Rickettsia infection in Bangladesh

Mohammad Zahiruddin
Professor of Medicine
Sir Salimullah Medical College, Dhaka.

Is it an emerging infection in Bangladesh ?

Introduction

- Rickettsia may be responsible for certain febrile illness of unknown origin.
- It is often misdiagnosed and treated as other febrile illness because of its similarity of symptoms and lack of confirmation by laboratory investigations.
- And when untreated Rickettsial diseases can be fatal sometime.

- The name *Rickettsiaceae* came in honor of Howard Taylor Ricketts for his brilliant experiments in the field of these infections.
- Ricketts, as well as another famous rickettsiologist, Von Prowazek, died of rickettsia during their study period.

With Tribute to Howard Taylor

- Howard Taylor Ricketts, 1871-1910. Ricketts identified the causative agent of Rocky Mountain spotted fever.

Cont..

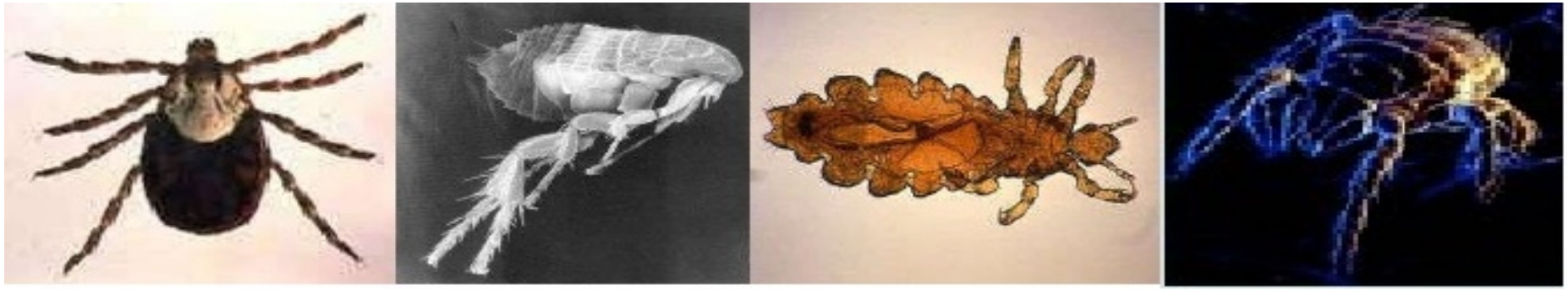
- Rickettsial diseases are a group of infections caused by the obligate intracellular bacteria *Rickettsia*.
- It is a Gram-negative, non flagellated, non-motile, non-spore forming, highly pleomorphic bacteria.
- They are small, cocco-bacilli that can present as cocci or bacilli. They comprise a group of microorganisms that phylogenetically occupy a position between bacteria and viruses

Cont…

- From 1873 to 1920, 66% of 431 reported cases resulted in death in USA by Rocky mountain spotted fever.
- During 1983-1998, Five to thirty-nine deaths were reported annually to public health authorities.
- In Southeast Asia alone, an estimated one million cases of scrub typhus occur annually.
- There are 50,000–80,000 deaths per year caused by this disease.
- Although this number of deaths is probably an underestimate.

Rickettsia Transmission

- Maintain in animal and arthropod reservoirs (ticks, mites, lice, fleas by transovarian transmission).
- Transmitted to humans by arthropod vectors
- Humans are accidental hosts: acquired by arthropod bite or contact of arthropod excreta with abraded skin



Pathogenesis

Infection is conveyed to human through the skin from excreta of arthropods but the saliva of some biting vectors is infected

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Multiply in endothelial cells of small blood vessels

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Causing vasculitis & producing lesion in the skin and multiple organs

↓

Endothelial proliferation associated with a perivascular reaction

↓

Thrombosis of the vessels

Classification of Rickettsial fever

Rickettsial illness can be classified into 3 biogroups:

- Spotted fever bio-group (15 rickettsioses)
- Typhus group
- Scrub typhus bio-group (Tsutsugamushi disease)
- Other rickettsioses and closely related illnesses

Cont..

Spotted fever bio-group (15 rickettsioses)

- Rocky Mountain spotted fever (RMSF), caused by *Rickettsia rickettsii*
- Rickettsialpox, caused by *Rickettsia akari*
- Boutonneuse fever (ie, Kenya tickbite fever, African tick typhus, Mediterranean spotted fever,Israeli spotted fever, Indian tick typhus, Marseilles fever)
- Rickettsia felis infection

Cont…

Typhus group:

- Louse borne (epidemic) typhus, caused by *Rickettsia prowazekii*
- Murine (endemic or flea borne) typhus, caused by *Rickettsia typhi*
- Brill Zinsser disease (ie, relapsing louse borne typhus)

Cont…

Scrub typhus bio-group (*orientia Tsutsugamushi*)

3 major subtypes: karp, Gilliam, Kato.

Other rickettsioses and closely related illnesses

Rickettsia slovaca

Rickettsia sibricia

Coxiella burnetii

Presentation

- Fever with rigors
- Headache
- Malaise
- Prostration
- Confusion
- Myalgia
- Cough
- Hepatosplenomegaly
- Lymphadenopathy
- Rash :macular, papular, petechial, hemorrhagic
- Eschar (dark crusty ulcer at the site of bite)

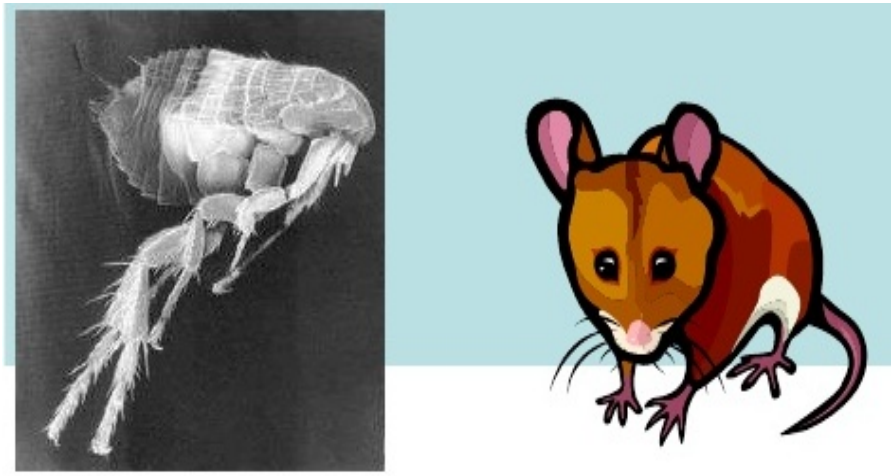
Epidemic (louse-borne) typhus/ Classisal typhus

- Organism: *R. prowazekii*
- Reservoir: Humans
- Vector: Human body louse (pediculus humanus)
- Geographical area: Worldwide
- Incubation period: 12-14 days
- Rash appears on 4^{th} -6^{th} day and appears first on the anterior folds of the axillae, sides of the abdomen or backs of hands, then on trunk and fore arms.

Cont..

- During the 2nd week symptoms increase in severity and patient dies from toxaemia, cardiac or renal failure, or pneumonia.
- 20-30% fatal if untreated
- Recrudescent typhus: Reactivation of organism which remained latent for years after recovering from epidemic typhus

Endemic (flea-borne) typhus/ Murine typhus



- Organism: *R. typhi*
- Reservoir: Rats
- Vector: flea
- Geographical area: Worldwide (warm, coastal ports).
- Incubation period: 8-14 days.
- Symptoms resemble to mild louse-borne typhus.

Scrub typhus

- Organism: *Orientia tsutsugamushi*
- Reservoir: Rodents
- Vector: Trombicula mite
- Geographical area: South-east Asia
- Incubation peroid: 9 days
- Eschar surrounded by an area of cellulitis present (75%).
- Rash: Maculopapular rash appears on about 5^{th} to 6^{th} day and spreads to the trunk, face and limb, including the palms and soles.

Cont..

- Patient also come with remittent fever, tachypnea, hepatosplenomegaly, generalized painless lymphadenopathy.

- In severe infection, patient is prostrate with cough, pneumonia, confusion and deafness.
- Cardiac failure, renal failure and hemorrhage may develop.

Rocky mountain spotted fever

- Most serious form.
- Organism: *r. rickettsii*
- Reservoir: Rodents, ticks
- Vector: Ioxodes tick
- Geographical area: North, central and south america
- Incubation period: 7 days
- Rash begins as macules on hands or feet and spreads centripetally and become petechial or hemorrhagic in 50% cases.

Complications

- Bronchopneumonia
- CCF
- Multi organ failure
- Myocarditis, endocarditis
- Glomerunephritis
- Meningoenchephalitis
- DIC
- Shock

Differential diagnosis

- Dengue
- Malaria
- Typhoid
- Meningococcal sepsis
- Leptospirosis

Laboratory Diagnosis

Objective:

Diagnosis of Rickettsial infection and exclusion differential diagnosis.

Routine investigations:

- Complete blood count with ESR
- Blood film examinations
- Liver function tests
- Chest X-ray P/A view
- NS1 antigen detection

Specific investigations:

Specimen:

- Blood & skin biopsy.

Serological diagnosis:

- Detection of rising titer of anti-rickettsial antibodies by ELISA.
- Weil-Felix reaction.

Direct detection in clinical specimen:

- PCR
- Immunofluorescence

Culture:

- Tissue culture or chick embryo.

Rickettsia infection: Bangladesh perspective

- In 1993, WHO reported that rickettsia infections are the major causes of febrile illnesses throughout the Asia-Pacific region.
- It is also present in several parts of the Indian subcontinent
- From India in 2010 reported that 45.6% had spotted fever group and 30.7% scrub typhus & untreated cases can have fatality rates as high as 30-35%.

- For India, the reported numbers are an underestimate due to lack of community based data and non-availability of confirmatory laboratory tests.

- Rickettsial disease in India has been documented from Jammu, Kashmir, Himachal Pradesh, Uttaranchal, Rajasthan, Assam, West Bengal, Maharashtra, Kerala and Tamil Nadu

Cont…

- Since Bangladesh is very adjacent to the India, it is very likely that the same *Rickettsia* would be responsible for certain febrile illnesses.
- Investigations facilities for rickettsia diseases are not well available in Bangladesh.
- Only Weil-Felix test is available which has less specificity.
- Physicians often treat febrile patient empirically with doxycycline when other causes of fever are excluded.

Cont..

- There is little published evidence for the occurrence of rickettsia infection in Bangladesh.
- One case series of 40 rickettsia infection was reported in 2007.
- Study was done in Mymensingh medical college hospital during 2003 to 2005.
- Diagnosis was done on the basis of clinical suspicions, exclusions of other causes of fever and positive Weil-Felix test.

In this series their results were:

Presenting features of the cases (no-40)

fever	40(100%)
headeche	33(82%)
rashes	15(37.5%)
splenomegaly	15(37.5%)
arthralgia	15(37.8%)
hepatosplenomegaly	12(30%)
lymphadenopathy	5(12%)

Distribution of cases according to types of Rickettsia fever (n=40)

Types	Number
Scrub Typhus	19(47.5%)
Spotted fever(Indian tick typhus)	16(40%)
Scrub typhus with enteric fever	5(12.5%)

Ref: Miah MT, Rahman S, Sarker CN, Khan GK, Barman TK, 2007. Study on 40 cases of Rickettsia. Mymensingh Med J 16: 85–88

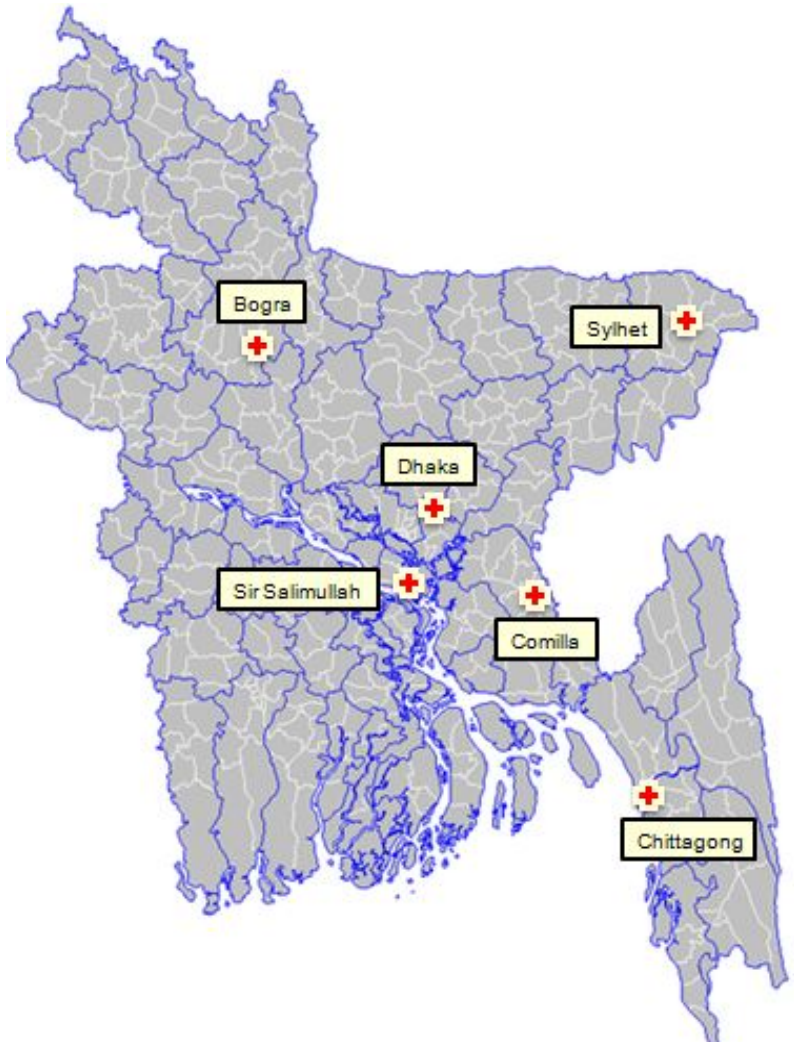
Cont..

- Another prospective sero-epidemiological study was conducted in six major teaching hospital in Bangladesh.

- It was done in June to August 2010.

- Diagnosis was made from blood test by detection of IgM enzyme-linked immunosorbent assay for *Orientia tsutsugamushi*(Scrub Typhus) and *Rickettsia typhi* (Murine typhus).

Place of study:



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Dhaka Medical College, Dhaka

Sir Salimullah Medical College, Dhaka

Comilla Medical College, Comilla

Shaheed Ziaur Rahman Medical College, Bogra

MAG Osmani Medical College, Sylhet

SEROSURVEY OF O. TSUTSUGAMUSHI AND R. TYPHI IN BANGLADESH (cut off =0.2)

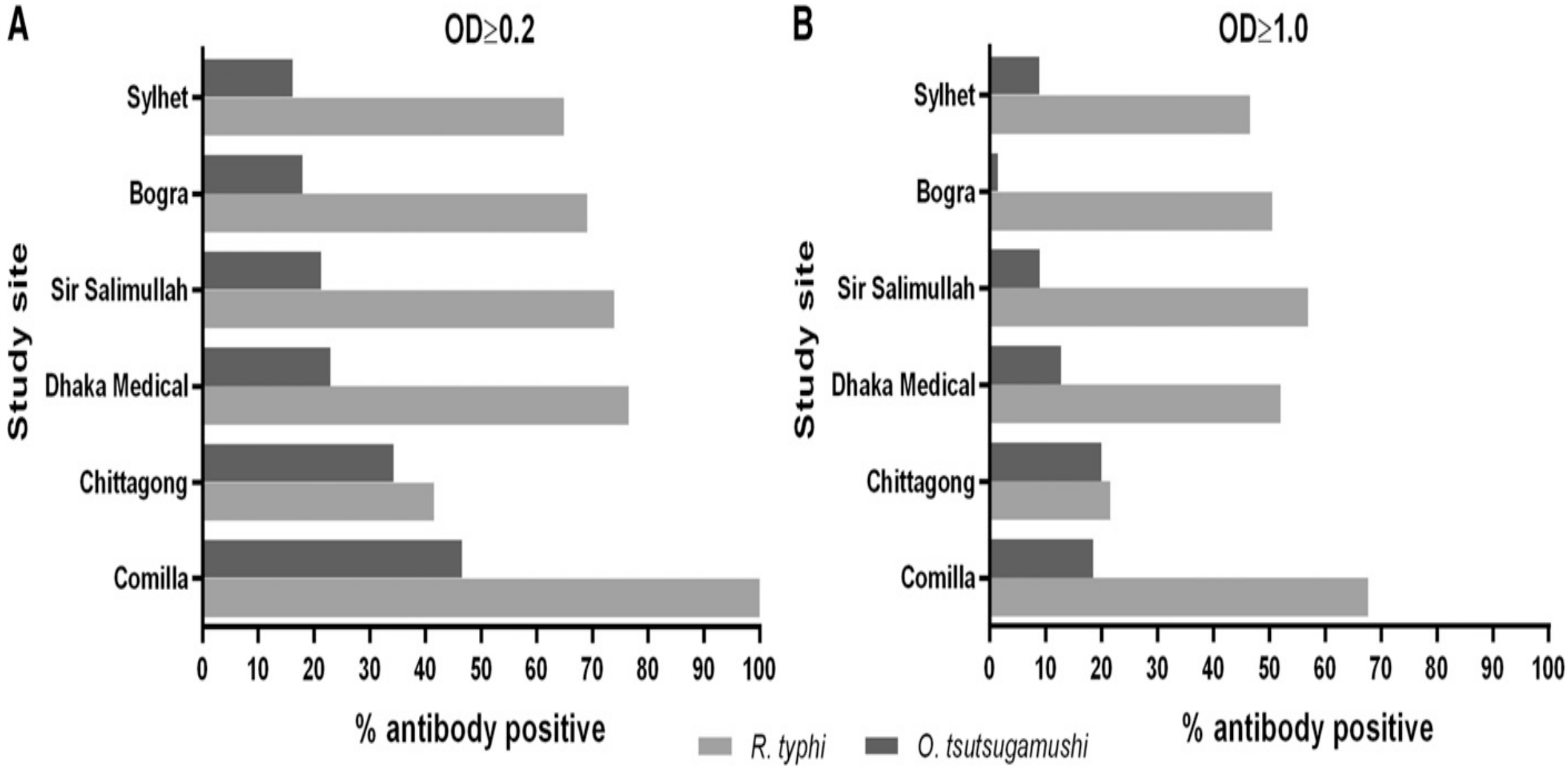
Type of rickettsia	Number (total-1209)
Orientia tsutsugamushi (Scrub typhus)	287 (23.7%)
Rickettsia typhi (Murine typhus)	805 (66.6)

Ref: Rapeephan R. Maude,* Richard J. Maude, Aniruddha Ghose, M. Robed Amin, M. Belalul Islam, Mohammad Ali,M. Shafiqul Bari, M. Ishaque Majumder, Ampai Tanganuchitcharnchai, Arjen M. Dondorp, Daniel H. Paris,Robin L. Bailey, M. Abul Faiz, Stuart D. Blacksell, and Nicholas P. J. Day. Am. J. Trop. Med. Hyg., 91(3), 2014, pp. 580–583

SEROSURVEY OF O. TSUTSUGAMUSHI AND R. TYPHI IN BANGLADESH (cut off >1)

Type of Rickettsia	Number (Total=1209)
Orientia Tsutsugamushi (Scub Typhus)	109 (9%)
Rickettsia Typhi (Murine Typhus)	543 (44.9%)

Ref: Rapeephan R. Maude,* Richard J. Maude, Aniruddha Ghose, M. Robed Amin, M. Belalul Islam, Mohammad Ali,M. Shafiqul Bari, M. Ishaque Majumder, Ampai Tanganuchitcharnchai, Arjen M. Dondorp, Daniel H. Paris,Robin L. Bailey, M. Abul Faiz, Stuart D. Blacksell, and Nicholas P. J. Day. Am. J. Trop. Med. Hyg., 91(3), 2014, pp. 580–583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% antibody positive
R. typhi
O. tsutsugamushi

- A molecular approach for diagnosis of *Rickettsia* among patients with fever of unknown origin was done in Mymensingh Medical College Hospital with the joint initiative of department of Medicine and Microbiology.
- Study period was July 2012 to September 2013.
- Total number of patients were 155 from both Medicine and Pediatric department.
- Blood were collected from each of the patient for Weil felix test ,ELISA and PCR.

- All the samples were tested by Weil-Felix test. In Weil felix test OXK,OX2 and OX19 strains of proteus are used to detect rikettsial antibody

- ELISA were done only Weil felix test positive cases.

- PCR were done for all the specimens (155)

Their study results were:

Age group	Male (n=74)	Female (n=81)	Total (n=155)
Up to 15 years	09	17	26
15 – 30 years	36	35	71
30 – 45 years	23	22	45
> 45 years	06	07	13
Total	74 (48%)	81 (52%)	155 (100%)

Distribution according to age and sex

Presentation of the cases:

Clinical features	No. of presenting cases	percentage
Fever	155	100%
Headache	98	63%
Body ache	65	41%
Cough	12	7.2%
Rash	03	02%
Conjunctival hge.	01	0.6%

Test results were:

Name of test	No. of patent	No. of positive test
Weil-Felix	155	136 (88%)
ELISA IgM	129	31 (24%)
PCR	155	61 (39%)

Ref. F. Ferdouse, M.A. Hossain, S. K. Paul, S. Ahmede, M. C. Mahmud *et all*
DOI: http://dx.doi.org/10.3201/eid2108.150328ll.

Cont…

- Out of the 61 PCR positive products, 16 were sequenced in Sapporo Medical University, Japan.

- Among these 16, 13 were found to be 99.9% consistent with *Rickettsia felis.*

Beside these studies, few case report of typhus fever had been published in different journals of Bangladesh.

Summery and conclusions

- Rickettsia may be responsible for certain febrile illness of unknown origin in Bangladesh.

- In Southeast Asia, an estimated one million cases of scrub typhus occur annually and there are 50,000–80,000 deaths per year caused by this disease.

- There is little published evidence for the occurrence of rickettsia infection in Bangladesh.

- In the contest of recent studies, scrub and murine typhus should be considered as possible causes of febrile illness in Bangladesh.

Cont..

- PCR based diagnostic study has revealed that *Rickettsia Felis* may be an emerging infection.
- Still diagnostic facilities for Rickettsia infections are limited in Bangladesh.
- ELISA, Immunofluorescence study and PCR based diagnostic method should be available for appropriate diagnosis.
- More studies are needed to identify types of rickettsia and their strains in the vectors, reservoirs, and humans, as well as to determine the incidence and spectrum of clinical disease in Bangladesh.

WARNING:

RICKETTSIA FELIS IS EMERGING

BE AWARE OF CAT FLEAS

Thank
you