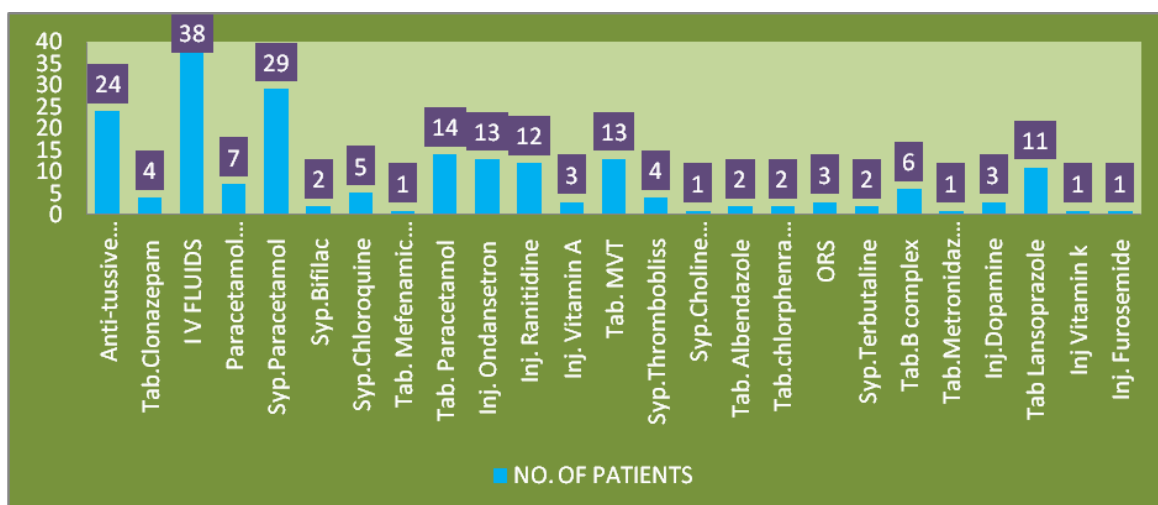


Fig. 2: Symptomatic Relieving Drugs Distribution

Out of 47 prescriptions, 47 patients were prescribed with paracetamol followed by 24 patients with anti-tissuives for symptomatic relief and 38 patients were given IV fluids as supportive therapy.

Table 3: Duration of Therapy

DRUGS	DURATION OF THERAPY		
	0-3 DAYS	3-6DAYS	>6DAYS
CEFTRIXONE	6	12	3
AZITHROMYCIN	5	14	0
DOXYCYCLINE	2	6	11
CEFOTAXIM	5	9	1
AMIKACIN	3	11	2
AMOXICILLIN+CLAVULANIC ACID	4	3	0
GENTAMYCIN	1	1	0

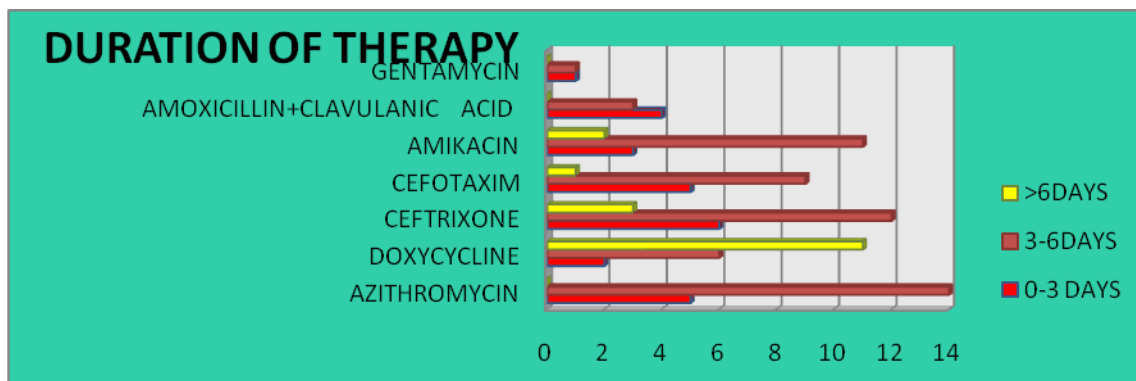


Fig. 3: Duration of Therapy

From the data obtained above – Empirical Therapy of ceftriaxone, gentamycin, ampicillin & amoxicillin were given as pre- diagnostics measure. After confirmatory test for scrub typhus, either doxycilline for 7 days or azithromycin for 5 days therapy is being initiated. Thus the given treatment regimen totally complies with the standard DHR-ICMR treatment guidelines of scrub typhus.

Table 4: Adverse Drug Reaction

DRUG	TYPE OF ADVERSE EVENTS
AZITHROMYCIN	Abdominal pain
CEFTRIAZONE	Rash
LANSOPRAZOLE	Constipation

Table 5: Calculation of Incidence Proportion of area

DRUG	NO. OF ADR REPORTED	GIVEN TOTAL NO.OF PATIENTS	INCIDENCE OF PROPORTION
AZITHROMYCIN	1	20	5%
CEFTRIAZONE	1	21	4.76%
LANSOPRAZOLE	1	11	9.09%

INCIDENCE PROPORTION

Formula:

Number of new cases of disease or injury During specified period / Size of population at start of period

FOR AZITHROMYCIN:

No .of new cases of ADR's = 1
Size of population = 20
Incidence proportion = $(1/20)*100$
= 5%

FOR LANZOPRALOZE:

No .of new cases of ADR's = 1
Size of population = 11
Incidence proportion = $(1/11)*100$
=9.09%

FOR CEFTRIAXONE:

No .of new cases of ADR's = 1
Size of population = 21
Incidence proportion = $(1/21)*100$
= 4.76%

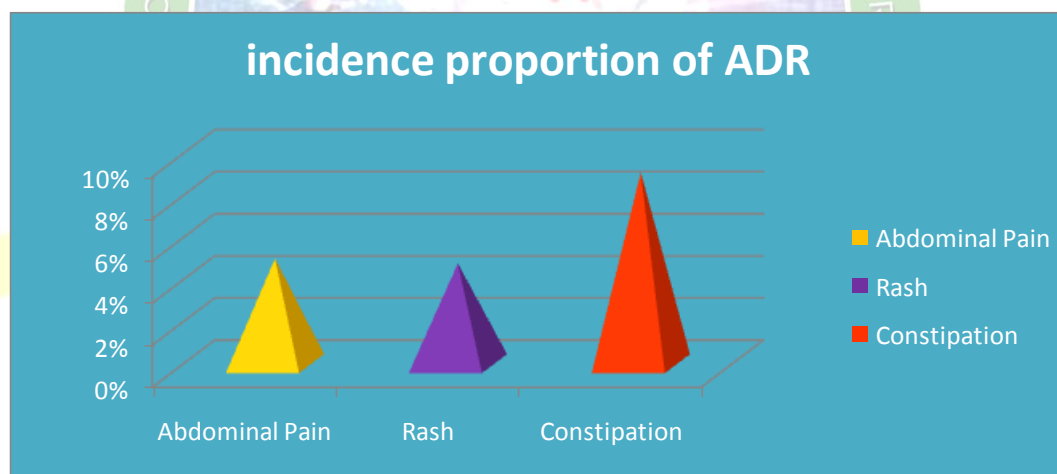


Fig. 4: Incidence proportion of area

The incidence proportion of ADR of Azithromycin, ceftriaxone and Lansoprazole were 5%, 4.76% and 9.09% respectively. Even though Azithromycin has high incidence of ADR it is one of the most frequently prescribed drug in our hospital. This is because our study was undertaken at a tertiary care teaching hospital where most of the patients seeking treatment are from poor socio economic class. So, they are prescribed medications available at hospital pharmacy which they can avail free of cost.

CONCLUSION

The motive of this study was to observe medicine use in comparison with DHR-ICMR guidelines and to observe adverse drug reactions (if present any). Out of total population enrolled in this study, Mostly prescribed with Ceftriaxone and Azithromycin as the primary therapy & others as adjuvant therapy. Antibiotic therapies of Ceftriaxone, Amikacin, Ampicillin, Amoxicillin+ Clavulanic acid, Gentamycin are given as empirical therapy before confirmation of diagnosis. Later changed to Doxycycline or Azithromycin as primary therapy. Thus the given treatment regimen in our hospital completely complies with the standard DHR-ICMR treatment guidelines of Scrub Typhus. The incidence proportion of ADR's of Azithromycin, Ceftriaxone and Lansoprazole were 5%, 4.76% and 9.09% respectively. Even though Azithromycin has incidence of ADR (abdominal pain) it is one of the most frequently prescribed drug in our hospital. This is because our study was undertaken at a tertiary care teaching hospital where most of the patients seeking treatment are from poor socio economic class. So, they are prescribed medications available at hospital pharmacy which they can avail free of cost.

REFERENCES

1. Bavaro MF, Kelly DJ, Dasch GA et al: History of US military contribution to the study of Rickettsial diseases. *Mil Med.* 2005; 170 (4 suppl): 49-60.
2. Mathai E, Rolain JM, Verghese GM et al. Outbreak of Scrub Typhus in Southern India during the cooler months. *Ann. New York Acad Sci.* 2003; 990:359-64.
3. Somashekar HR, Moses PD, Pavithran S, et al. Magnitude and features of scrub typhus and spotted fever in children in India. *J Trop Paediatr* 2005;16.
4. Sharma A, Mahajan S, Gupta ML, et al. Investigation of an outbreak of Scrub Typhus in Himalayan region of India. *Jpn J Infect Dis* 2005; 58: 208-10.
5. Watt G, Parola P. Scrub typhus and tropical rickettsioses. *Curr Opin Infect Dis.* 2003;16 (5):429-36.
6. Liu Q, Panpanich R. Antibiotics for treating scrub typhus. *Cochrane Database of Systematic Reviews* 2002; Issue 3 Art No. CD002159.

7. DHR-ICMR Guidelines for Diagnosis and Management of Rickettsial Diseases in the India-2015.
8. Jang M, O, H. C. Jang et al 2014.Outcome of intravenous Azithromycin therapy in patients with complicated scrub typhus compared with that of Doxycycline therapy using propensity-matched analysis. *Antimicrobial Agents Chemother* 58 (3): 1488-1493.
9. Kim D-M, Yu K D, Lee J H, Kim H K, Lee S H. Controlled trial of a 5-Day Course of Telithromycin versus Doxycycline for treatment of mild to moderate scrub typhus. *Antimicrobial agents and chemotherapy* 2007; 51 (6): 2011-15.

