

RISK FACTORS FOR ACQUIRING SCRUB TYPHUS IN AN ADULT POPULATION IN SOUTH INDIA



A Dissertation submitted in partial fulfillment of

M.D (General Medicine) branch I Examination of the Tamil Nadu

Dr. M.G.R. UNIVERSITY, CHENNAI to be held in 2015

DECLARATION BY THE CANDIDATE

This is to declare that dissertation entitled “ RISK FACTORS FOR ACQUIRING SCRUB TYPHUS IN AN ADULT POPULATION IN SOUTH INDIA “ is my original work towards partial fulfilment of M.D (General Medicine) Branch I Examination of the Tamil Nadu Dr. M. G. R. UNIVERSITY, CHENNAI to be held in 2015

Candidate

Dr. Tina George

Post graduate

Department of General Medicine

Christian Medical College

Vellore - 632004

CERTIFICATE

This is to certify that the dissertation entitled “RISK FACTORS FOR ACQUIRING SCRUB TYPHUS IN AN ADULT POPULATION IN SOUTH INDIA” is the bonafide original work of Dr. Tina George , towards the M.D. Branch- I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai to be conducted in 2015.

Guide:

Dr. Sudha Jasmine

Associate Professor of Medicine,

Department of Medicine -III ,

CHRISTIAN MEDICAL COLLEGE,

VELLORE - 632004.

CERTIFICATE

This is to certify that the dissertation entitled “RISK FACTORS FOR ACQUIRING SCRUB TYPHUS IN AN ADULT POPULATION IN SOUTH INDIA” is the bonafide original work of Dr. Tina George , towards the M.D. Branch- I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai to be conducted in 2015.

Head of Department :

Dr. Anand Zachariah,

Head of the Department,

Professor of medicine,

Department of Medicine- I,

CHRISTIAN MEDICAL COLLEGE,

VELLORE - 632004.

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PG Registrar
Department of General Medicine
Christian Medical College
Vellore 632 002

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Risk factors for acquiring scrub typhus in an adult population in South India.
Dr. Tina George, PG Registrar, Medicine, Dr. Sudha Jasmine, Dr. Thambu David,
Dr. Samuel George Hansdak, Medicine, Dr. John Jude, Microbiology, Dr. J.V.
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1. Institutional Review Board approval
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Additional Vice Principal (Research)

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1. Format for application to IRB submission
2. Patient Data Form
3. Information sheet and consent form (English, Tamil, Telugu and Hindi)
4. Cvs of Drs. Sudha Jasmine Rajan, Samuel George Hansdak, Antonisamy, John Antony Jude Prakash, Thambu David, , JV Peter
5. A CD containing documents 1 – 4.



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A sum of Rs. 7720/- (Rupees Seven Thousand Seven Hundred and Twenty only) will be granted for Two years.

Yours sincerely

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Institutional Review Board

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Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Sudha Jasmine, Department of Medicine

CONTENTS

INTRODUCTION.....	17
SCRUB TYPHUS – THE PAST.....	20
EPIDEMIOLOGY.....	24
CLINICAL FEATURES.....	27
The Eschar.....	28
Renal failure in Scrub typhus.....	30
Acute respiratory distress syndrome in Scrub typhus.....	30
Myocardial dysfunction.....	31
Hepatic and gastrointestinal manifestations.....	31
Neurological manifestations.....	31
Features suggestive of poor prognosis in Scrub typhus.....	31
DIAGNOSIS AND TREATMENT OF.....	32
SCRUB TYPHUS.....	32
Laboratory evidence for Scrub typhus.....	33
Treatment.....	34
Resistance to treatment.....	35
THE BACTERIA- ORIENTIA TSUSUGAMUSHI.....	36
Reclassification of the <i>R.tsusugamushi</i>	37
Structure of the bacteria-.....	39
Strains of <i>Orientia tsusugamushi</i>	41
Strains in South East Asia and India.....	44
PATHOGENESIS OF SCRUB TYPHUS.....	45
Host factors affecting disease.....	48
Leptotrombidium.....	50
Chigger.....	52
Life cycle of the Trombiculid Mite.....	53

Infection.....	56
Species.....	56
Host preference.....	58
ECOLOGICAL ASPECTS OF DISEASE TRANSMISSION	59
Ecology of Scrub Typhus	60
Widespread presence of Scrub typhus in India and around the world.....	61
Effect of climate:	62
Effect of Vegetation	63
Theories of wide spread presence of Scrub typhus	64
Effect of human activity	65
Indian Ecology-	65
RISK FACTORS FOR SCRUB TYPHUS.....	66
Risk factors for acquiring Scrub typhus	67
Risk factors identified in Korea-	68
Risk factors identified in Beijing.....	69
Risk factors studied in South China	69
Risk Factors in Taiwan.....	70
Risk factors in North India	71
Risk factors in South India	72
Scrub typhus in Tamil Nadu.....	72
Scrub Typhus in Vellore.....	72
Justification for the study	73
PATIENTS AND METHODOLOGY.....	75
Study type-	76
Setting and Duration-	76
Study population-	76
Inclusion criteria.....	77
Cases.....	77
Controls	78
Exclusion criteria.....	79
Methodology	80

Preliminary work.....	80
Questionnaire construction.....	80
Enrollment of cases	82
Enrollment of Geographical control.....	82
Enrollment of the clinical control.....	82
Interviews	83
Consent.....	83
Health education.....	83
Bias.....	83
Confounding factors	84
Statistical methods.....	Error! Bookmark not defined.
Sample size.....	Error! Bookmark not defined.
Analysis	87
Institutional review board.....	88
Funding.....	88
RESULTS.....	89
Sex distribution.....	94
Age distribution.....	95
Socioeconomic distribution of cases and controls.....	95
Seasonal distribution of cases from Tamil Nadu.....	100
Seasonal distribution of cases from Andhra Pradesh	101
Clinical signs	102
Time to defervescence of fever	102
Antibiotic Usage.....	103
RISK FACTORS FOR ACQUIRING SCRUB TYPHUS	105
Discussion	119
CONCLUSION	124
Bibliography.....	128
ANNEXURE.....	133
ANNEXURE 1 – ENGLISH PATIENT DATA FORM	133
TAMIL QUESTIONNAIRE	143
TELEGU QUESTIONNAIRE	145

HINDI QUESTIONNAIRE.....	151
ANNEXURE 2	154
ANNEXURE 3	161
MODIFIED KUPPUSWAMY SCALE FOR SOCIOECONOMIC STATUS AND INCOME GROUPS 2012.....	162
ANNEXURE 4 SOFA SCORE	163
ANNEXURE 5 -PATIENT HEALTH EDUCATION PAMPHLETs	164
Patient data	160

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I would like to thank my parents and my husband whose encouragement and cheerfulness have been a constant relief.

And finally I would like to thank God for his continued blessings

ABSTRACT

TITLE- RISK FACTORS FOR ACQUIRING SCRUB TYPHUS

DEPARTMENT- DEPARTMENT OF GENERAL MEDICINE

NAME OF THE CANDIDATE- TINA GEORGE

DEGREE AND SUBJECT-M.D. POSTGRADUATE STUDENT OF GENERAL MEDICINE

NAME OF THE GUIDE- DR SUDHA JASMINE

OBJECTIVES- To determine the behavioral and environmental risk factors for acquiring scrub typhus among adults who present to a tertiary care hospital in South India

METHODS- This was a hospital based case control study comparing the exposure of known cases of Scrub typhus to a geographical and clinical control arm in a 1:1:1 ratio. 75 patients were enrolled in each arm. Data was gathered by administration of questionnaires.

Conditional univariate and multivariable logistic regression were performed for relating Scrub typhus with the risk factors concerned.

RESULTS- On univariate analysis patients with Scrub typhus were found to be more likely to - live in Kuchcha houses (OR and 95 % CI 4.12(1.10-15.44), spend more than 7 hours per week sowing (OR and 95% CI(7.61(0.91-63.52), lie-down or sit on mud or grass OR and 95% CI 3.43(1.47-7.96), lie down directly on the ground OR and 95% CI 2.44(1.12-5.30) and lie down on the ground for more than 7 hours a week OR and 95 %CI 3(1.1-8.30), as compared to their geographical controls. They were more likely to – not have a toilet inside their house OR and 95% CI 2(1-4), use an outdoor toilet OR and 95% CI 3.61(1.4-9.3), have fire wood in or around their house OR and 95% CI 1.78(0.92-3.43), involved in sowing OR and 95% CI 8 (1.00-63.96),

spend more than 7 hours per week sowing OR and 95% CI 7.61(0.91-63.52), be involved in tilling OR and 95 % CI 7.61(0.91-63.52), be involved in harvesting OR and 95% CI 3.00(1.19-7.557), be involved in watering plants OR and 95 % CI 3.33(0.91-12.11), and not use footwear OR and 95% CI 2.13(0.91-4.92) as compared to their clinical controls. However on multivariate analysis ,these factors were not independently co-related to acquisition of Scrub typhus.

Further studies, preferably in the community may help gain more accurate information and hence facilitate preventive strategies.

INTRODUCTION

Scrub typhus is a Rickettsial infection caused by *OrientiaTsusugamushi*. It is an acute febrile illness with a potentially devastating course if left untreated.

The bacteria itself is carried in a vector called the Trombiculid mite and has a trans-ovarian transmission. The larval stage of the vector is the sole feeding stage and is the infective stage. The larvae are called chiggers.(1)

This disease was earlier thought to be confined to an area referred to as the Tsusugamushi triangle, and was common in areas of scrub vegetation where recent deforestation had occurred, however the disease is being encountered in unexpected areas and at unexpected times.

Within India itself there are reports of the disease from the foothills of the Himalayas to the arid areas of Tamil Nadu.(2,3)

Identifying this disease based on its clinical manifestation, presence of a typical eschar and lab parameters have decreased the morbidity due to this disease, However drug resistance to doxycycline used in treatment has now become the new challenge. In this scenario preventive measures are becoming increasingly important.(4)

As of today no vaccines are present for preventing this disease, however a deeper understanding of the risk factors that predispose to the same, may guide the formulation of a preventive strategy. In Korea studies on patient behavior and practices have yielded information on the probable risk factors for acquiring scrub typhus. Similar studies in Darjeeling have also been undertaken which have helped in community measures against acquiring scrub typhus.

In South India, large series have shown that up to 47 % acute febrile illnesses presenting to hospital can be due to Scrub typhus, however there are is no data on what environmental or behavioral factors predispose this population to acquiring this disease. This is hence an effort in that very direction and will hopefully stir more effort into preventing human infection with this deadly disease.(3,5,6)

AIM

To determine risk factors for acquiring Scrub typhus in an adult population presenting to a tertiary care center in South India

OBJECTIVES

- a) To determine the behavioral risk factors for acquiring scrub typhus among adults who present to a tertiary care hospital in South India.
- b) To determine environmental risk factors among adults who present to hospital with confirmed diagnosis of Scrub typhus

SCRUB TYPHUS – THE PAST

Scrub typhus is one among many rickettsial diseases that have infected mankind. It gets its name from the initial observation that the disease was contracted in areas which have scrub vegetation. Like other Rickettsial infections, it can have a non-specific presentation, with rapid deterioration.

Rickettsial infections have been notorious for the epidemics they have caused. History is rife with instances of rickettsial infections causing the downfall of many a nation. Armed forces of countries during the world wars have suffered more casualties at the hands of rickettsial diseases than in battle itself. Mortality rates in the pre-antibiotic era were nearly 50-60%. The interest in these diseases and contributions in the research of these diseases has thus largely been from medical professionals affiliated to the military.

The ancient Chinese seem to have known about Scrub typhus as is evident from their ancient writings as early as 313 A.D. (7)

Scrub typhus was first described in Japan in 1810 and almost 100 years later the organism was identified by Ogata and named *Rickettsia tsutsugamushi*. Lewthwait and Savor established that the etiological agent outside Japan was the same. In 1995 it was re-classified in a new genus called *Orientia* and was given the name *Orientia tsutsugamushi*. (7-9)

The disease came back into the limelight during the Second World War when it caused 14.6 deaths per 100,000, deaths which was the largest contribution of an infectious disease during World War II. Most of the cases were from Burma. This prompted the establishment of the Typhus society which is responsible for

much of the research on the ecology and transmission of this disease.(7) It was given the name Scrub typhus by Fletcher to emphasize the environment that predisposed to the infection.(10)

In India scrub typhus was known in the early 1930s when British forces in Burma fell prey to it.

In the Burma campaign in 1944 the British forces reported 5000 cases of Scrub with a 7 % fatality ratio (350 deaths). The US army posted in Assam in 1943 also reported cases of Scrub typhus(7) The disease was rediscovered during 1990 when a unit of the Indian army was sent to the Indo-Pak border(11) In South India there have been reports from all the four states of South India.

In the Christian Medical College among patients with acute febrile illnesses that presented to a tertiary care center during one year the prevalence of Scrub typhus was found to be 47.5% with a case fatality rate of 12.2%(6,12)

The high mortality rates with Scrub typhus are attributed to secondary Acute Respiratory Distress Syndrome(ARDS), multiorgan dysfunction (MODS) or Septic shock.The interest in Scrub typhus waned after the Second World War, but because of a resurgence of the disease in recent times in South East Asia there has been a renewed interest in this disease.(10,13) Around 1 billion people are at risk of acquiring this disease and approximately 1 million cases are reported annually. (14) Case fatality rates of up to 50 percent have been observed in untreated patients in South Korea.(5)

EPIDEMIOLOGY

Scrub typhus is a disease endemic to the Asia Pacific region, within the area called the Tsusugamushi triangle. (15)



Picture 1- The Tsusugamushi triangle- Areas where scrub typhus is endemic. Triangle formed by Japan and Russia in the north, Pakistan and Afghanistan in the west to northern Australia in the south(16)

This includes Japan and Russia in the north, Pakistan and Afghanistan in the west to Northern Australia in the south.(17)(18) However due to extensive travel this disease is being identified in areas outside this geographical area as well. This dissemination of the disease can be attributed to hardiness of the vector as well as the bacteria. It also reflects the role that human practices have made in the dissipation of the disease.

Scrub Typhus had always been considered a disease of the tropics. Most cases occurred in the rainy season in areas that had been recently deforested. In South East Asia, areas where lallang grass was found were considered to be endemic for the disease. However, there are reports of the disease from the foothills of the Himalayas to the deserts of the Middle East .(19,19–21)

It probably reflects the effect of the changing climatic conditions on the epidemiology of the disease. Scrub Typhus is endemic to India and is found in many parts of the country.(2,3,6,22)

This disease has been seen from Kashmir to Assam, Eastern and Western Ghats. There have been case reports of Scrub typhus from Darjeeling, Himachal Pradesh, Bihar and Kerala. In our institution Scrub typhus is prevalent during the cooler months. It has been shown to have a prevalence rate of around 47% during the cooler months(17)(12)(23)

CLINICAL FEATURES

Scrub typhus presents with diverse clinical features. It has an incubation period of 7-10 days. It begins with features similar to flu like symptoms and can progress to involve multiple organs.

Acute respiratory distress syndromes, acute renal failure, hepatic injury in the form of a mild transaminitis are the more common manifestations of scrub typhus. (12)

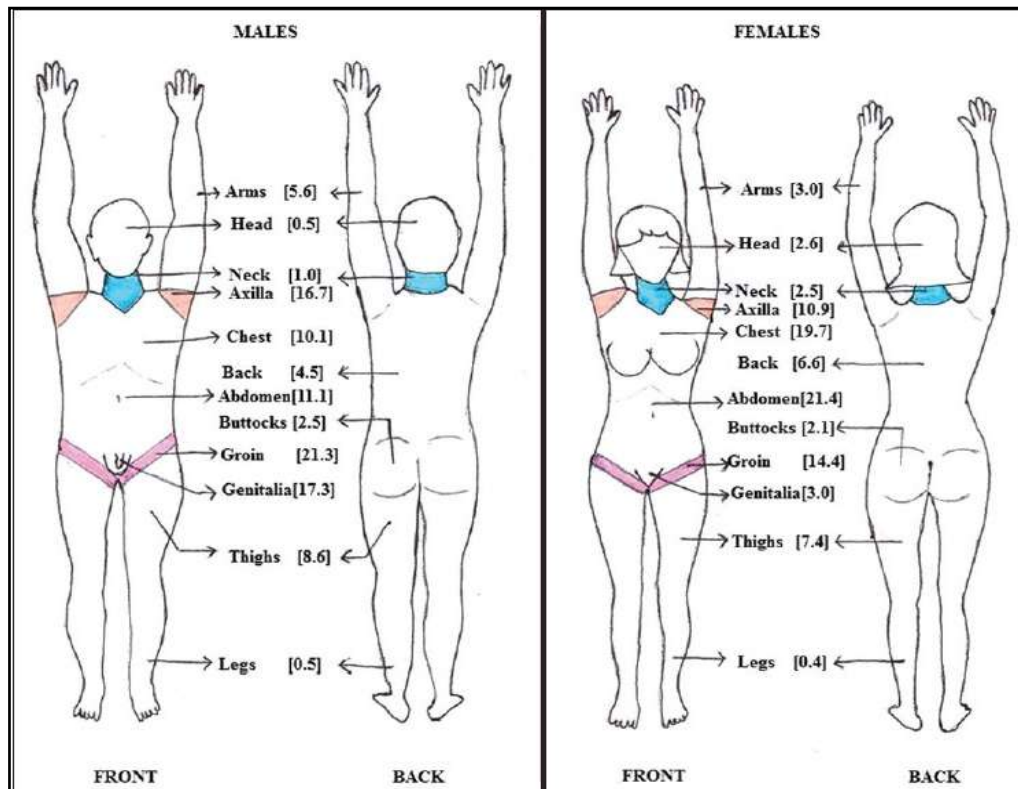
Scrub typhus can be associated with an eschar which is a rash 5-20 mm in size. It is formed at the site where the chigger has bitten the host. It goes through stages of papule formation and ulceration before the formation of an eschar. The margins of the eschar are erythematous.(24)



Picture 2- Showing an eschar on the lower abdomen. Central necrotic skin with peripheral erythema are characteristic of the eschar.(25)

The Eschar

The eschar is almost pathognomonic of Scrub typhus and is a vital clue towards the diagnosis of Scrub typhus. It is seen in almost 90% of patients with Scrub typhus. (26) It is still uncertain whether the eschar is a reaction to the bite of only an infected chigger. There is also a wide variation in the distribution of these eschars between men and women and probably correspond to the exposed areas in them. Usually eschars have been found in the skin creases. This includes the axilla, groin, nape of neck, below the breast. From a recent study done in South India the following distribution of eschars was found.(27)



Picture 3 – Distribution of eschars in men and women(27)

If treated early Scrub typhus has a good prognosis, however delay in treatment leads to severe disease which can be complicated by any one or more of the following.

Renal failure in Scrub typhus

Early cases of Scrub typhus can present with mild acute renal failure. However in later stages of the disease the patients may present with oliguric or even anuric renal failure. In a study done in a tertiary care center in South India the incidence of renal failure was found to be 19.6% (12)

The mechanism of injury to the kidney is not clearly known. Hypo perfusion of the kidneys secondary to shock, microangiopathy or direct affection of renal tubular cells leading to acute tubular necrosis have also been considered. A systemic vasculitis could also explain the renal involvement. (28,29)

Acute respiratory distress syndrome in Scrub typhus

In patients with scrub typhus, respiratory involvement is an ominous sign. Respiratory system involvement can range from a mild interstitial pneumonia to ARDS needing ventilatory support. The incidence of this complication in a tertiary care center in South India was close to 25% (12)

Myocardial dysfunction

Myocardial dysfunction has been reported with Scrub Typhus. This presentation can be fulminant. (30)

Hepatic and gastrointestinal manifestations

Scrub typhus causes a mild hepatitis which is considered to be due to the organisms tropism for the sinusoids. Only rarely is severe hepatitis with hyperbilirubinemia encountered. Other GI manifestations such as nausea and vomiting with mild pancreatitis is also known.(31)

Neurological manifestations

Neurological manifestations of this disease can range from headaches, meningitis to seizures and focal deficits. It is considered to be secondary to the vasculitis and ischemia caused .(12)

Features suggestive of poor prognosis in Scrub typhus

Chrispal et al in a cohort of patients with Scrub typhus had found that Acute Respiratory Distress Syndrome, Metabolic acidosis, Septic shock and altered sensorium were risk factors for mortality in Scrub typhus. Thus early identification and treatment is imperative.(12)

DIAGNOSIS AND TREATMENT OF SCRUB TYPHUS

With increasing awareness about the disease, and hence a higher index of suspicion, diagnosis is being made early. In addition to the typical presentation and the typical eschar lab parameters are useful in differentiating Scrub from other acute febrile illnesses that occur during the same period.

Laboratory evidence for Scrub typhus

Culture- As for all infectious disease the gold standard test is the isolation of the organism from the blood. This technique is cumbersome as the bacteria in question is an intracellular pathogen and needs to be cultured in yolk sac and then isolated. Also for the direct handling of the bacteria bio-safety Level 3 environments are needed. Serological tests are cheaper, faster, easier and do not require bio-safety level 3 facilities.

Serological evidence

Many serological tests are available for testing for Scrub typhus. They include the Weil Felix test, IFA and the IgM ELISA for Scrub typhus. The IgMELISA is easy to administer and is not operator dependent like the IFA. (32)

Molecular techniques

PCR from blood or tissue can also be used for diagnosis and strain identification.(33)

It has been found that high Alanine amino transferase (ALT) and Aspartate amino

transferase (AST) levels, with thrombocytopenia and leukocytosis have an 80 % specificity and positive predictive value for scrub typhus. (21)

The combination of clinical features, baseline blood investigations and the IgM ELISA is done in CMC to assist in diagnosis.

The criteria being used for diagnosis of scrub typhus in the past have been as follows.

1 Acute febrile illness (fever <14days) and the presence of a positive eschar and scrub IgM ELISA, or

2 AFI plus a positive scrub IgM ELISA plus clinical response to Doxycycline.

3 AFI plus scrub IgM ELISA seroconversion on convalescent sera, or;

4 AFI plus a positive scrub IgM ELISA with other serology's negative.(12)

Treatment

Doxycycline is the drug of choice and a single dose of 200 mg is usually enough. A prolonged course of 1 week of medication is given in more severe infections. The other drug that can be used is Azithromycin

In 2010 a Cochrane review showed that the effect of Azithromycin, Tetracyclines, Doxycycline and Rifampicin was equal.(34)

Response to treatment is usually seen within 48 hours when the fever defervesces.(8)

Resistance to treatment

With the rampant use of antibiotics bacteria are becoming resistant to the antibiotics.

The first ever report of resistant in the rickettsial species was in scrub typhus and was reported from Northern Thailand. Resistance to doxycycline was proved with susceptibility studies.(35) Hence there is an urgent need to spread awareness about this disease and also look at preventive strategies.

THE BACTERIA- ORIENTIA
TSUSUGAMUSHI

Rickettsial infections are caused by the bacteria family Rickettsiaceae and genus Rickettsia

The genus had 3 main groups

1. The typhus group. This group consists of the bacteria that cause epidemic typhus. *R. prowazekii* is the prominent bacteria in this group and is transmitted by body louse.
2. The spotted fever group. This group consisted of the bacteria causing spotted fevers. *R. rickettsii*, *R. conorii*, *R. africae* belong to this group.
3. The Scrub typhus group which had only a single species called the *Orientia tsusugamushi*.

The bacteria was first discovered by the Japanese. The first name proposed was *Theileria tsusugamushi* by Hayashi in 1920. Later in 1930 Nagayo proposed the name *Rickettsia orientalis*. Ogata in 1931 proposed *Rickettsia tsusugamushi*. (8,9) However *Rickettsia tsusugamushi* due to many differences in its structure and function as described below was re-classified in a genus of its own

Reclassification of the *R. tsusugamushi*

In 1995 due to the following differences it was proposed to separate the Scrub Typhus causing bacteria into a genus of its own.

1. Differences in cell wall- lack of peptidoglycan layer and lipopolysaccharides makes the cell wall of the *Orientia* genus thinner . In addition its cell wall was also found to have a thicker outer leaflet and a thinner inner leaflet
2. Due to the lack of peptidoglycans and lipopolysaccharides these bacteria were found to be more resistant to penicillin than the other species in the genus *Rickettsiaceae*.
3. The protein composition of these organisms was found to be different from that of the rest of the species in the genus *Rickettsiaceae*. Proteins which range from ~~54-~~ to 58-kDa and are called 56-kDa are the most abundant and are located on the cell surface. They are heat labile. This is different from the other species of the *Rickettsiaceae* genus as they have larger proteins which can have heat labile and heat stable sites.
4. *R.tsutsumushica* can be grown in the yolk sacs of developing chicken embryos and cultured in various cell lines like the HeLa, **BHK**, Vero, and L929 cell lines.
5. Budding forms of the bacteria are seen during replication in the *Orientia* genus and are not seen in the other species
6. Electron-lucent halo zones are usually seen around growing cells of the other *Rickettsia* species but are not seen with the *Orientia* genus.

7. The *Orientia* genus was found to have many strains and they had differed in their virulence for mice . This was not seen with other species of the genus *Rickettsiaceae*.

8. DNA sequencing and phylogenetic studies also supported the evidence that the bacteria causing Scrub Typhus was in fact separated from those causing spotted fever and plague.

Due to the above mentioned differences *R. tsusugamushi* was renamed *Orientiatsusugamushi* and a new genus *Orientia* was created with one species alone in it.

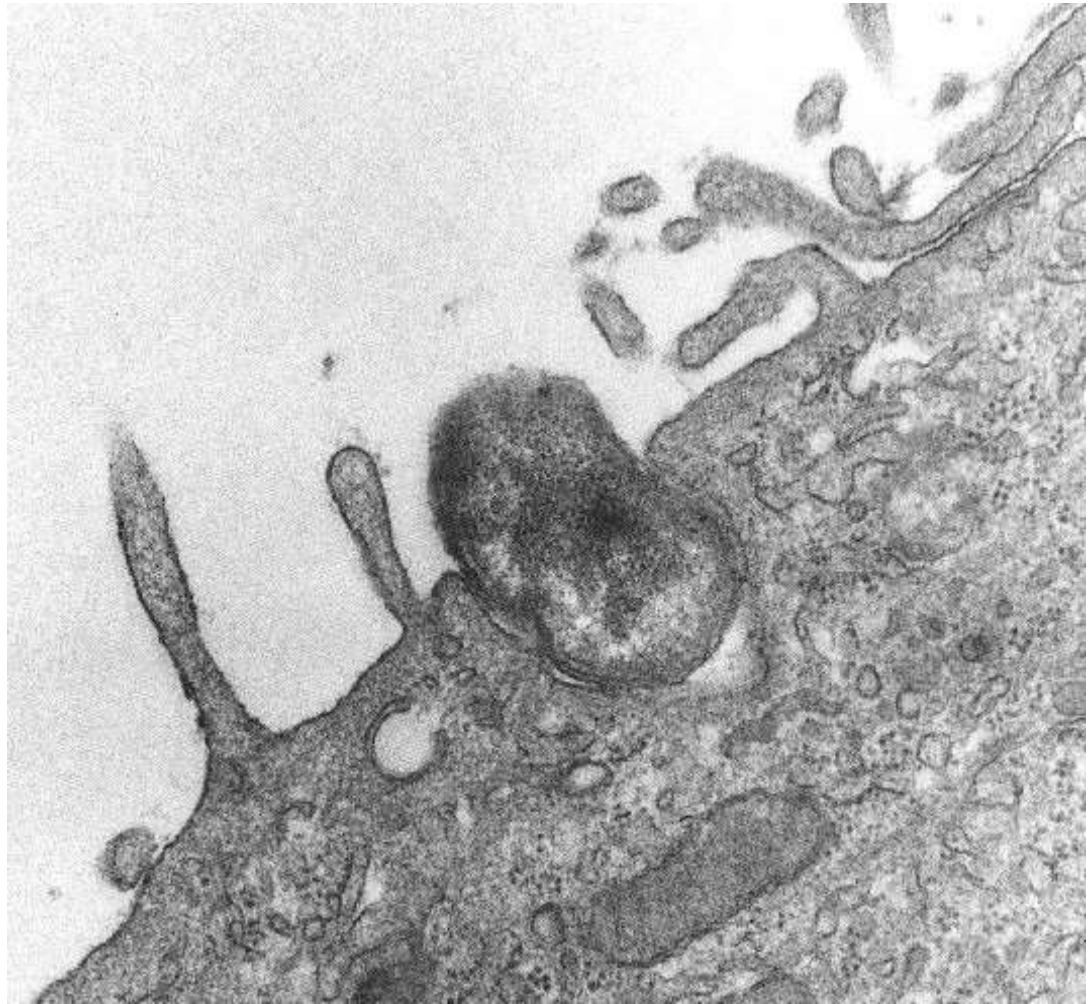
The name honoured both Nagayo and Ogata(9)

Structure of the bacteria-

Orientiatsusugamushi is gram negative rod shaped bacteria. It is 0.5-0.8 micrometers wide and 1.2 -3 micrometer long.

They are obligate intracellular organisms. They can survive in both human and arthropod hosts and they can propagate disease in humans.

The bacterial cell has a soft cell wall and cell membrane and is deficient in peptidoglycans and Lipopolysaccharides. The 56 K Da is the primary protein and the main antigenic protein of the organism. Below is an electron microscopy picture of the bacteria being ingested by a macrophage.



Picture 4 Showing *Orientia susugamushi* being phagocytosed by a macrophage

Strains of *Orientiatusugamushi*

Earlier the *Orientiatusugamushi* was divided into strains based on the differences a surface antigen which was a 56 kDa protein on the cell surface. This protein specifically differentiated it from other rickettsial bacteria.

Using antibodies against this antigen 3 major strains of this bacteria were identified. They were Gilliam, Karp, and Kato. Other antigenic types, which were also identified were Shimokoshi, Kawasaki, Kuroki.(9)

With the advent of techniques such as the PCR the entire genome has now been characterized. Based on PCR , many more strains have been identified. They have been classified in a phylogenetic tree as shown below in Figure 1 .(18)

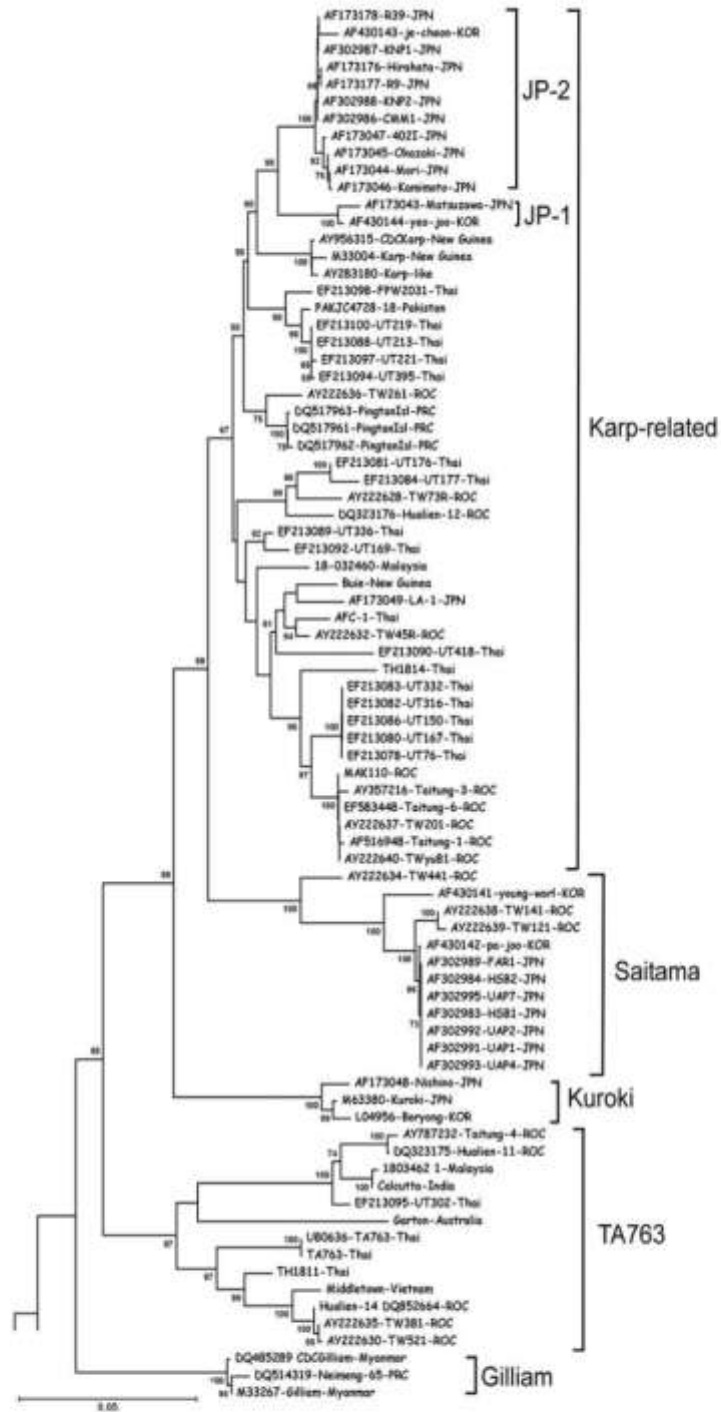


Figure 1 The phylogenetic tree of *Orientiatusugamushi*. Cell surface antigen 56kDa is the basis for this classification

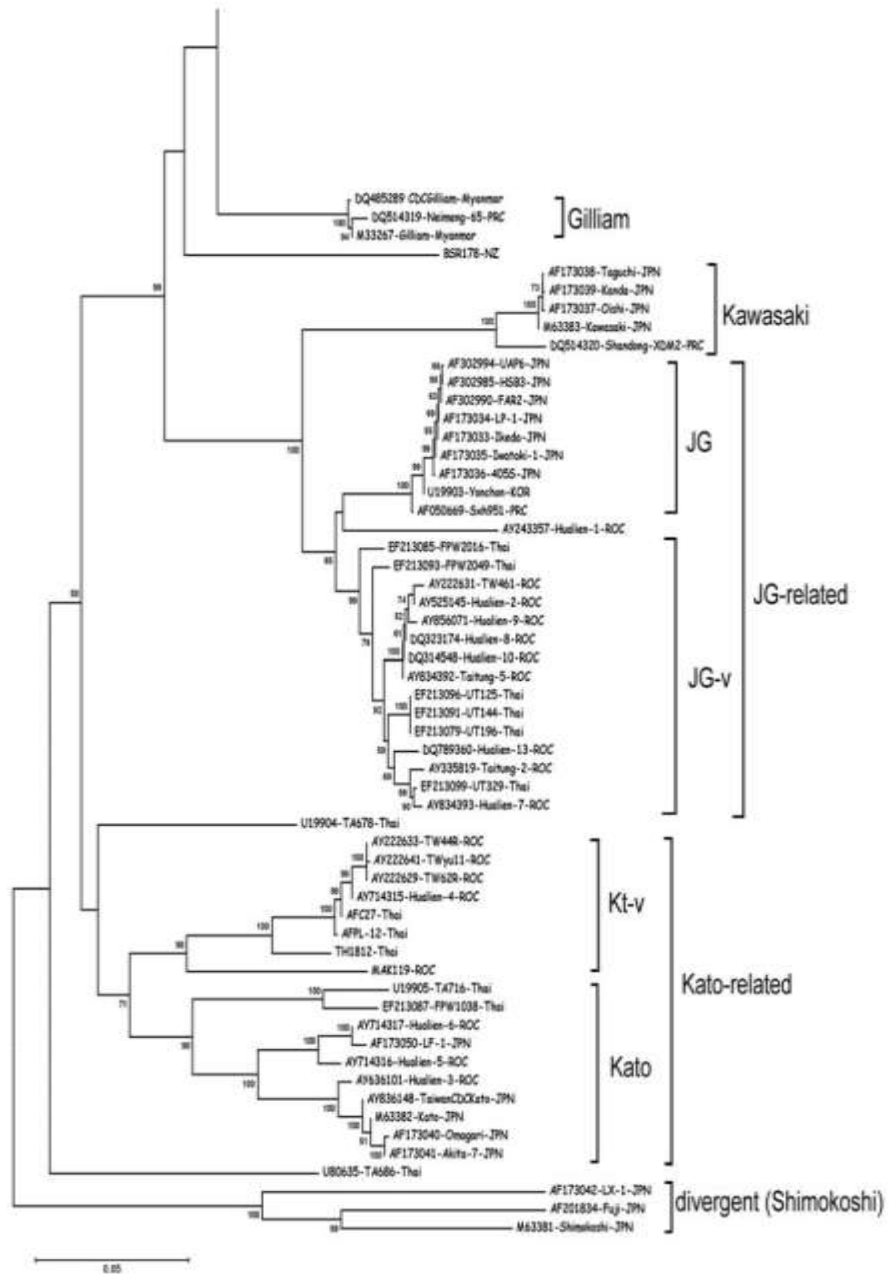


Figure 1 continued The phylogenetic tree of *Orientiatsugamushi*. Cell surface antigen 56kDa is the basis for this classification

The difference in these strains is not restricted to their genotypes and phenotypes. They are also different in their geographical distribution. The various strains differ in their virulence not only in humans, but also in mice.

These factors have been a major hindrance to the development of a vaccine against this infection.(18)

Strains in South East Asia and India

There is a lack of data about the distribution of the various strains of *O.tsusugamushi* in India.

The common strains found in China are the Gilliam strains (90%)Kuroki in Japan and Karp in Vietnam.(36–38)

Recent studies from south India by Verghese et al have demonstrated the presence of 3 main strains in South India. These strains are the Kato like(65.3%), Karp like(30.7%) and Gilliam(3.8%).(39) There is no epidemiological data on the strains most prevalent in North India in recent times.

New strains of the bacteria are being reported from various parts of the country. Mahajan et al reported more than 2 genotypes. One between Karp and JP-1 . The other between Saitama and JG type in 21 patients who were diagnosed with Scrub typhus in the Himalayas.(40)

PATHOGENESIS OF SCRUB TYPHUS

Humans are an accidental host to the bacteria *O. tsusugamushi*. The bacteria are transmitted by the bite of the vector, which is the larval form of the Trombiculid mite.

It is transmitted from one generation of vectors to the next transovarially.

In vitro studies have shown that the bacteria is an obligate intracellular organism.

This bacteria grows in the perinuclear cytoplasm and then release themselves by pushing through the cytoplasm of the host cell. The bacteria doubles every 9-18 hours.(9)

In patients infected with Scrub typhus, the bacteria causes a large variety of clinical manifestations, involving every organ system and if left untreated leads to multi organ dysfunction with ARDS and often death.

The injection of the bacteria into the host skin causes a local papule formation which finally ulcerates and leaves an Eschar. Initially it was though that the bacteria multiply here and later travel via the lymphatics. However this theory did not explain the spread of the infection to multiple organ systems.

Subsequently Moron et al from post mortem studies showed the presence of the bacteria in the endothelial cells and proposed that the endothelial invasion causes a generalized inflammation of the blood vessels and hence involves multiple organ systems.(41)

It was later proposed by Walsh et al that the bacteria invade the white blood cells themselves and are hence directly carried in the blood stream to the various organs.(42)

This leads to an immune response from the host which has been demonstrated to be both humoral and cell mediated. This leads to a systemic inflammatory response which causes the multi organ dysfunction.

The severity of the illness is related to both the strain of bacteria as well as the host factors. Bacteria have evolved to find ways to evade the host immune system. One such way is by suppressing the glycoprotein 96 expression in infected macrophages. These proteins are responsible for MHC1 mediated cell response and antibody production. Thus, by down regulating the same the bacteria evades destruction.(43)

Lately the mechanism by which the organism invades host cells which are not phagocytic cells has also been studied in greater detail.

It has been found that Integrin mediated signaling is used by the bacteria to cause actin re-arrangement at the site of infection in non-phagocytic cells. This allows the bacteria to gain entry into these cells.(44)

Of interest is the finding that in patients with HIV infection *Orientiatsusugamushi* infection causes a drop in the viral load. This finding may prove useful in further development of a vaccine for HIV.(45)

Watt et al in experimental studies to examine inhibitory effects of Scrub typhus plasma in HIV -1 infected patients. This showed HIV -1 copies in ART naïve patients decreased three fold or more. The virus burden remained low for 8 weeks in 70 percent patients transfused with 500 ml units of plasma from patients with Scrub typhus. The cause for variability in results is not known.(46)

Host factors affecting disease

O.tsusugamushi infection has been present in rodents and small animals since ancient times, however disease is not seen as frequently in these hosts as compared to humans.

This variability in response to the same bacteria has lead to further research in the genetic susceptibility of hosts.

Michael Groves and Osterman studied the genetics of rodents which showed disease and those that did not show disease after infection with *O.tsusugamushi*. They also studied the progeny of resistant and susceptible species. They were all resistant, hence showing that the resistance to the disease is a dominant trait associated to a single gene or a cluster of genes.(47)

Despite the duration for which Scrub Typhus has tormented mankind, still there seem to be lacunae in the knowledge of its full pathogenesis.

THE VECTOR

Scrub typhus is a zoonosis and as such is perpetuated by mites unlike most other rickettsial infections. Mites are hardy creatures and cause a variety of infections. They also can occupy a variety of habitats. Probably this feature contributes to the gradual omnipresence of the diseases caused by them

Scrub typhus also has become notorious for its presentation in unexpected geographical and climatic conditions. This disease was associated with a mite even prior to the knowledge of the causative organism.

The Japanese who were the first to identify the pathogen of Scrub typhus were also the first to identify that it was transmitted by mites. To ward off the mite they constructed effigies of the same and displayed them(18). It was also thought intermittently that the vector for Scrub typhus may be the Ixodid ticks. However due to failure to experimentally infect the tick , the idea was abandoned. (19) Subsequently the role of the mite as well as its larval forms was established.

Much of the work in identifying the mite and various characteristics of the mite and its behaviour are credited to the work of the US typhus commission which was set up during the World War 2.

Leptotrombidium

The mite transmitting Scrub typhus belongs to Acariformes subclass of the class Arachnida .they belong to the family Trombiculidae and to the genus Leptotrombidium. There are more than 3000 known species within this group in Asia alone.

The species of *Leptotrombidium* associated with causation of disease vary in differing geographical areas. They also differ during different months of the year and with changes in temperature and humidity.

The risk factors for acquiring scrub typhus are very closely related to the behavior and survival of these mites.

These mites are different from other members of the class Arachnida and are thus easily identified because their abdomen is not segmented. They thus have a single body called idiosoma with the 4 pairs of legs and mouth parts which are at the cephalic end and have an anterior attachment(Figure 2). (48)

These larvae of these mites commonly infest rodents and ground dwelling animals. They have also been known to be found on various birds. This is postulated to be one mechanism of its widespread presence. Humans are the accidental hosts of these mite larvae.(10)

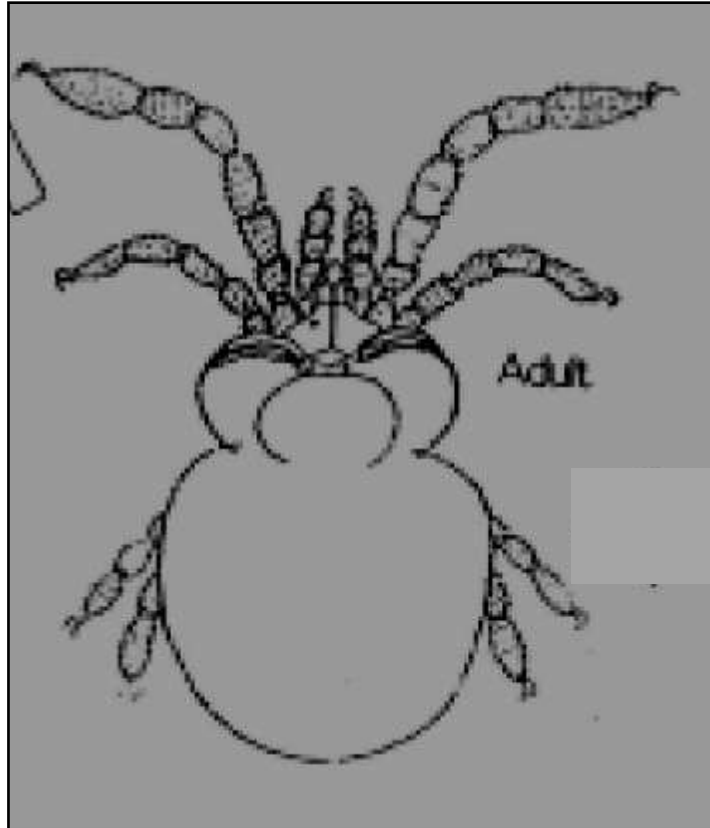


Figure 2-8 legged adult mite. Single body with 4 legs and mouth parts anteriorly

Chigger

The true vector of the bacteria *O. tsusugamushi* is not the adult trombiculid mite but its larva which is called the chigger.

They are smaller than the adult and are 4 legged (Figure 3). They have fewer setae than the adult mite. They are parasite on warm blooded animals. In the entire life

cycle of the mite this is the only parasitic stage and hence it is this stage of the mite that transmits the disease. (10)

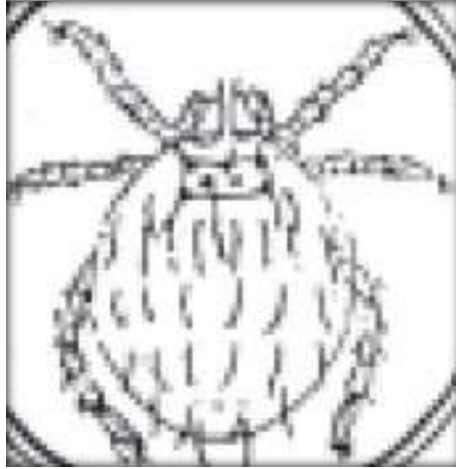


Figure 3 : Chigger mite with 6 legs

Life cycle of the Trombiculid Mite

The adult trombiculid mites lay eggs close to the ground and on dead leaves. Each female adult may lay up to 450 eggs. From these eggs the pre larval and then the larval stage with 6 legs emerges. They stay close to each other and are usually seen on the tips of the leaves or their undersurface, usually 6-10 mm from the ground. They are active in the unfed state. From observational studies it was found that in the presence of carbon dioxide the chiggers stretch their legs and similar behavior is with the approach of a warm blooded animal.

They drop from the leaves onto the host. They attach themselves onto the host and move to find a suitable location on the body of the host. Usually they settle in skin creases as clusters.

Once attached to the skin they feed on dead epidermal cells and fluids, however blood is not drawn. They produce a sucking tube from their saliva. This is called a stylosome. After feeding for 2-3 days the chigger gets engorged. It subsequently falls off the host.

The unfed larva are usually small and measure around 220 x 150 micrometer and the as they get engorged they may measure up to 560 x 400 micrometer

The fallen chigger has a quiescent phase for 3 days after which they moult once and an 8 legged nymph stage emerges which feed on the fluid content of dead arthropods or eggs of hatched arthropods. The nymph enters another quiescent stage and moults yet again and the adult emerges. There are male and female mites. These mites undergo indirect fertilization. The male adult drops the sperm in a sack in the soil and the female adult takes them inside fertilization occurs in the female.(49) This life cycle of the mite takes up to 8 weeks. (10) In laboratory conditions the mite can survive up to 15 months.

The chigger usually attaches to small ground animals, mostly rodents. Infection in these animals does not cause disease as frequently as in humans and as such humans are considered an accidental host.

Other hosts such as bigger mammals and birds play a role in spread of the mites to newer areas and hence in the spread of the disease.

This complex life cycle of the trombiculid mite is illustrated in the picture below (Figure 4)

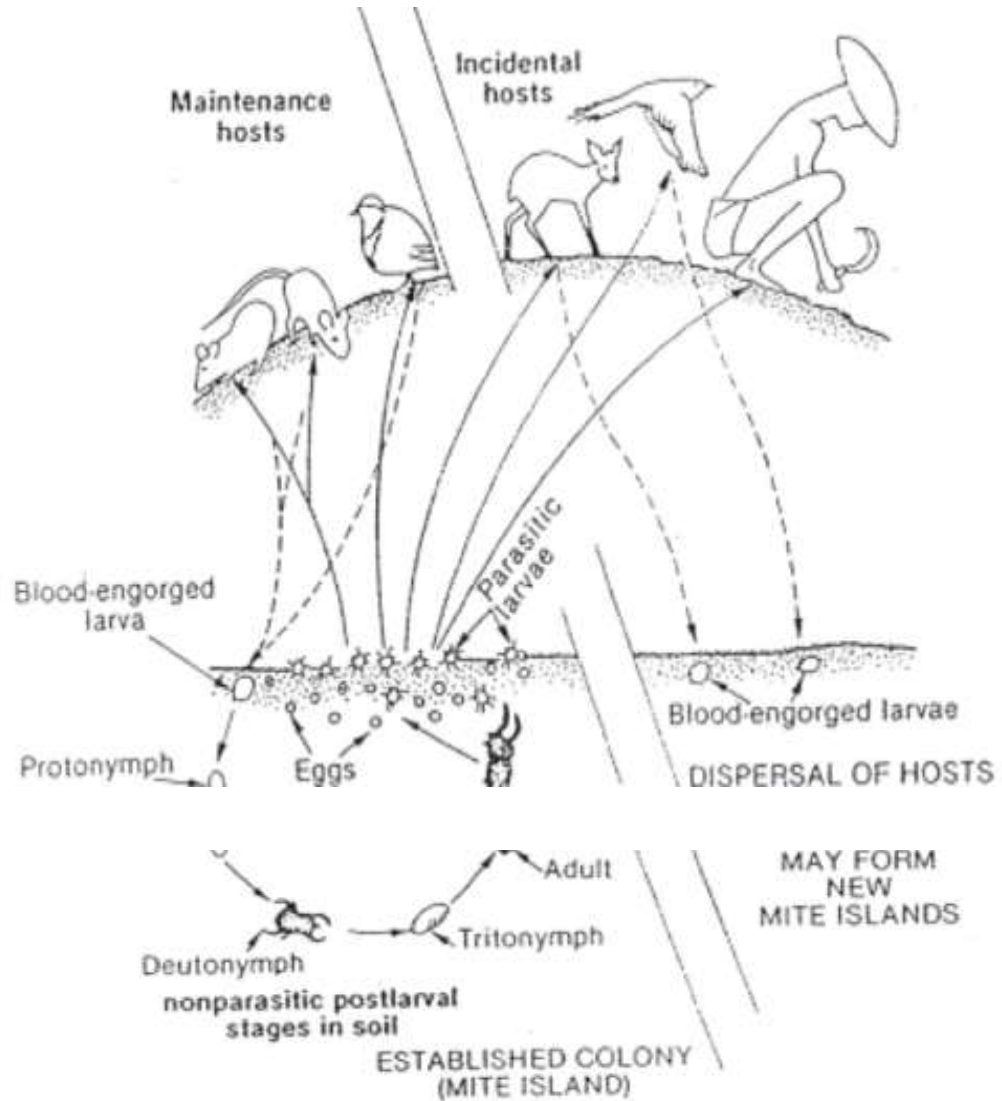


Figure 4 Life cycle of the trombiculid mite

Infection

For many years the mode of transmission of the bacteria *Orientia* *susugamushi* was unclear. It was believed that the carriers of the disease were the rodents and the chiggers or mites merely the intermediate host. However it was discovered that only the chigger stage of the mite could feed and was parasitic. Hence the mite was not just an intermediate carrier but a reservoir of the infection as well. It is still not clear how the infection entered the mites, however experimental studies have shown the maintenance of infection in a generation of mites for upto 20 generations . (50)

This led to the discovery that there was transovarian spread of the infection from one generation to the next. Thus the presence of small mammals may in fact prevent human infection.

Species

There are more than 3000 species of mites in the Leptotrombidium family which are present in South East Asia. Each species is adapted for a certain geographical and climatic condition. The various species and their area of prevalence is shown in the table below.(50,51)

Two trombiculid species *Leptotrombidium deliense* and *Shoengastiella ligula* are the recognized vectors in India. *Leptotrombidium makamushi* is the recognized vector

in Japan and other SouthEast Asian countries, but it has been identified in India as well(52,20)

Table 1 : Vectors of Scrub typhus and their area of prevalence	
Vector	Area of prevalence
L.deliense	Australia, India, China, Malaysia, Pakistan
L. akamushi	Japan
L. scutellare	Japan
L. fletcheri	Indonesia, Malaysia
L. imphalum	Thailand

Host preference

The mite and its chigger infest any kind of animal. From small rodents, to bigger mammals and birds. Certain species have a preference for certain hosts. Not only do these chiggers have a preferential host they may also have a specific area on the host to attach to.

Audy studied these patterns and found that the same species of chiggers could have varying patterns of infestation on different hosts. The *L.deliense* species infests the ears of rats, but the abdominal area of the tree shrews. It was hypothesized that the area of attachment had more to do with the grooming habits of the animal than the chiggers preference itself. The areas where the animal finds it difficult to access or does not groom, seem to be the areas where the chiggers attach. In animals where the chigger attaches in more approachable areas , nest or burrow infestation and attachment during sleep seem to be the plausible explanation.(53)

**ECOLOGICAL ASPECTS
OF DISEASE TRANSMISSION**

Ecology of Scrub Typhus

Scrub typhus was originally discovered in Japan where it was seen among plantation workers .

During World War 2 the soldiers and labourers alike were petrified of the disease that lurched in the long grasses called Lallang.

Since then the disease had been associated with areas where wild grass grew.

Dr Fletcher during the World War II changed the name of this disease. Up to the second world war the disease was called Tsusugamushi disease which in Japanese translates to “tsusuga” meaning disease and “ mushi” meaning insect. After the association with its presence in wild grasses was understood the disease was aptly called Scrub typhus.

Early in the knowledge of the disease certain characteristics about the outbreaks of the disease were identified. These were

1. The disease was obviously associated with particular types of terrains
2. The cases were usually restricted to small foci
3. Large number of people exposed for a short duration acquired the disease
4. There was usually no history of a bite by an insect.

These characteristic features of an outbreak were evident to Dr Audy and his workers in the British army posted in Ceylon. 756 cases of Scrub Typhus were admitted after just 4 days of exposure to an infective area in Ceylon during World War 2. It was noticed that all infections can occur in one platoon and spare the adjoining ones and hence the concept of islands of infection was conceived. These characteristics of the epidemic were eventually

found to be in cohesion with the activity of the chiggers themselves that lived in groups called mite islands(19)

Widespread presence of Scrub typhus in India and around the world

Since the times of the World War 2 Scrub typhus was associated with scrub like dry vegetation. It was thought to only be found in the fringes of the forests, or areas where forests had been cut down and scrubby overgrowth had taken over. It was believed that *L. Deliense* was associated with woody terrain and *L.akamushi* with the grassy fields. Subsequently species such as *Aindica* were associated with urban areas where they infested rodents. This theory of restricted areas where scrub typhus was found and the concept of the tsusugamushitriangle changed with the observation of Scrub typhus from untouched areas of the world.

Scrub Typhus has been isolated from areas as isolated as the Himalayas, Sikkim, Darjeeling and Western parts of Pakistan.

In Himachal Pradesh, a mountainous part of North India is at an altitude of 350-7000 meters above sea level . . 21 cases of Scrub typhus were isolated by Mahajan et al and vector species *Leptotrombidiumdeliense* and *Gahrliepia(schoengastilla)*spp. were isolated. (40)

Sikkim which is in the northeastern part of India had an outbreak of Scrub typhus. S Gurung et al collected sera from 204 patients with a pyrexia of unknown origin in the year 2011 and 63 had Scrub typhus.(54) Similarly from Meghalaya

entomological surveillance has found rodents infested with Chiggers carrying *O. tsusugamushi*.(55)

There have been outbreaks in Southern most parts of India and the western most points of the country as well.

The Maldives which are a small group of islands off the shore of India in the Indian ocean also had an outbreak of Scrub typhus in the year 2002(56)

However Europe and North America remain mostly free of this disease. The only reported cases from there are seen in travelers returning from endemic areas.(57)

Effect of climate:

For many years Scrub typhus was considered a tropical disease with maximum incidence during the rainy seasons. The *L. deliense* and *L. akamushi* are known to proliferate better in these conditions. However the works of Audy et al showed that these mites are very hardy and can withstand extremes of temperature. In laboratory experiments these mites have been frozen to 120 degrees Celsius for weeks and seem to be normal after thawing.(19)

Thus it comes as no surprise that chiggers have been found as high up as in the Himalayas, in desserts of Australia.

Effect of Vegetation

It was believed that chiggers were found mostly in scrub like vegetation, however a jungle cycle of these vectors had been identified.

Sequential studies on chigger populations also have shown that in the same area over time the species and the numbers of the vector can change. This change with time had been attributed to two main factors.

1. Change in the population of the primary hosts of the chiggers. In studies done in Malaya the population of *L. deliense* was followed over a period of time after the deforestation at the same site. With time, the number of *L. deliense* decreased and the number of *L. akamushi* increased. At the same time it was also notice that there was a change in the species of rats trapped in the same areas with time from deforestation.(19)
2. In some studies it has also been shown that cultivated land or that which has periodically ploughed is less likely to harbor chiggers than that which is left barren and unattended. This is a major cause of the disease being reported in new urban areas which are formed from encroaching upon farm land. (58)

Theories of wide spread presence of Scrub typhus

Thus as illustrated above there are various ecologies where this vector and hence the disease can be found. It is because the presence of this disease is unsuspected that people fall prey to it.

How this disease has spread so far and wide and its presence in places untouched by man are still a mystery, though there are a few theories to explain the same.

1. The first theory being that the vector commonly attaches itself to birds and hence can be transferred to places which are untouched by humans.
2. The second theory invokes the concept of ecological islands. It was the finding of scrub infection present on mountains separated by large areas of semi deserts like in Malakand in the Himalayas which lead to this hypothesis. The hypothesis claims that in the Tertiary Period the land in that area was a continuous stretches of forest where scrub typhus was found , and that in the era of the Pliocene upward thrusts of the land separated small areas from each other. This lead to some ecological islands on mountains and some in valleys. (19)

Effect of human activity

Throughout history there are examples of manmade disasters. The spread of Scrub typhus can be added to that list. It is the activities of a man during peace time and during war that have led to the increase in scrubby lands. It is the industrialization and gradual encroachment into the forests and the sea that have dispersed vectors carrying this deadly disease to various parts of the world.

Indian Ecology-

In India the disease was initially studied at the Indo Burma border and was known to be a monsoon phenomenon. However in South India the disease is also seen in the cooler months.(12)

RISK FACTORS FOR SCRUB TYPHUS

Risk factors for acquiring Scrub typhus

Since the resurgence of Scrub Typhus it has become apparent that the disease is wide spread. There is a new interest in the disease. During World War 2, many a soldier fell prey to this disease and preventive measures such as spraying clothes with pesticides, checking for the mite and dusting the scrubby areas with pesticides was also resorted to. The identification of a medication to treat this rickettsial illness was a break through which changed the course of the war. Soldiers were not afraid of the bushes anymore. However with the growing use of these drugs and inappropriate dosages and duration, there is a risk of resistance to first line agents. (59)

In this scenario it seems that preventive measures may play a major role in the control of this disease. Preventive strategies being considered are generation of a vaccine. However, the multiple strains of the bacteria and difference in the strains present in various parts of the world, have made this task difficult. Other preventive measures which target decreased host vector interaction are gaining impetus in this setting. For such measures, a sound knowledge of what puts the host in the realm of the vector and hence, the bacteria, is important.

Risk factors identified in Korea-

D.M. Kim et al conducted a case control study in Korea to identify epidemiological risk factors for scrub typhus.

Cases of Scrub typhus residing in South west Korea in the age group of 40-75 years were screened and 156 patients were included. A control group consisting of the patients neighbours was formed. Baseline data was collected and analyzed

The analysis proved that fruit farming, gathering chest nuts and taking breaks in areas adjacent to agricultural operations was associated with higher odds of acquiring scrub typhus. This was consistent with the presence of *L pallidum* and *L. scutellare* which are usually active in the cool dry autumn conditions when chest nut harvesting takes place.

These findings were grounds for public health measures which were instituted. It helped narrow down the population and the specific tasks which lead to higher risks of Scrub and hence to more targeted interventions for its preventions.

The research group made recommendations to farmers to take indoor breaks, and if outdoor breaks were preferred to use mats to sit on. They recommended not removing any clothing while working and advised dusting of clothes and daily showers. The use of insect repellants was also promoted.(60)

Risk factors identified in Beijing

Since the occurrence of Scrub typhus in urban areas, studies in urban and suburban areas have also been done to look at risk factors for acquiring Scrub typhus.

In Beijing a case control study done by YanningLyu et al identified 56 patients with scrub typhus identified by PCR and serological methods. The control arm was a neighborhood control and age and occupation were matched.

The study showed a that people working in vegetable fields and hilly areas, carrying out harvesting activities in autumn had odds ratios and confidence intervals as follows 3.7 (1.1–11.9), 8.2 (1.4–49.5), and 17.2 (5.1–57.9), respectively.(61)

Risk factors studied in South China

Wei Et al studied the factors responsible for increasing reports of Scrub typhus in Southern China. They observed that the incidence of Scrub typhus had tripled from 2006 to 2012 in Southern china.

A summer peak was noticed and people over the age of 40 were affected more often. The Karp strain of *O.tsusugamushi* was the common strain identified.

People with a history of activity in a park, sitting in the lawn and sitting near rat holes had a higher risk of acquiring Scrub Typhus. Other factors were not looked at and chiggers were not characterized.(62)

Subsequently Tiegang Li et al studied the relationship of risk of scrub typhus with meteorological factors in Southern China from 2006 to 2012

It was found that each one degree rise in temperature corresponded to almost 15 percent increase in monthly number of cases. Also a 1hPa rise in atmospheric pressure lead to a decrease of 8% cases and an increase of 1 mm of rainfall caused an increase of up to 1% cases. These studies show how the change in global climatic conditions, are affecting the incidence of Scrub typhus. Better preventive strategies can be planned with these factors in mind.(63)

Risk Factors in Taiwan

Taiwan which is consists of a varying landscape is also known to have Scrub typhus. Pui et al analyzed the meteorological factors that played a role in the incidence of Scrub typhus. They also looked at the relationship between the use of forest land, farm worker density with scrub typhus.

Areas where Scrub typhus was not endemic had a higher incidence when the humidity increased in that area. There was also a positive co-relation with number of wet days and duration of sunshine.

Taiwan could be classified into 3 types of Scrub typhus. Type 1 where there was no change with climate. Type 2 where Scrub typhus was higher in higher temperatures in the warm season . Type 3 where Scrub typhus correlated with higher surface temperatures and longer hours of sunshine.

In the mountainous areas higher risk of Scrub typhus was associated with farm workers density , management of wood and the type of area.(64)

Risk factors in North India

In India, the burden of Scrub typhus has gradually been increasing. In 2008 there was an outbreak of Scrub Typhus in Darjeeling and the vector identified was *Schoengastiella ligula* was identified as the vector. This sprung interest in preventive measures in those parts of India.

Sharma et al studied the risk factors for scrub typhus using a case control model. 62 patients were studied and a neighbourhood control was identified. These patients and their controls had similar environments and the role of their activities was studied. Unmatched controls were also used for finding the role of the environment in the incidence of Scrub Typhus.

It was identified that cases lived closer to bushes and had wood piles. They commonly worked in farms and had rodents at home.

These studies helped in making proposals to the municipalities for prevention of the disease.(3)

Risk factors in South India

In South India There has been an increase in the incidence of Scrub typhus. It has been observed that the cases reported usually cluster in the cooler months.(12)

However to the extent of my knowledge there is no data on the co-relation of other meteorological factors associated with Scrub typhus, or epidemiological data on risk factors for infection with Scrub typhus.

Entomological data is also lacking regarding the vector and its activities in South India.

Scrub typhus in Tamil Nadu

The resurgence of Scrub typhus in South India led to interest in the disease in Tamil Nadu as well. In 2004 patients with fever of more than 10 days were evaluated for Scrub typhus. 9.6% patients were found to have Scrub typhus. This increased the interest in Scrub typhus(65)

In Rural South India 50 percent of undiagnosed prolonged fevers occurring during the cooler months were caused by Scrub typhus.(23)

Scrub Typhus in Vellore

Vellore is a district in north east Tamil Nadu. It is a city. It has an area of 87.91 sqkm. Vellore is at 12.92 degree North and 79.13 degree east. It is 220m above the sea level. It lies within the Eastern Ghats and has a semi-arid climate with high temperatures all round the year. Rainfall is scanty. April to June are the hottest months and it is coolest from December to January. The monsoons occur usually during October November and December and are a part of the north east monsoons. As per the 2011 census Vellore had a population of 4, 23,425.

Christian Medical College Vellore is a tertiary care hospital situated in the city of Vellore. The annual number of inpatients in the medical wards in this hospital is 38,600

The number of inpatients in the department of medicine was 10,200

In recent studies published from this institution Scrub typhus has been contributing to a major burden of acute febrile diseases. In 2010, 47.5 % patients who presented to this hospital were diagnosed with Scrub Typhus. These cases were seen mostly in the winter months.(6)

The case fatality rate was 14.6% as recorded in 2007. However since then the awareness of the disease and early treatment have led to a case fatality rate to decrease to 7.6%(39)

Justification for the study

Scrub typhus causes significant morbidity and mortality in South India during the cooler months. Scrub typhus spreads through the bite of an infected chigger and with increasing urbanization and clearing of forests these mites will soon be present

in every ecological habitat, and this will determine the acquisition of this disease. Also the onset of resistance to this disease may require more effective preventive measures as prevention may literally be better than cure.

From what is known there has not been any study to look at risk factors for acquiring scrub typhus in South India in spite of the common occurrence of this disease. The knowledge of such risk factors, especially those which are modifiable, could help shape public health measures to prevent the transmission of this disease.

Thus my hope is that my dissertation will help to shed some light on such possibly useful information.

PATIENTS AND METHODOLOGY

Study type

This study was a prospective case control study which intended to determine environmental and behavioral risk factors for acquiring scrub typhus. A case control model was chosen as it would help establish associations between the risk factors and the disease.

Setting and Duration

This study was conducted from the January 2013 to June 2014 in the medical wards of the Christian Medical College Hospital Vellore in Tamil Nadu in South India , which is a tertiary care center.

Study population

Patients who were admitted to the CMC Hospital medical wards and medical intensive care units.

Inclusion criteria

Cases

All adults (>18yrs) presenting to Christian Medical College with an acute febrile illness defined as fever for less than 14 days were evaluated for scrub typhus. A case definition based on work done by Chrispal et al was used(12). Consecutive cases of Scrub Typhus were recruited.

1 Acute febrile illness (fever <14days) and the presence of a positive eschar and scrub IgM ELISA, or;

2 AFI plus a positive scrub IgM ELISA plus clinical response to Doxycycline.

3 AFI plus scrub IgM ELISA seroconversion on convalescent Sera, or;

4 AFI plus a positive scrub IgM ELISA with other serology's negative.

Controls

This study was designed to be a case control study in order to look at specific environmental and behavioural risk factors. Hence 2 sets of controls were chosen. The Geographical controls were patients who shared an environment similar to the case. In this arm as the environment was matched, the role played by activities could be ascertained.

The second control arm was a clinical control who presented to the same hospital with fever and a diagnosis other than scrub typhus was chosen. In this arm the environmental factors could be compared as environment was not matched for.

As behavior varies with both the sex and age of individuals, they were considered confounding factors and it was decided to match all arms for the same. However in view of practical constraints of getting both age and sex matched geographical controls it was decided to match for sex alone, as in our society gender plays a larger role in determining activities of a person

The two control arms were defined as follows

Clinical Control

A sex matched patient, admitted in any of the medical wards with an acute febrile illness (<14days) with a diagnosis other than scrub typhus.

Geographical control

First sex matched bystander or visitor from the same neighborhood as the patient who came to visit the patient in hospital

Exclusion criteria

Patients less than 18 years and those who did not have an appropriate geographic control were excluded.

Patients who belonged to states other than the 4 South Indian states, namely Tamil Nadu, Karnataka, Andhra Pradesh and Kerala were excluded, as the study was planned for looking at risk factors in a south Indian population.

Methodology

Preliminary work

As this was a hospital based study evaluating the geographical and behavioural risk factors for acquiring scrub typhus, home visits to patients houses and their neighbours` houses was conducted prior to initiation of the study, and development of the questionnaire to get a better perspective and understanding of their homes and surroundings. It helped in adding risk factors to be looked at over and above risk factors which had been studied previously.

Questionnaire construction

Based on these visits and on previous studies a questionnaire was made consisting of 80 major questions with sub questions. This questionnaire was translated into Tamil, Telegu and Hindi. (Annexure1)

The questionnaire was piloted amongst the patients in the general wards and some corrections were made. Also it was noticed that most patients were unable to read and hence in order to standardize the collection of data it was decided that the questionnaire would be administered by the primary investigator.

The questionnaire consisted of the following parts (Annexure 1)

- The demographic data of the patient, or control. Socioeconomic status was stratified using the Modified Kuppuswamy scale(Annexure 3)and income ranges were stratified as per the scales of 2012.(66)
- Details of the illness of the cases and clinical controls-This was collected as per the patient records at the time of first contact with the doctor either in the outpatient department or in the emergency department. Data regarding the investigations of the patients were collected from the clinical workstation.

The SOFA scale was used to assess the severity of illness at presentation.

- Environment related questions- These questions related to the environment of the enrolled patients and both sets of controls
- Activities and behavior related questions- These questions related to the behavior and activities of the patient and controls in the 2 weeks prior to illness for the patients and controls

Questions pertaining to hours spent in any given activity were collected for each day and multiplied by 7 for the entire week.

Enrollment of cases

All inpatients admissions during the period of recruitment were screened and all consecutive patients with acute febrile illness who were confirmed to have scrub typhus as per the case definition were enrolled after informed consent. The interview was conducted at the time of recruitment after informed consent, however when a patient was too sick to be interviewed, the interview was postponed till pre discharge. If the patient was deteriorating the questionnaire was administered to the next of kin who lived with the patient.

Enrollment of Geographical control

At the time of interview, the first bystander of the same sex from the same area was also interviewed. This person was interviewed separately. If such a person was not there, a bystander of any other patient in the same ward from the same area as the case was recruited as the geographical control. If this was also not possible then the case was excluded.

Enrollment of the clinical control

Any sex matched patient who was admitted to the hospital after the case with an acute febrile illness other than Scrub typhus was recruited.

Any person with an acute febrile illness suspected to be scrub typhus but did not fulfill criteria for scrub typhus were also recruited as clinical controls.

Interviews

Interviews were conducted individually by the principal investigator for all cases and controls separately.

Consent

Consent was obtained prior to all interviews and consent forms were prepared for the same in Tamil, Telegu and Hindi (Annexure 2)

Health education

After the interviews, a health education session on the prevention of scrub typhus was done and pamphlets were distributed. These were designed and translated in all languages.(Annexure 3)

Bias

The following biases were anticipated

1-Selection bias of cases- This was overcome by including all consecutive cases who met the inclusion criteria.

2-Selection bias of controls- This was overcome by interviewing the first sex matched by stander from the same locality who visited the patient after he/she was recruited for the study.

The second control was a sex matched patient from the medical wards who was admitted after the case with an acute febrile illness otherthan Scrub typhus.

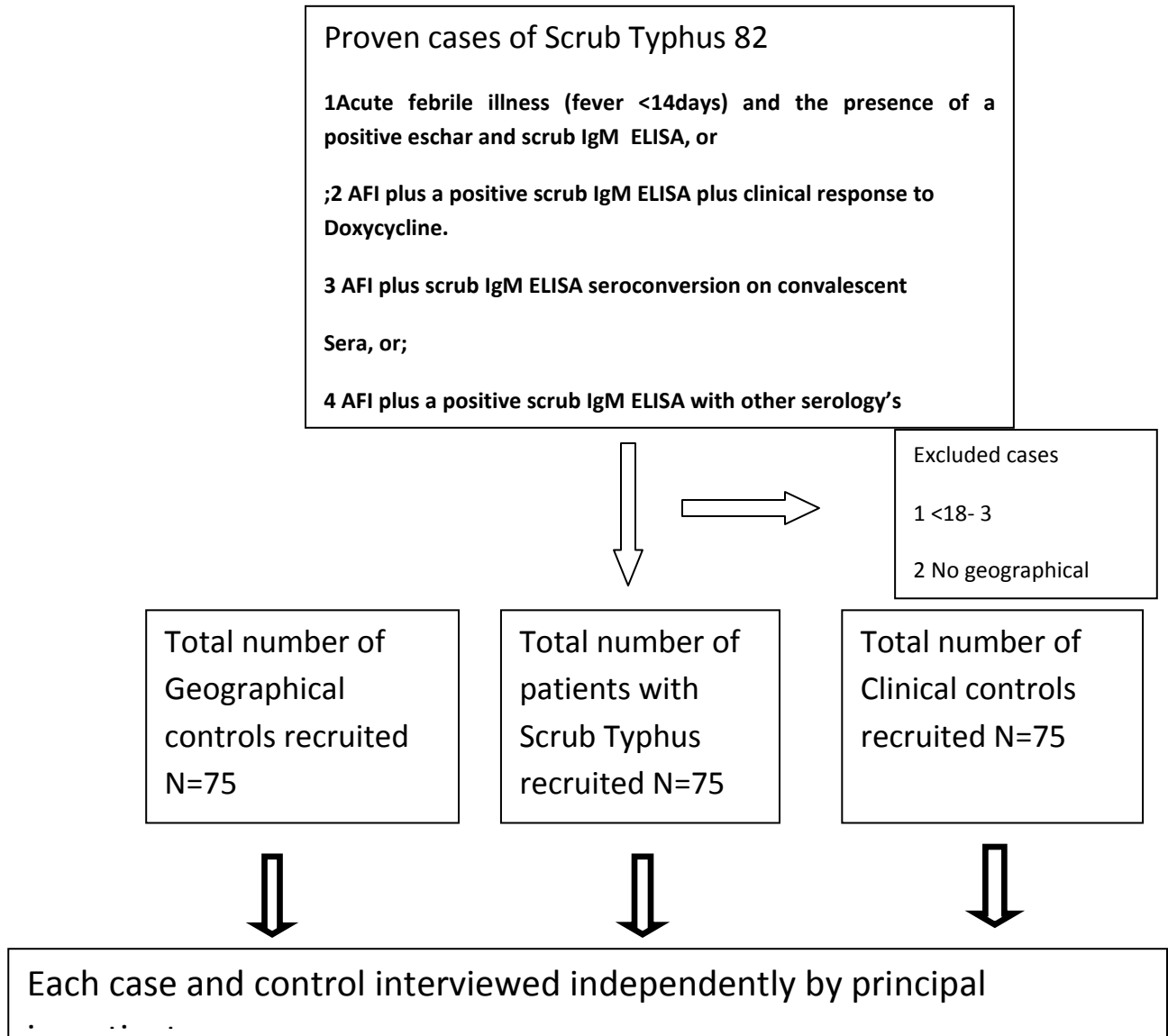
3-Investigator bias- The questionnaire was administered by the principle investigator to every case and control.

Confounding factors

Age and Sex are confounding factors as they determine activities of a person and hence can affect the results of activity based risk factors.

Hence it was decided to match for both during the selection of both cases and controls. However practical constraints during the piloting proved that only age or sex matching was possible. Hence it was decided to match only for sex in both control

STROBE FIGURE



Statistical Methods

Sample size

A sample size of 225(75 cases and 150 controls) was required to detect an odds ratio of 3 with 10 percent exposure in controls and 80 percent power with a two sided significance level of 0.05. The odds ratio of 3 was taken based on previous studies done in Darjeeling. The following formula was used to determine the sample size

Multiple Controls per Case (1 : C)

Formula

$$n = \frac{(C+1)n'}{2C} \quad n' = \frac{m}{P_e}$$

Where,

$$m = \frac{\left\{ \frac{Z_{\alpha}}{2} + (Z_{1-\beta} \sqrt{P(1-P)}) \right\}^2}{(P - 1/2)^2}$$

$$P = \frac{OR}{1 + OR}$$

$$P_e = [(P_2 * (1-P_1))] + [P_1 * (1-P_2)];$$

$$P_1 = \frac{(OR)P_2}{1 + (OR - 1)P_2}$$

n : Number of cases per group

n*c : Number of controls per group

P_1 : Calculated proportion in the case group

P_2 : Expected proportion in the control group

OR : Estimated Odds ratio

C : Number of controls per case

n' : Number of required pairs to detect m discordant pairs in the exposure group.

m : Minimum number of required discordant pairs.

α : Significance level

$1-\beta$: Power

Note: Use the 'C' value = 2 in case of 1:2 Allocation Ratio; use C = 0.5 for 2:1

Allocation Ratio

Analysis

Data entry software Epidata Version 3.1 was used for entering data and analysis was done using STATA version 13

The variables analysed consisted of nominal variables, ordinal variables, continuous and discrete variables.

Univariate analysis was done between cases and controls comparing different variables. Outcome of continuous variables with a normal distribution was

compared between the groups using t test of significance and the Mann Whitney U test for those that do not have a normal distribution. Categorical variables were analysed using the chi square test of significance. Conditional univariate and multivariable logistic regression were performed for relating the scrub typhus with the risk factors concerned. Thus, conditional odds ratios and its 95% CI were presented. Logistic regression was used to study the association between several risk factors and the outcome

Institutional review board

The thesis proposal was reviewed and accepted by the Institutional review board and the Ethics committee.

Funding

This project was funded by the fluid research fund.

RESULTS

During the period from January 2013 to May 2014, 82 consecutive cases of Scrub typhus were collected. However of the cases collected, 3 were below 18. Four of the cases did not have any sex matched geographical control till the time of discharge. Hence 75 cases and their geographical controls and clinical controls were recruited. Each case, clinical control and environmental control was interviewed separately by the principal investigator.

Informed consent was obtained for each case and control in their own language.

The data was entered in Epidata version 3.1 and was analyzed in STATA version 13.

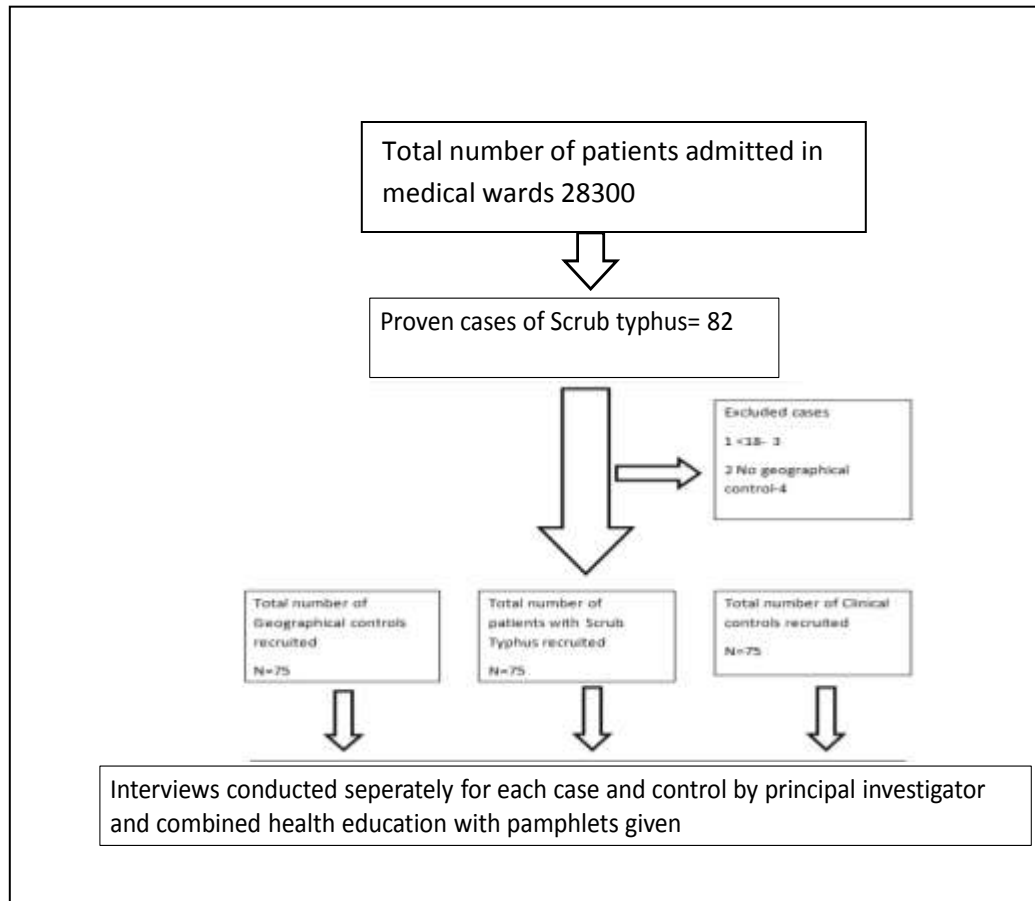


Figure 5 STROBE FIGURE

Baseline characteristics

Table 2 Baseline characteristics of demographic features of cases and controls			
Demographic features	Case	Geographical control	Clinical control
Sex(Female)n(%)	44(58.67)	44(58.67)	44(58.67)
Age mean(SD)	44.7(27-61)	38.6(28-48)	44.8(27-61)
Socioeconomic status(SES)			
Low SES	9(46.6)	10(44)	10(48)
Middle SES	31(41.3)	32(42.6)	29(38.6)
High SES	35(12.5)	33(14.0)	36(14.0)
Farming in the previous 2 weeks	15(20)	14(18.6)	7(9.3)

Table 3 Baseline clinical characteristics of the cases of Scrub typhus	
SYMPTOMS	n (%)
Headache	20 (26.67)
Nausea/ vomiting	24 (32)
Cough	14 (18.67)
Altered Sensorium	6 (8)
Seizures	1 (1.33)
Myalgia	14 (18.67)
Abdominal Pain	15 (20)
Breathlessness	28 (37.33)

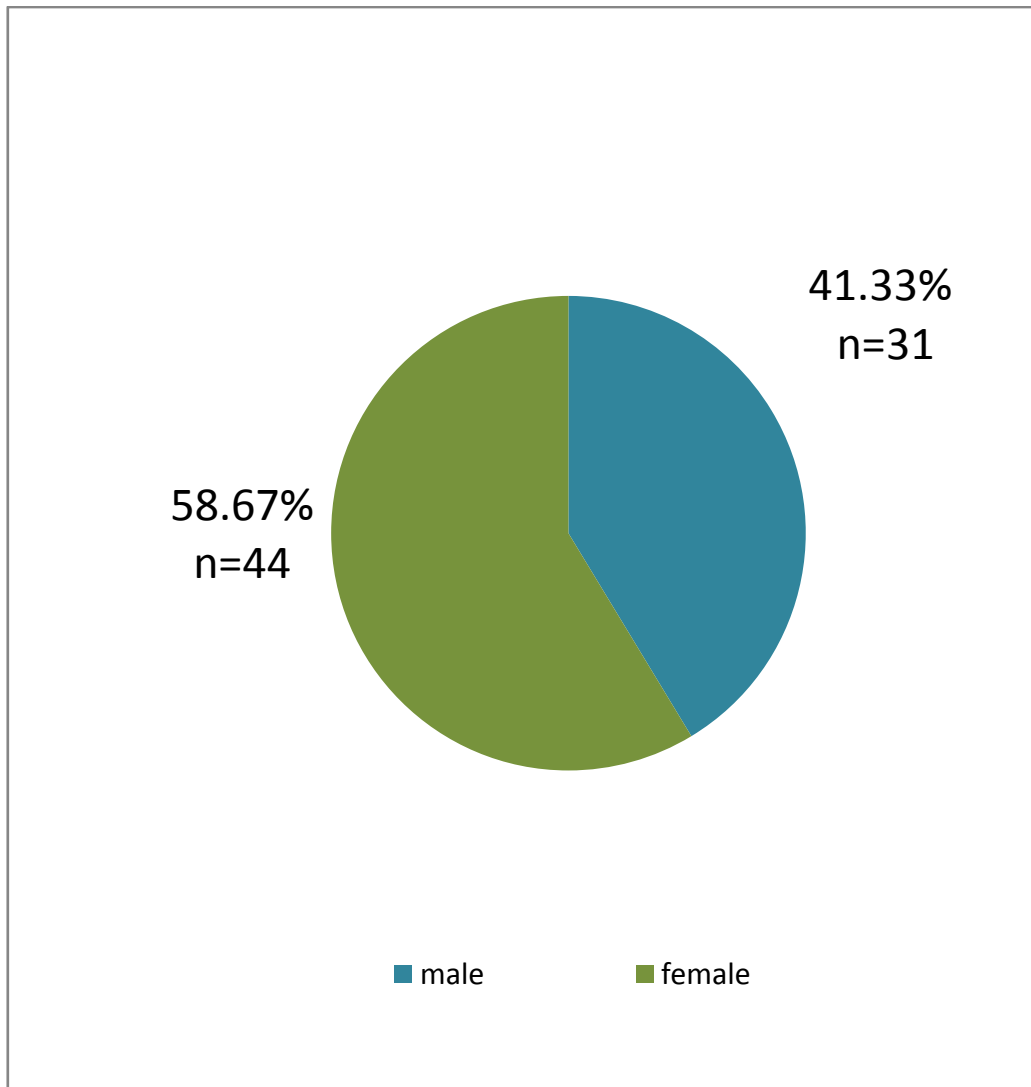
Arthralgia	4(3)
Jaundice	1(1.33)
Oliguria	4(5.33)
Bleeding	1(1.33)
SIGNS	n(%)
Pallor	18(24)
Icterus	9(12)
Oedema	5(6.67)
Eschar	48(64)
Hepatomegaly	5(6.67)
Splenomegaly	3(4)
Crepitations	17(22.67)
Neck Stiffness	3(4)
LVS3	1(1.33)
LAB PARAMETERS	N(%)
WBC COUNT	
Leucopenia(<4000)	0(0)
Normal(4000-11000)	31(41.3)
Leucocytosis(>11000)	44(58.6)
Thrombocytopenia	68(90.7)
Transaminitis	73(98.7)
SOFA AT ADMISSION	
>=10	5(6.6)
<10	70(93.3)

Sex distribution-

Of the 75 cases who were recruited , there was a larger proportion of women than men.

The controls were sex matched as per study protocol.

Figure 6 Sex distribution among cases of Scrub typhus recruited.



Age distribution-

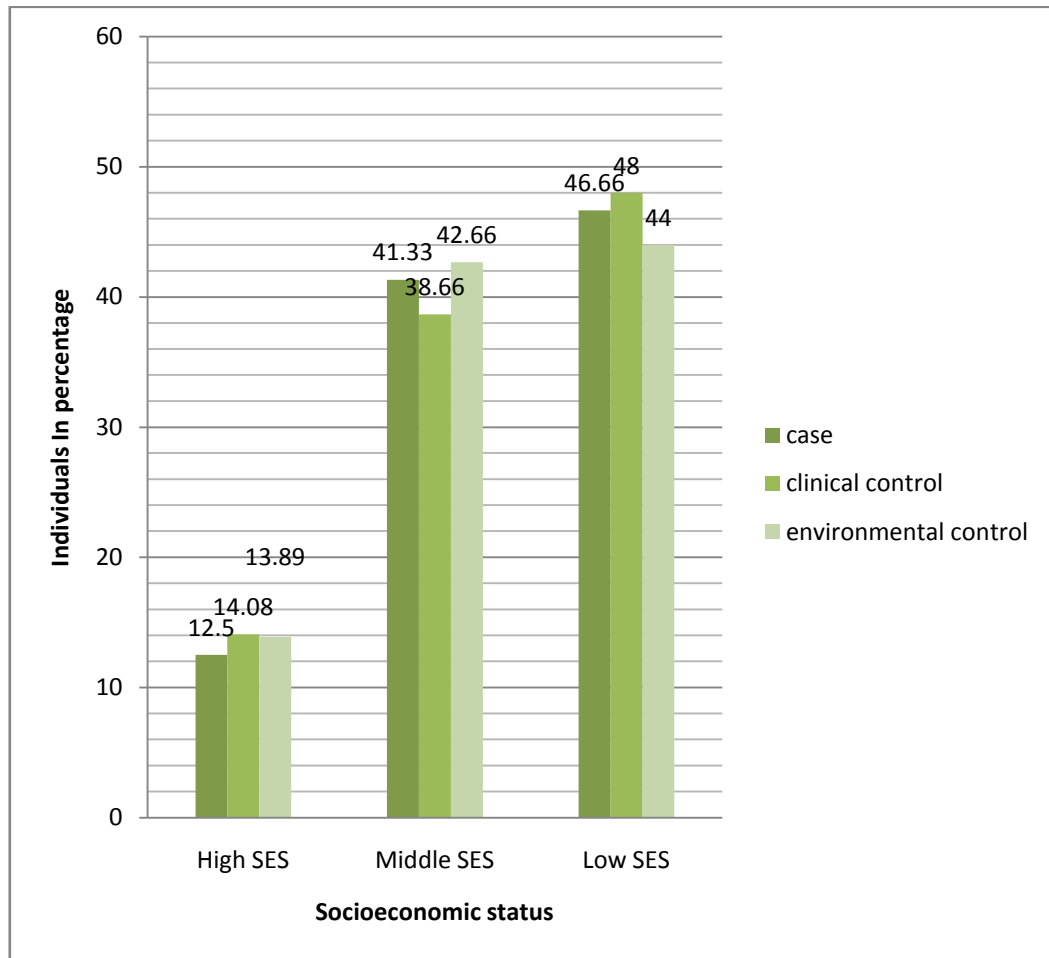
Most cases belonged to the 4th decade of life in both the cases and the clinical controls.

The average age of patients with Scrub typhus was 44.7(27-61), and among clinical controls was 44.8(27-61). However the mean age in the environmental controls was 38.6(28-48)

Socioeconomic distribution of cases and controls-

The average socioeconomic status of most of the patients, both cases and controls was from the lower socioeconomic strata

Figure 7 Socioeconomic status of patients and controls



.Figure8 People involved in farming in 2 weeks preceeding their illness

among cases, clinical controls and environmental controls

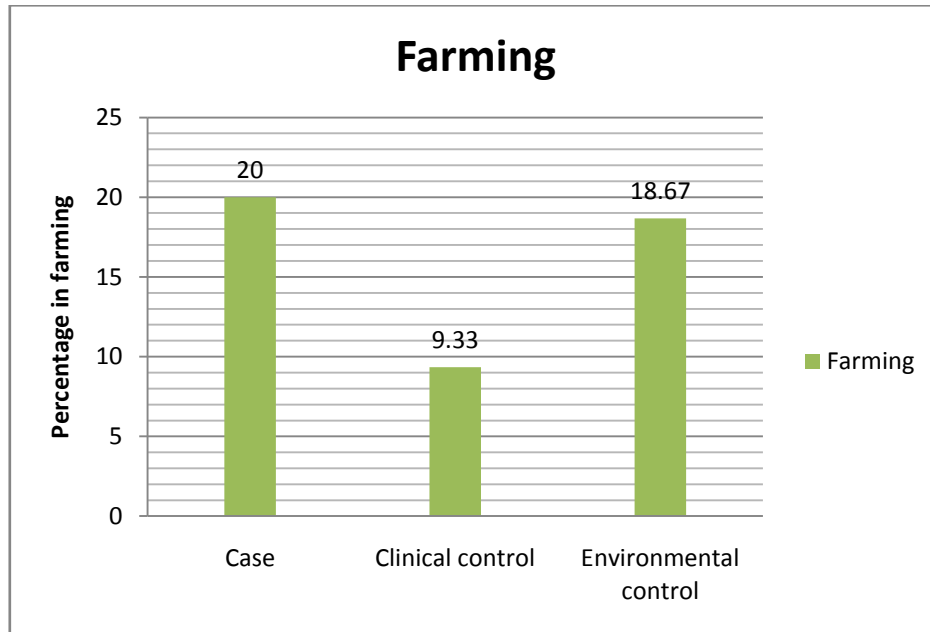
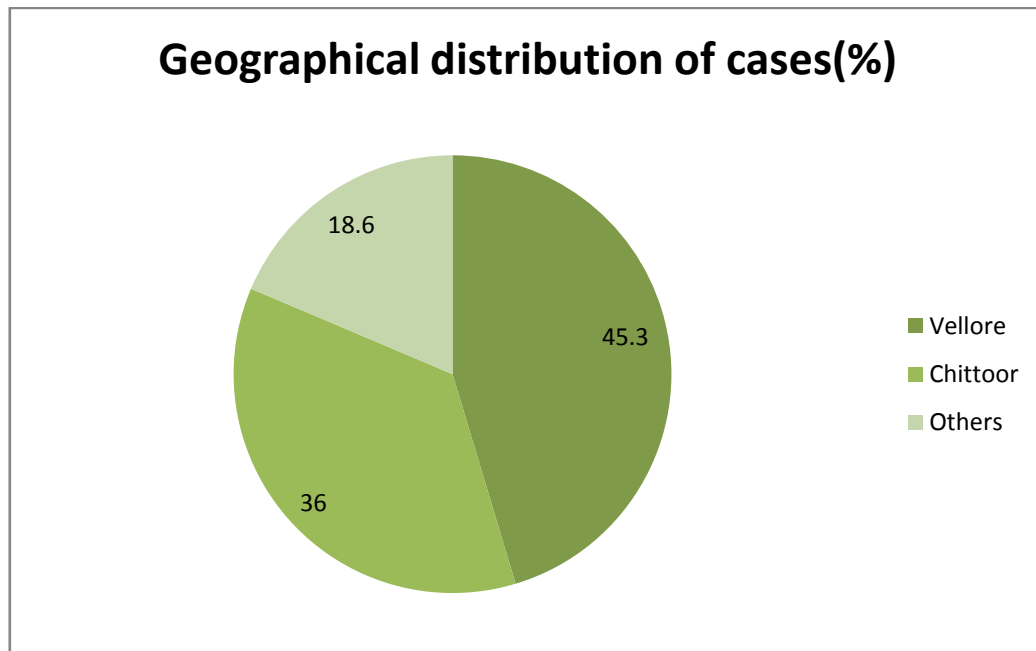


Figure9 Geographical distribution of cases



Among the 75 cases who were recruited there were almost equal number of urban and rural 53% and 47 % respectively. Most of the cases were from the district of Vellore and a few from the southern parts of Tamil Nadu. However there were a sizeable number of cases from Andhra Pradesh as well (38.7% ie 29 cases). Below is a map showing the distribution of the cases from the various parts of both states.

45 % of the patients diagnosed as scrub typhus were from Vellore, 36% were from Chittoor, which is part of adjoining state of Andhra Pradesh and almost a third of the cases were from other adjoining villages and cities

Within the Vellore district the cases of Scrub typhus were distributed mostly within Vellore, Gudiyatham and Katpadi towns. (Figure 11)

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Figure10 : Distribution of cases of Scrub typhus

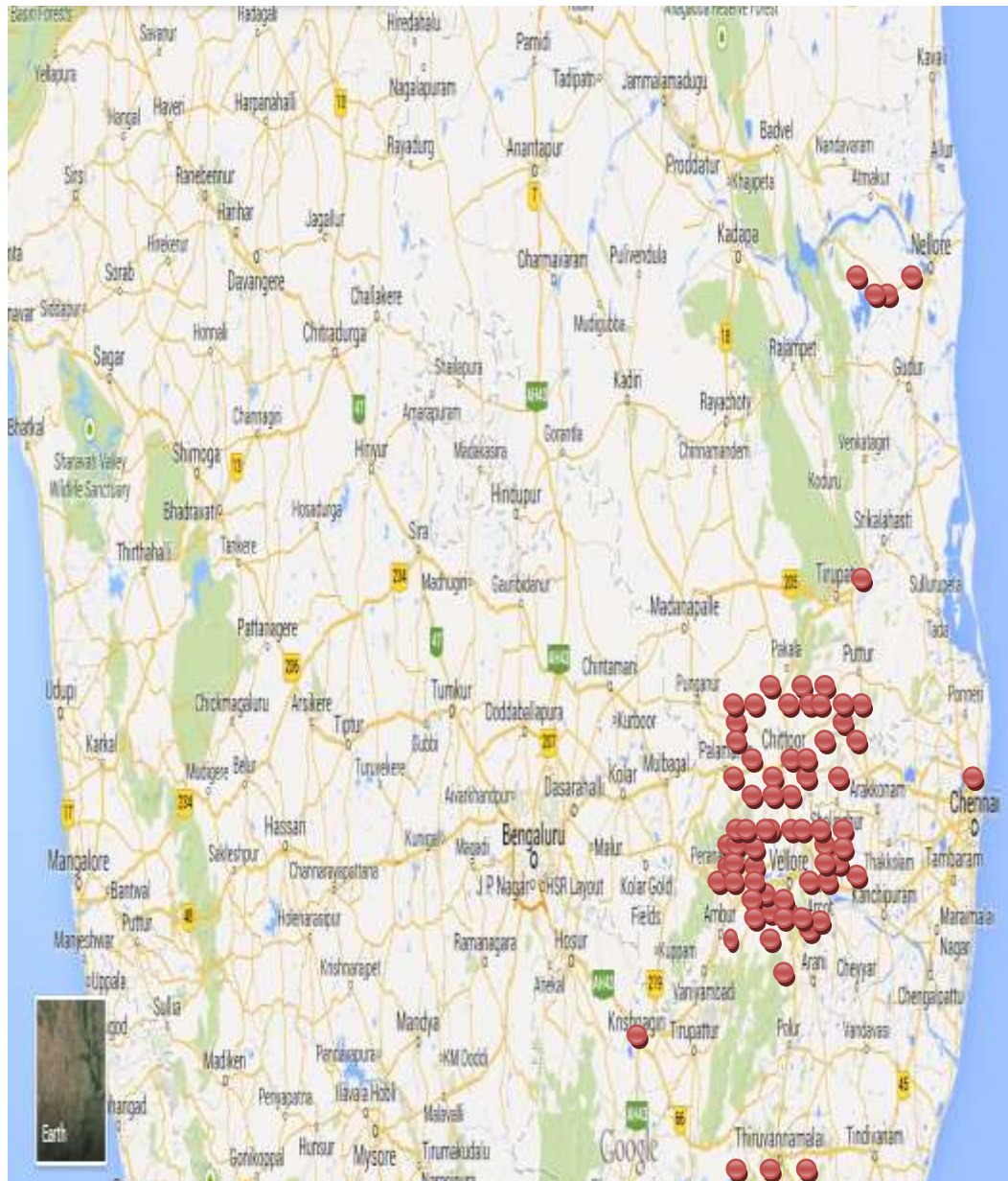
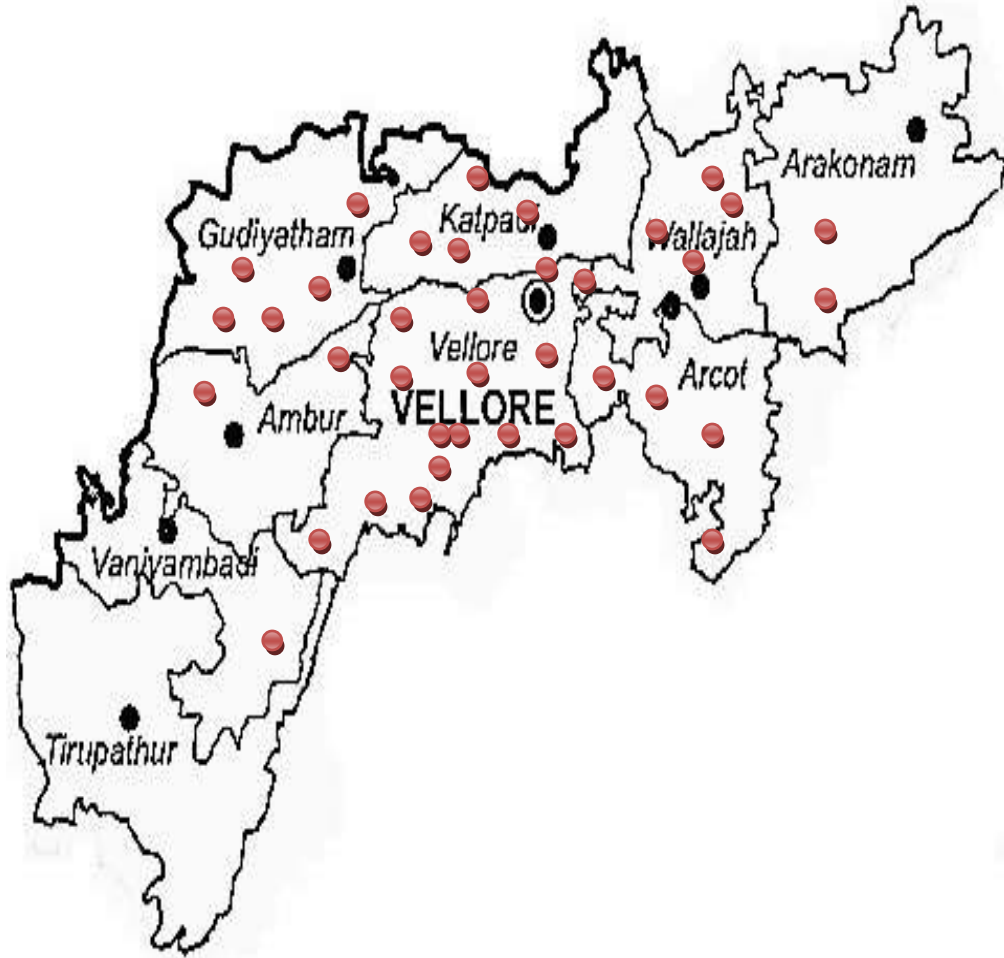


Figure11 : Distribution of cases of Scrub typhus within Vellore district

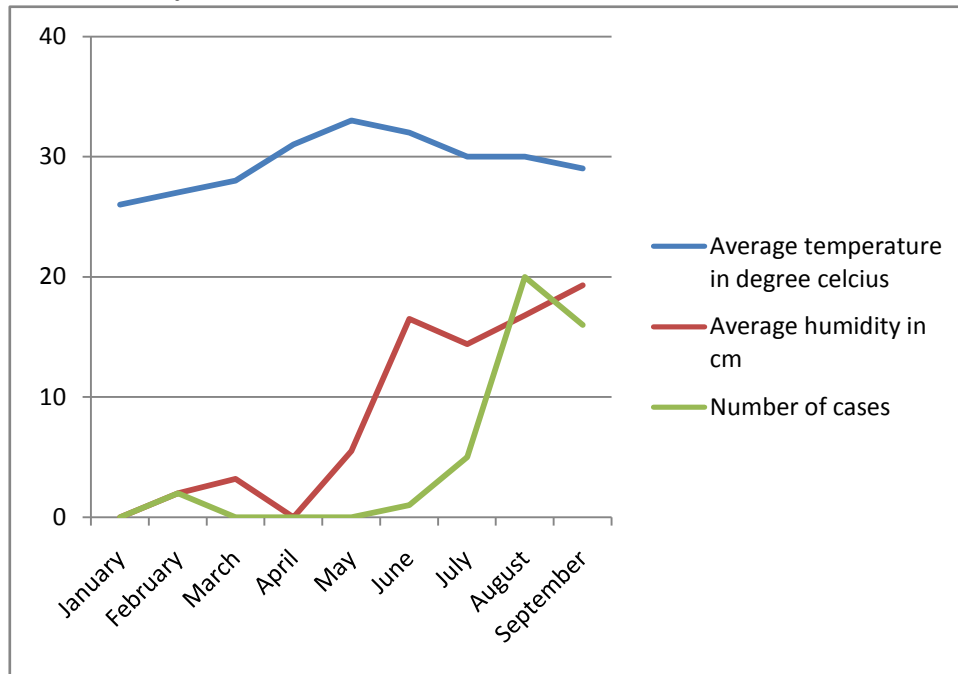


Seasonal distribution of cases from Tamil Nadu

During the period of January 2013 to October 2013, 75 cases of Scrub typhus were recruited. The cases were clustered during the period of July to August . However the sample collection was completed in mid October.

During this period the temperature in the district had started to decrease and the humidity had started to increase. This relationship is demonstrated in the Graphs below for both Vellore(Figure 12) and Chittoor(figure 13)

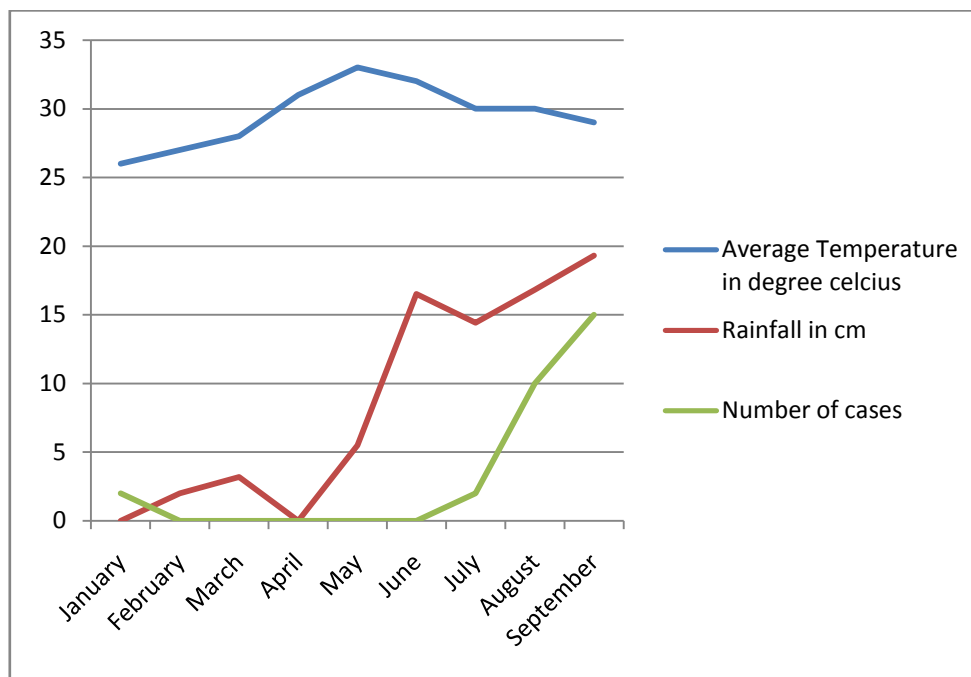
Figure 12: Graph showing the monthly distribution of cases in the period from January 2013 to October 2013 in CMC hospital with the average temperature and humidity in Vellore district



Seasonal distribution of cases from Andhra Pradesh

The cases of Scrub typhus from Andhra Pradesh were also clustered from August to September and were on the rise.

Figure 13: Graph showing the monthly distribution of cases in the period from January 2013 to October 2013 in CMC hospital with the average temperature and humidity in Chitoor district



Clinical characteristics

The common clinical symptoms that patients with Scrub Typhus, presented with were breathlessness, nausea, vomiting and headaches.

Clinical signs- The common clinical signs which were present among the cases were an Eschar which was present in more than 50% of the cases, followed by pallor and crepitations. Features to suggest meningitis and myocarditis were infrequent at presentation.

Nearly 60% of patients had leukocytosis, 90.7 % had thrombocytopenia and 98.7 % had elevated transaminases on laboratory evaluation at presentation.

The SOFA score was used as a severity score for cases and for clinical controls. The median SOFA scores for the cases was 5 and for the controls was 2.

Time to defervescence of fever

Among the cases of Scrub typhus the time to defervescence was less than 48 hours in 77 % of the patients as compared to 22 % in whom defervescence took longer.

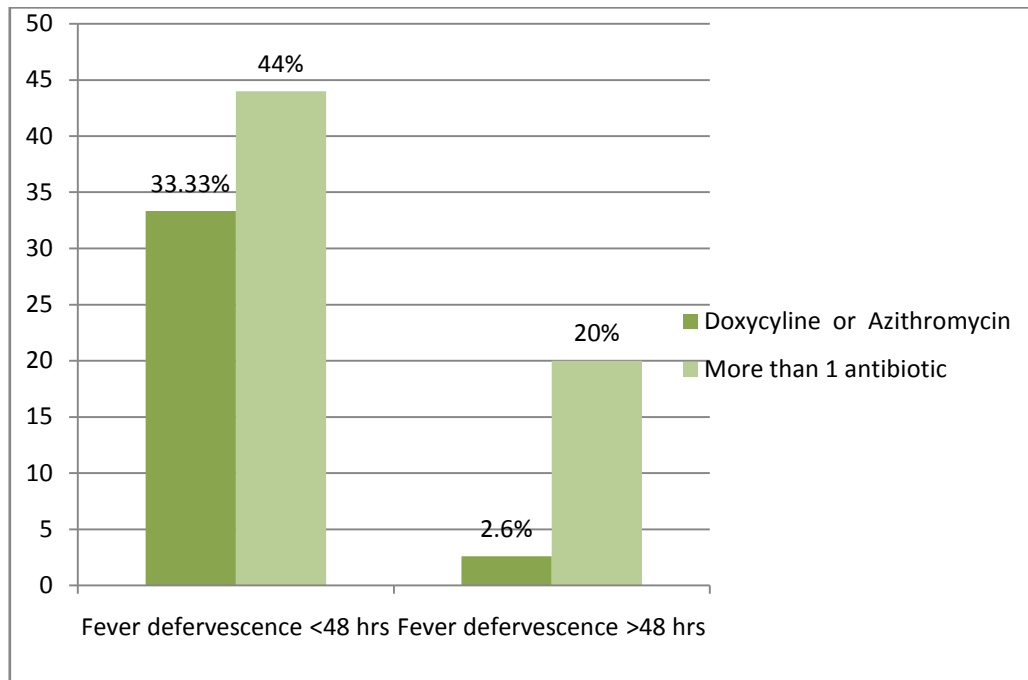
Table 4 Time to defervescence among cases of scrub typhus	
Time to defervescence	n(%)
<= 48 hours	58(77.33)
>48 hours	17(22.67)

Antibiotic Usage

Among those who had an earlier response to treatment more than 50% used more than 1 antibiotic.

Table 5: Antibiotics used among cases with fever defervescence <48 hours	
Doxycycline or Azithromycin	25(43.10%)
Both or more than 2	33(56.89%)

Figure 14 Antibiotics used and fever defervescence among cases of Scrub Typhus



Nearly two thirds of patients with scrub typhus received more than 1 antibiotic. More than 75% of cases showed a response to treatment within 48 hours. However, nearly one fourth

of them had a delayed response. This is a disturbing trend probably signifying loss of exquisite sensitivity to doxycycline, considering that response to doxycycline used to be part of case definition of scrub typhus until very recently.

RISK FACTORS FOR ACQUIRING SCRUB TYPHUS

Housing

It was found that 14 % of the cases lived in Kuchcha houses. These included both thatched and mud houses, whereas only 4 % of the controls lived in similar houses.

Table6 Univariate analysis showing the odds ratio for type of house and disease					
Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Geographic control n(%)	Odds ratio (95% Confidence interval(CI))
Kuchcha house (exposure)	11(14.66)	12(16)		3(4)	4.12(1.10-15.44)
Pucca house	64(85.33)	63(84)	0.90(0.39-2.14)	72(96)	
TOTAL	75(100)	75(100)		75(100)	

Sanitation-

The following table shows the crude odds ratios for various sanitation risk factors for acquiring scrub typhus. Not having a toilet in the house, use of an outdoor toilet among those who did not have toilets were risk factors for cases as compared to the clinical controls.

Table 7 Univariate analysis showing odds ratios for toileting facilities and disease					
Variable	Case n(%)	Clinical control n(%)	Odds ratio (95% CI)	Geographic control n(%)	Odds ratio (95% CI)
No toilet in the house	59(78.67)	47 (62.67)	2(1-4)	55(73.33)	1.67(0.60-4.58)
No bathroom in the house	51(68.92)	41(55.41)	1.76(0.8-3.49)	49(65.33)	1.28(0.47-3.45)
Using outdoor toilet	24(40.67)	9 (18.75)	3.61(1.4-9.3)	22 (44.89)	1 (0.32-3.10)
Open defecation	35 (59.32)	39 (81.25)	1.1(0.5-2.6)	33 (67.34)	0.70(0.32-1.56)
Defecation at less than 1 meter from scrub (open or toilet outside)	24 (32)	27(36)	1.37(0.67-2.8)	20(26.66)	1.66(0.60-4.58)

Surroundings of the house and risk of Scrub typhus-

The table below shows the crude odds ratios for environmental risk factors for scrub typhus . The presence of firewood in or around the house was found to be more among cases than in their clinical controls.

Table 8 Univariate analysis of environmental risk factors					
Variable	Case	Clinical	Odds ratio	Geographic	Odds ratio
	n(%)	control n(%)	(95%CI)	control n(%)	(95%CI)
Scrub vegetation less than 5 meters from the house	48(72)	43(69.33)	1.32(0.68-2.55)	62.66(47/75)	1.05(0.54-2.05)
Firewood in or around the house	57(76)	48(64)	1.78(0.92-3.43)	59(78.66)	3(0.81-11.08)

Presence of animals and rodents and risk of Scrub typhus

The presence of cattle or rodents in or around the house did not have significant crude odds ratios for disease, when compared to clinical controls or geographic controls. Neither did working with cattle predispose to the Scrub typhus

Table 9 Univariate analysis showing odds ratio for presence of animals in the surroundings and disease					
Variable	Case n(%)	Clinical controln(%)	Odds ratio (95% CI)	Geographic control n(%)	Odds ratio (95% CI)
Rodents in the house	42(56)	38(50.67)	1.25(0.64-2.41)	33 (44)	0.4(0.15-1.03)
Cattle in or around the house	28(37.33)	22(29.33)	1.35(0.72-2.53)	28(37.3)	1.11(0.45-2.73)
Working with cattle	14(18.67)	10(13.33)	1.44(0.61-3.38)	17(22.7)	0.7 (0.26-1.83)
Working with cattle for >7hr/wk	6(8)	3(4)	2.08(0.50-8.67)	7 (9.33)	0.85(0.27-2.68)

Farming and gardening practices and risk of Scrub typhus-

Farming and gardening practices were such as sowing , tilling , harvesting or weeding showed a higher association with disease. Also watering of plants or fields also showed a significant association with disease. To our knowledge this was the first time the duration of exposure was accounted for. It was observed that spending 7 or more hours a week in sowing, and spending more than 15 hours a week in harvesting or weeding activities was associated with disease.

Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Geographic control n(%)	Odds ratio (95%CI)
Time spent in farming >30 hrs a week	8 (10.66)	3(4)	2.82(0.71-11.08)	5 (6.6)	1.64(0.5-5.28)
Involved in sowing	8(10.67)	1 (1.33)	8 (1.00-63.96)	7(9.46)	1.25(0.33-4.65)
Time spent in sowing 7 or more hours/wk	7(9.33)	1(1.33)	7.61(0.91-63.52)	1(1.33)	7.61(0.91-63.52)
Involved in tilling	7(9.33)	1 (1.33)	7.61(0.91-63.52)	2(2.67)	6(0.72-49.83)
Time spent tilling >15hr/wk	2.66(2)	1(1.33)	2.02(0.17-22.84)	0	5.13(0.24-108.81)
Involved in harvesting or weeding	24(18)	6(8)	3.00(1.19-7.557)	12(16)	1.75(0.73-4.17)
Time spent in harvesting or weeding >10hr/wk	6(8)	4(5.3)	1.54(0.41-5.70)	6(8)	1.37(0.45-4.16)

Watering plants	11(14.67)	4(5.33)	3.33(0.91-12.11)	6(8)	2.67(0.70-10.05)
Time spent watering >5hrs/wk	6(5)	1(1.3)	5.28(0.60-46.37)	2 (2.66)	2.05(0.36-11.58)
Exposure to forest or scrub vegetation	15(20)	10(13.3)	1.62(0.67-3.92)	13(17.33)	1.22(0.50-2.71)
Duration of exposure in forest>7hr/wk	5(6.66)	5(6.66)	1.00(0.27-3.60)	6(8)	0.82(0.23-2.81)

Clothing and risk for Scrub typhus-

Men who did not wear a shirt or those whose legs were not covered during work were considered exposed and women who wore sari to work were considered exposed. The table below shows the crude odds ratios for the same. There is no significant difference between the three groups with regard to clothing practices.

Table11Univariate analysis showing odds ratio for clothing and the disease					
Variable	Case	Clinical	Odds ratio	Geographic	Odds ratio
	n(%)	control	(95%CI)	control	(95%CI)
		n(%)		n(%)	
Men with exposed areas	30(96.77)	30(96.77)	0.57(0.17-1.95)	31(100)	0.625(0.20-1.91)
Women with exposed areas	39(88.63)	32(72.72)	1.75(0.51-5.97)	37(84.09)	1.5(0.42-5.31)

Hygiene practices and the risk of Scrub typhus-

In the table below the univariate analysis shows the relationship of various hygiene practices and Scrub typhus. Patients with Scrub typhus are more likely to not be changing underclothes before going to bed, however there is no significant difference between the three groups..

Table 12 Univariate analysis showing odds ratios for hygiene practices and the disease					
Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Geographic control n(%)	Odds ratio (95%CI)
Not wearing undergarments	40(53.33)	39(52)	1.16(0.39- 3.47)	41(54.67)	0.87(0.31- 2.41)
Not changing overclothes before sleeping	49(65.33)	43(57.33)	1.40(0.72- 2.71)	43(57.33)	1.40(0.72- 2.71)
Not changing under clothes before sleeping	25(71.4)	21(58.33)	1.57(0.35- 4.05)	13(37.14)	1.41(0.7- 2.76)
Not bathing after outdoor activity	58(77.33)	60(80)	0.88(0.42- 1.79)	53(70.67)	1.83(0.68- 4.96)

Resting and sleeping activities and risk for Scrub typhus-

The table below shows the relationship between the resting and sleeping habits and the risk of disease. Lying down or sitting directly on mud or grass especially for periods greater than 7 hours a day appeared to be significant risk factors in univariate analysis.

Table 13 Univariate analysis showing odds ratios of resting and sleeping practices and disease					
Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Geographic control n(%)	Odds ratio (95%CI)
Lying down / sitting on mud/grass/scrub	44(58.67)	31(41.33)	1.81(0.98- 3.33)	27(36)	3.43(1.47- 7.96)
Lying directly on ground(without mat)	41(54.67)	29(38.67)	0.50(0.045— 5.51)	28(37.33)	2.44(1.12- 5.30)
Duration of lying on ground >7hrs/wk	9(12)	6(8)	2(0.50-7.99)	11(14.66)	3(1.1- 30)
Sleeping on floor	44(58.67)	41(54.67)	1.17(0.61- 2.24)	48(64)	0.71(0.31- 1.60)

Cooking and washing practices and the risk of Scrub typhus-

Squatting on the ground to cook and drying clothes outside were not associated with significant risk of acquiring Scrub typhus

Table 14 Univariate analysis showing odds ratios for cooking and washing practices and Scrub typhus					
Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Geographic control n(%)	Odds ratio (95%CI)
Squatting on floor to cook	15(20)	15(20)	1(0.43-2.30)	19(25.33)	0.63(0.24- 1.64)
Hours spent squatting >7hr/wk	7(9.3)	3(4)	1(0.06- 15.98)	5(6.66)	2(0.18- 22.05)
Drying clothes outside	69(92)	73(97.33)	0.33(0.06- 1.65)	71(94.67)	0.5(0.09- 2.73)

Protective measures and Scrub typhus

The table below shows the effect of protective measures and Scrub typhus. In all three groups no one had heard of Scrub typhus or knew how it spread. Use of insecticides is considered as a protective factor. Only 2.6% of clinical controls, 4% geographic controls used insecticides in their farms, However none of the cases used insecticides in their farm.. The other factors such as use of insect repellants and foot ware were analysed and is shown below in table10

Table 15 Univariate analysis showing odds ratio for lack of protective measures and scrub typhus					
Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Geographic control n(%)	Odds ratio (95%CI)
Not using insect repellants when outdoors	75(100)	73(98.65)	5.13(0.24-108.81)	74(98.67)	3.04(0.12-75.84)
Not using foot ware	19(25.33)	10(13.33)	2.13(0.91-4.92)	15(20)	1.44(0.61-3.37)

Multivariate analysis of case vs Geographical control

It was found that even though cases and their geographical controls shared the same locality there was a difference in their living conditions and practices. In previous studies done in Korea it has been found that outdoor defecation and passing urine in the grass were risk factors for Scrub infection.(5) In our population too, the practice of open defecation is common and it was hypothesized to be a probable risk factor for acquiring Scrub typhus. Also the closeness to vegetation was hypothesized to be a risk factor. These factors though significantly associated with disease on univariate analysis did not show any significance in the multivariate analysis.

From previous work done by Kundavaram et al it was seen that the commonest site for the eschars was the groin followed by the abdomen. It was considered that the kind of clothing amongst patients in our population may be a factor contributing to this distribution. In turn clothing and exposure during working hours may be a factor predisposing to scrub typhus.

In our population taking rest during lunch hours on the grass is a common practice, very much like the practices in South Korea. As this was found to be a risk factor in their population it was analysed and found to be associated to disease in our population as well. The duration of exposure was also considered to increase the possibility of exposure and was also included in the multivariate analysis.

Besides these practices, the practices of harvesting or weeding were hypothesized to be risk factors and were also considered in the multivariate analysis.

All the above mentioned factors showed significant association to the disease in the univariate analysis, however in the multivariate analysis they did not.

. Lying down or sitting directly on the grass had a high odds ratio of 10, however the difference was not statistically significant. These results are presented in Table 16 below

Table 16 Multivariate analysis of risk factors for scrub in case vs. geographic control				
Variable	Case n(%)	Geographic control n(%)	Odds ratio (95%CI)	Modified odds ratio(95%CI)
No toilet in the house	78.67(59/75)	73.33(55/75)	1.67(0.60-4.58)	1.64(0.42-6.44)
Defecation at less than 1 meter from scrub (open or toilet outside)	32 (24/75)	26.66(20/75)	1.66(0.60-4.58)	1(0.26-3.87)
Involved in harvesting	24(18/75)	16(12/75)	1.75(0.73-4.17)	1.03(0.37-2.84)
Not changing under clothes before sleeping	71.42 (25/36)	37.14 (13/33)	1.41(0.7-2.76)	1.35(0.65-2.81)
Lying down / sitting on mud/grass/scrub	58.67(44/75)	36(27/75)	3.43(1.47-7.96)	10.91(0.82-144.5)
Duration of lying on ground >7hrs/wk	28(21/75)	14.66(11/75)	3(1.1-8.30)	1.2(0.34-4.733)
Lying directly on ground(without mat)	54.67(41/75)	37.33(28/75)	2.44(1.12-5.30)	0.25(0.02-2.67)

Multivariate analysis of case vs clinical control

In the comparison to the clinical controls practices such as outdoor toilet use, involvement in sowing , harvesting, and lack of use of protective measures was considered. In addition presence of firewood around the house was also considered. Though, there was a difference in the number of people using outdoor toilets in the cases and clinical controls, Cases using outdoor toilets almost 3 times as much as the controls, it did not reach significance on the multivariate analysis. Also cases were more likely to be involved in sowing, harvesting and lying down on open grass as compared to the clinical controls, however these factors did not reach significance on the multivariate analysis.

This could probably be because, the terrain of the areas around the city of Vellore, which are the main areas of referral to the Christian Medical College are quite similar. As such there may be no true difference in the environment of these two groups. That being said the cultural practices and activities are also quite similar. Hence we cannot conclusively say that any specific environment or activity predisposes to the acquisition of Scrub typhus in our population, but factors such as lying or sitting on grass and sowing may be associated with disease.

Table 17 Multivariate analysis of risk factors for scrub in case vs clinical control

Variable	Case n(%)	Clinical control n(%)	Odds ratio (95%CI)	Modified odds ratio(95%CI)
No toilet in the house	78.67(59/75)	62.67(47/75)	2(1-3.99)	1.37(0.37-4.94)
Using outdoor toilet	40.6(24/59)	18.75(9/48)	3.61(1.4-9.3)	1.48(0.36-5.96)
Firewood in or around the house	76(57/75)	64(48/75)	1.78(0.92-3.43)	1.51(0.62-3.65)
Involved in sowing	10.67(8/75)	1.33(1/75)	8 (1.00-63.96)	7.08(0.68-72.88)
Involved in harvesting	24(18/75)	8(6/75)	3.00(1.19-7.557)	1.88(0.63-5.64)
Lying down / sitting on mud/grass/scrub	58.67(44/75)	41.33(31/75)	1.81(0.98-3.33)	1.95(0.78-4.90)
Not using foot ware	25.33(19/75)	13.33(10/75)	2.13(0.91-4.92)	0.82(0.26-2.54)

Discussion-

Scrub typhus is a re-emerging zoonosis. In the pre-antibiotic era methods to prevent the spread of Scrub typhus included spraying and dusting clothes with insecticides, and burning areas at the fringe of forests. With the discovery of antibiotics to treat this disease there was a decline in preventive measures and gradually this zoonosis has been detected in multiple varying ecologies. This points to a very hardy bacterium and also a hardy vector. The mortality due to this disease though less, due to earlier treatment and early identification may rise again as there are newer reports of resistance to this disease.

In view of this scenario preventive measures have again become important.

As is documented from studies in various parts of South East Asia and in both North and South India, the disease can affect any age group and sex; however there is a predilection towards women. In my study also almost 60% of the patients recruited were women and most cases were in the 4th decade.

Most of the patients in all three groups belonged to the lower socio economic group, however a sizeable number were also present in the middle socioeconomic group (46.6%, 48% and 44% respectively in cases, clinical and geographic control). Though Scrub typhus was originally considered a disease of predominantly the farmers and agricultural workers, in this study, only 20% of the cases were involved in farming and only 47% were from the rural areas. This is probably due to a referral bias as this study was done in a tertiary care hospital which is accessed by those who can afford care. Effective treatment of Scrub typhus is now available at the peripheral health centers with increasing awareness of the disease, this could have also contributed to this result.

81% of the cases were from the district of Vellore and from neighbouring Chittoor, although it is part of the state of Andhra Pradesh. There were only a few cases from the other parts of Tamil Nadu and Andhra Pradesh. There were no cases from the other 2 states of Kerala and Karnataka in South India. Thus this sample may not be representative of South India.

As is seen in figure 8 the distribution of cases seems to be concentrated both in Vellore and in Chittoor to the months of August to October. The cooler months from November, December which is also the time of North East Monsoon from which Tamil Nadu gets most of its rainfall, (starts from October to December) were not part of the study as the sample size was completed in October. There is a lag period from January to July. In my study the incidence of Scrub typhus starts at the end of the summer months, continues through the monsoons and into the cooler months. This may suggest that there is a wide variety in the vector transmitting this disease. However worth noting is that the fluctuations are more in humidity over the months than in the temperature. Further entomological studies may be helpful in delineating the reason for this pattern of the disease.

Most patients with Scrub typhus were found to have a fever defervescence within 48 hours (77.33%). Of these patients however 56 % required more than 1 antibiotic. Resistance to Doxycycline and Azithromycin has not been seen in our institution, however the use of more than 1 antibiotic may be an indication of this, or of superadded infections in these patients. This requires further investigation.

Geographic risk factors for acquiring Scrub typhus

In this study living in a Kuchcha house , not having a toilet in the house, presence of firewood in and around the house were risk factors for Scrub typhus with odds ratios of 4.12(1.1-15.44),2(1-4),1.78(0.92-3.43).

In a risk factor analysis study done in Darjeeling, 73 percent of the cases lived in wood houses(3). In China, houses with yards without cement floors which may be comparable to Kuchcha houses in India, had higher odds of disease odds ratios of 4.2(1-17). (61)

. These findings are similar to the Darjeeling risk factors studies , where having piles of wood in the yard was found to be significantly associated with disease odds ratio of 3.6(1-14) and contrary to the Sharma et al 's findings bushes at close range to the house was not a significant risk factor(Odds ratio1.05(0.54-2.05)as compared to odds ratio of 11(3.1-38) in the Darjeeling study (3)

However on multivariate analysis none of these factors were found to be independent risk factors for acquiring scrub typhus

Presence of animals or rodents and working with cattle was not different in the three groups with odds ratios of 1.25(0.64-2.41) and 0.7(0.26-1.83) . This too was in contrast to Sharma et al's findings that presence of rodents and rearing domestic animals is associated with Scrub typhus(odds ratio of 3.6(1.4-11), 2.4(1.1-5.7) respectively). This could be due to different cultural practices between the different regions of India.

Activities predisposing to Scrub typhus

Farming activities such as sowing and harvesting, using an outdoor toilet were found to be significantly associated with disease in the univariate analysis, odds ratio 8(1-63.96), 3(1.19-7.5) and 3.61(1.4-9.3) respectively, however were not independently associated with disease. Other activities like, lying directly on mud or grass were also associated with disease, odds ratio 2.44(1.12-5.30), however this was not independently associated with the same.

This is similar to findings of Kweon et al in Korea where urinating on the grass predisposed to Scrub typhus with an odds ratio 1.5(1.1-2.1).

Use of protective measures and awareness of Scrub typhus

All the patients and controls were unaware of Scrub typhus disease and how it spreads. There were only 1 percent of clinical and geographical controls that used insect repellants. None of the cases used the repellants while working outdoors. In studies done in Korea knowledge of the disease and preventive measures were found to be protective factors with(Odds ratio 0.45(0.24-0.83)).(67)

Other factors such as not bathing after outdoor activities, and not changing over clothes or underclothes before sleeping, did not prove to be independently related to disease, odds ratio 0.88(0.42-1.79), 1.40(0.72-2.71) and 1.57(0.35-4.05). This was

contradictory to the results from North India where bathing and changing clothes were protective (odds ratio 0.4(0.1-0.9), 0.2(0.1-0.5)) (3)

Completely covered clothing was found to be a protective factor in the Korean studies with OR of 0.5(0.3-0.9), however exposed clothing was not a significant risk factor for acquiring Scrub typhus in this study. (OR and 95% confidence intervals(CI) 0.6(0.2-1.9) for men and 1.5(0.42-5.31) for women. This again could be due to prevalence of dressing practices where everyone wears a saree or dothi hence was not different between the three groups.

Thus for the factors investigated, there was no significant difference in the exposure of the cases or controls. It is thus possible that the entire population was equally exposed to the vectors and hence the bacteria, however the acquisition of disease may be dependent on the vector characteristics or the host characteristics. These aspects were not considered during this study.

Also protective factors were used only in minimum numbers by cases and controls and hence their effect cannot be adequately gauged. Intervention studies may be more suited to find the usefulness of such measures. In spite of its strengths which include exhaustive information on the surroundings and practices of patients and their controls, there were shortcomings which may have skewed the results.

CONCLUSION

In this population examined, there seem to be no significant environmental factors or practices which predispose a person independently to acquiring scrub typhus. However, on univariate analysis patients with Scrub typhus were found to be more likely to -live in Kuchcha houses [OR and 95 % CI 4.12(1.10-15.44)], lie down or sit on mud or grass [OR and 95% CI 3.43(1.47-7.96)], lie down directly on the ground [OR and 95% CI 2.44(1.12-5.30)] and lie down on the ground for more than 7 hours a week [OR and 95 %CI 3(1.1-8.30)], as compared to their geographical controls.

They were more likely to – not have a toilet inside their house[OR and 95% CI 2(1-4)], use an outdoor toilet[OR and 95% CI 3.61(1.4-9.3)], involved in sowing [OR and 95% CI 8 (1.00-63.96)], be involved in harvesting [OR and 95% CI 3.00(1.19-7.557)], as compared to their clinical controls.

LIMITATIONS

Despite its strengths this study had its limitations as mentioned below.

1. Recall bias- As the questionnaire was administered at the hospital it relied on the patients and controls ability to recall their activities and surroundings. Hence the measurements and durations may not be accurate. Also in some cases where the patient was too sick the information was provided by the next of kin and maynot have been accurate. In certain cases due to lack of any geographical control cases had to be excluded.
2. Referral bias- As CMC is a referral center only the very sick patients are referred from far off districts. Most patients were hence from districts close to CMC. Hence the sample may not be representative of South India.
3. Accuracy of information- In very sick cases the interview had to be conducted with the next of kin and the reliability of personal details and activities may not have been accurate.
4. In this study the environmental controls selected were healthy, however the absence of subclinical infection and hence exposure to the vector and the bacteria cannot be ruled out.
5. Administration of the questionnaire- In view of most patients being unable to read, the questionnaire was administered by the primary investigator. Hence blinding was not possible.

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ANNEXURE

ANNEXURE 1 – ENGLISH PATIENT DATA FORM

PATIENT DATA FORM 1

Patient demographic data:

	Question		
1.	Patient name (in Caps)		
2	Informant		
3.	Hospital ID No		
4	Age		
5	Sex	1. Male	2. Female
6	Date of admission		
7	Residence	1. VelloreCity 2. Others	
8	Residential Address		
	KUPPUSWAMY SCALE FOR SOCIO ECONOMIC STATUS	SCORING	SCORE GIVEN
9.	Education of the family head	7 6 5 4 3 2 1	<input style="width: 40px; height: 20px;" type="text"/>

10	Occupation of the family head	10 6 5 4 3 2 1	<input type="checkbox"/>
11	Family income per month	1.26-29-Upper 2.15-25-Middle 3.<10- Lower .	<input type="checkbox"/> <input type="checkbox"/>
	Total Score		

12.Symptoms: 1=present 2= absent

	Symptomatology	Duration of symptom		Symptomatology	Duration of symptom
a	Fever		h	Myalgia	
b	Headache		i	Abdominal pain	
c	Nausea/Vomiting		j	Breathlessness	
d	Rash		k	Arthralgia	
e	Cough		l	Jaundice	
f	Altered sensorium		m	Oliguria	
g	Seizures		n	Bleeding	

13. Signs : 1=present 2=absent

a	Pallor		g	Tachycardia>100		m	Splenomegaly	
b	Icterus		h	SpO2		n	Petechiae	
c	Lymphadenopathy		i	Tachypnea >20		o	Crepitations	
d	Rash		j	Hypotension<90		p	Altered sensorium	
e	Oedema		k	Fever		q	Neck stiffness	
f	Eschar		l	Hepatomegaly		r	LV S3	
	Eschar loc							

14. Investigations

a	Hb		h	Potassium		o	Protein	
b	TLC		i	Bicarbonate		p	Albumin	
c	% Neutrophils		j	CPK		q	SGOT	
d	Platelets		k	Total bilirubin		r	SGPT	
e	Creatinine		l	Direct bilirubin		s	ALP	
f	Sodium				t	Chest	
g	Scrub IgM		n	Other serologies		u	Scrub IgM convalescent sera	

15. SOFA parameters

Parameter	0	1	2	3	4
Respiratory P/F	> 400	< 400	< 300	< 200	< 100
Platelets	> 150	< 150	< 100	< 50	< 20
Vasoactive	Nil	MAP < 70	Dopa < 5	Dopa > 5 or Adr/NA < 0.1	Dopa > 15 or Adr/Na > 0.1
GCS	15	13-14	10-12	6-9	< 6
Bilirubin	< 1.2	1.2 – 1.9	2.0 - 5.9	6.0 -11.9	> 12
Renal	< 1.2	1.2 – 1.9	2.0 – 3.4	3.5-4.9 or UOP < 500 ml	> 5.0 or UOP < 200 ml

16	Clinical status at discharge	1. Cured 2. Better 3. Same 4. Sequelae 9. Other _____ 5. Discharged at morbid state 6. Dead 7. Discharged against med. adv. 8. Abscond <input data-bbox="1282 567 1347 630" type="checkbox"/>
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17	Diagnosis	1. Scrub Typhus 2. Malaria 3. Typhoid 4. Leptospirosis 5. Others <input data-bbox="1396 798 1461 850" type="checkbox"/>
18	If scrub typhus , name of the antibiotic used	1. Doxycycline 2. Azithromycin 3. Both 4. Multiple –specify _____ 99. Not applicable <input data-bbox="1396 1018 1461 1081" type="checkbox"/>
19	Time taken for fever to defervesce	1. </=48 hours 2. >48 hours 99. Not applicable <input data-bbox="1396 1186 1461 1239" type="checkbox"/>
20	If more than 48 hours specify	_____ <input data-bbox="1396 1291 1461 1344" type="checkbox"/>

ENVIRONMENT

21	What kind of house do you live in	1. Concrete 2. Brick 3. Mud 4. Thatched	5. Others _____(if others then specify) <input data-bbox="1307 1564 1372 1627" type="checkbox"/> <input data-bbox="1274 1659 1339 1711" type="checkbox"/>
22	How many rooms do you have in your house?	1. One 2. Two 3. Three 4. More than three <input data-bbox="1226 1795 1291 1858" type="checkbox"/>	

23	How many people live in your house ?	_____
24a	Is there a toilet inside your house?	1. Yes 2. No
b	Is there a bathroom in your house?	1. Yes 2. No <input type="checkbox"/>
25	If not then where do you pass urine /stools	1. Toilet outside the house 2. Open space 3. Others <input type="checkbox"/> _____(specify if others)
26	If the answer to the above question is 1or 2, is there scrub vegetation in that area	1. Yes 2. No <input type="checkbox"/>
27	If yes then how close to the scrub do you go?	_____(in meters)
28	If the answer to question24b. is no,then where do you bathe?	1. Toilet outside 2. Common lake 3. Near a hand pump 4. Pond 5. Others <input type="checkbox"/> _____(specify if others)
29	Is there scrub vegetation around the area you bathe in?	1. Yes 2. No <input type="checkbox"/>
30	If yes how close to the scrub is it?	_____(in meters)
31	Do you have scrub vegetation close to your house?	1. Yes 2. No <input type="checkbox"/>
32	If yes, how far from your house is the closest scrub vegetation	_____
33	Do you have piles of fire wood inside your house?	1. Yes 2. No <input type="checkbox"/>
34	If no, do you have piles fire wood outside your house?	1. Yes 2. No <input type="checkbox"/>

35	If yes, how far from your house is it kept?	_____
36	Do you have rodents in your house?	1. Yes 2. No <input type="checkbox"/>
37	Do you have cattle inside your house?	1. Yes 2. No <input type="checkbox"/>
38	Do you have cattle outside your house?	1. Yes 2. No <input type="checkbox"/>
39	How far from your house is the cattle kept?	_____

Activities(in the past 2 weeks)(if yes for any activity last done before illness date)

40	Are you involved in farming?	1 Yes 2 No <input type="checkbox"/>
41	If yes, what do you farm?	1. Paddy 2. Wheat 3. Maize 4. Fruits 5. Tea 6. Rubber 7. Others _____ Specify if others Can have more than one answer <input type="checkbox"/>
42	How many hours a week are you involved in this activity?	_____
43	Are you involved in sowing seeds?	1.Yes 2. No <input type="checkbox"/>
44	If yes, for how many hours a week?	_____
45	Are you involved in tilling soil/digging soil?	1.Yes 2. No <input type="checkbox"/>
46	If yes, for how many hours a week?	_____
47	Are you involved in harvesting /weeding?	1. Yes 2.No <input type="checkbox"/>
48	If yes, for how many hours a week?	_____

49	Do you water plants in your garden?	1. Yes 2.No	<input type="checkbox"/>
50	If yes, for how many hours a week?	_____	
51	Do you spray your garden or field with insecticide?	1 Yes 2 No	<input type="checkbox"/>
52	If yes specify the insecticide used	_____	
53	If yes how many times a week?	_____	
54	Do you go into scrubby areas or forest vegetation during the day?	1. Yes 2.No	<input type="checkbox"/>
55	If yes, for what?	1. Collect firewood 2. Collect fruits 3. Collect fodder for cattle 4. Others Can have more than one answer	<input type="checkbox"/>
56	For how many hours a week are you involved in the above activity?	_____	
57	Do you work with cattle?	1. Yes 2.No	<input type="checkbox"/>
58	If yes, what work?	1. Grazing 2. Feeding 3. Cleaning 4. Others Specify if others More than one answer can be given	<input type="checkbox"/>
59	For how many hours a week are you involved in the above activity?	_____	
60	If answer to any question from 41 to 56 is yes, then what clothing do you wear during these activities? A)TOP	TOP 1. Fully sleeved shirt/blouse 2. Half sleeved shirt/blouse	BOTTOM 1. Half pants 2. Full pants 3. Saree folded above the knee 4. Saree full 5. Mundu full 6. Mundu folded 7. Others -specify _____

	B)BOTTOM C) UNDERWEAR	3. Sleeveless shirt /blouse 4. No shirt 5. others sp_____	<input type="checkbox"/>
		1. Yes 2.No	<input type="checkbox"/>
6 1	Do you wear gloves during working with vegetation or animals?	1. Yes 2.No	<input type="checkbox"/>
6 2	Do you use insect repellent while working outdoors?	1.Yes 2. No	<input type="checkbox"/>
6 3	If yes what insect repellent?	_____	
6 4	Do you wear footwear when you leave the house?	1. Yes 2.No	<input type="checkbox"/>
6 5	Do you change clothing before sleeping? a)overclothes b)underclothes	1. Yes 2.No 1. Yes 2.No	<input type="checkbox"/>
6 6	Do you have a bath after returning from outdoor activities?	1. Yes 2.No	<input type="checkbox"/>
6 7	Do you lie down /sit on the open grass/scrub/mud?	1. Yes 2. No	<input type="checkbox"/>
6 8	If yes, for how long during a week?	_____	
6 9	If yes, do you use a mat/ cloth to lie on?	1. Yes 2. No	<input type="checkbox"/>
7 0	Do you sleep on the floor inside your house?	1.Yes 2. No	<input type="checkbox"/>
7 1	If yes , do you use a mat/ cloth to lie on?	1. Yes 2.No	<input type="checkbox"/>

7 2	Do you squat on the floor to cook food?	1.Yes 2. No	<input type="checkbox"/>
7 3	If yes, for how many hours a week?	_____	<input type="checkbox"/>
7 4	Do you dry your clothes on the grass?	1. Yes 2.No	<input type="checkbox"/>
7 5	Do you dry your clothes outside?	1. Yes 2.No	
7 6	Do you play outdoors next to scrub vegetation?	1. Yes 2.No	<input type="checkbox"/>
7 7	If yes, for how many hours a week?	_____	
7 8	Do you pass within 5 meters of scrub vegetation during the day?(not applicable if other contact present)	1 Yes 2 No	<input type="checkbox"/>
7 9	If yes, how many times a day?	_____	
8 0	Do you know how people get scrub typhus?	1 yes 2 no	<input type="checkbox"/>

TAMIL QUESTIONNAIRE

21	எப்படிப்பட்ட வீட்டில் நீங்கள் வாழ்கிறீர்கள்?	1. கன்கிரீட் 2. செங்கல் வீடு 3. மண்வீடு 4. குடிசை 5. பிரபலகை	<input type="checkbox"/>
22	உங்கள் வீட்டில் எத்தனை அறைகள் உண்டு?	1. ஒன்று 2. இரண்டு 3. மூன்று 4. மூன்றிற்கு மேல்	<input type="checkbox"/>
23	உங்கள் வீட்டில் எத்தனை பெர் வசிக்கிறார்கள்?		<input type="checkbox"/>
24	உங்கள் வீட்டில் உள்ளே கழிப்பறை உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
25	இல்லைபென்றால், உங்கள் கழிப்பறை கடமைகளை எவ்ரு செய்வீர்கள்?	1. வெளியே உள்ள கழிப்பறை 2. திறந்த வெளி 3. பிரபலகை	<input type="checkbox"/>
26	மேற்கண்ட கேள்விக்கு 1 டு) 2 பதில் உண்மையாக இருப்பின், அந்த பகுதியில் புத்ர் செய்கள் உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
27	இருப்பின், புத்ர்செய்க்கு எவ்வளவு அருகாமையில் நீங்கள் செய்வீர்கள்?	மீட்டர்களில்	<input type="checkbox"/>
28	நீங்கள் எங்கே குளிப்பீர்கள்?	1. வீட்டுக்குள் உள்ளே குளிப்பவறை 2. வீட்டுக்கு வெளியே குளிப்பவறை 3. ஏரி 4. குழாயடியில் 5. குளத்தல் 6. பிரபலகை	<input type="checkbox"/>
29	அந்தப் பகுதியிலே புத்ர்செய்கள் உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
30	ஆம் என்றால் புத்ர்செய்க்கு எவ்வளவு அருகாமையில்	மீட்டர்களில்	<input type="checkbox"/>
31	உங்கள் வீட்டில் அருகாமையில் புத்ர்செய்கள் உண்டா	1. ஆம் 2. இல்லை	<input type="checkbox"/>
32	ஆம் என்றால், உங்கள் வீட்டிலிருந்து எவ்வளவு தொலையில் புத்ர்செய்கள் உண்டு.	மீட்டர்களில்	<input type="checkbox"/>
33	உங்கள் வீட்டிலுள் விறகுகள் அடுக்கி வைக்கப்பட்டுள்ளனவா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
34	இல்லைபெனில், வீட்டுக்கு வெளியே விறகுகள் அடுக்கி வைக்கப்பட்டுள்ளனவா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
35	ஆம் எனில், வீட்டுக்கு எவ்வளவு தொலையில் அது அடுக்கி வைக்கப்பட்டுள்ளது?	மீட்டர்களில்	<input type="checkbox"/>
36	உங்கள் வீட்டில் எலிகள் உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
37	உங்கள் வீட்டிலுள் ஆடு மாடுகள் உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
38	உங்கள் வீட்டிற்கு வெளியே ஆடு மாடுகள் உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
39	உங்கள் வீட்டிலிருந்து எவ்வளவு தொலையில் அனை வைக்கப்பட்டுள்ளன?	1. ஆம் 2. இல்லை	<input type="checkbox"/>

செயல்பாடுகள்

40	பயிற்சூழலில் நீங்கள் ஈடுபட்டுள்ளீர்கள்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
41	ஆம் என்றால் என்ன பயிற்சூழல்கள்?	1. நேல் 2. கோதுமை 3. கோளம் 4. பழங்கள் 5. தேயிலை 6. ரப்பர் 7. மற்றவை	<input type="checkbox"/>
42	வாரத்தில் எத்தனை மணிநேரம் இந்த வேலையில் ஈடுபடுகிறீர்கள்?	மீட்டர்களில்	<input type="checkbox"/>
43	விவாக விவாகப்பதில் நீங்கள் ஈடுபடுகிறீர்கள்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
44	ஆம் என்றால், வாரம் எத்தனை மணிநேரம்?		<input type="checkbox"/>
45	நிள்க்கை கிளையத்தில் / மணலகை தேண்டுவதில் ஈடுபட்டுள்ளீர்கள்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
46	ஆம் என்றால், வாரத்திற்கு எத்தனை மணி நேரம்?		<input type="checkbox"/>
47	அறுவடை செய்வதில் களைபெடுப்பதில் ஈடுபட்டுள்ளீர்கள்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
48	ஆம் எனில், வாரம் எத்தனை மணிநேரம்?		<input type="checkbox"/>
49	உங்கள் தேரட்டத்துக்கு நீங்கள் தண்ணீர் விடுவதுண்டா?		<input type="checkbox"/>
50	ஆம் எனில், வாரம் எத்தனை மணிநேரம்?		<input type="checkbox"/>
51	உங்கள் தேரட்டத்துக்கு / லபலுக்கு பூச்சி கொல்லி அடிப்பது உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
52	ஆம் எனில், அந்த பூச்சிக்கொல்லி பயன்படுத்துகிறீர்கள்?		
53	ஆம் எனில், வாரம் எத்தனை தடவை?		<input type="checkbox"/>
54	பகலில் புதர்ச்செடிபகுதியில் அல்லது காட்டுப்புதர் பகுதியில் செய்வதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
55	ஆம் எனில், எதற்காக?	1. விறகு பொறுக்க 2. பழம் சேர்க்க 3. புல் எடுக்க 4. வேறு	<input type="checkbox"/>
56	மேற்கண்ட செயல்பாட்டில் எத்தனை மணிநேரம் நீங்கள் ஈடுபட்டுள்ளீர்கள்?		
57	யாடுகளை நீங்கள் வேலை செய்கிறீர்கள்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
58	ஆம் எனில், என்ன வேலை?	1. புல் மேயலிடல் 2. உணவுபட்டல் 3. கத்தம் செய்தல் 4. மற்றவை (ஒன்றிற்கு மேலான பதில் கொடுக்கலாம்)	<input type="checkbox"/>
59	மேற்கண்ட பணியில் வாரம் எத்தனை மணிநேரம் ஈடுபடுகிறீர்கள்?		

60	41 முதல் 56 வரை உள்ள கேள்விகளுக்கு ஆம் எனில், இந்த பணிகளில் எடுபடும் போது உள்ள ஆடைகளை அணிவிக்கிறீர்கள்?	1. முழுக்கை உட்க / ஊர்க்கெட் 2. ஆளாக்கை உட்க / ஊர்க்கெட் 3. கையில்கை உட்க / ஊர்க்கெட் 4. உட்கையில்கை 5. அளாக்கை உட்க 6. முழுக்கை உட்க 7. முழுக்கை மேல் டிப்க்கப்பட்ட கேவை 8. பிறவை	<input type="checkbox"/>
61	பயிர்க்கோடு அல்லது விளக்குகோடு வேலை செய்யும் போது கொக்கிரட்டும் மருந்துகளை பயன்படுத்துவதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
62	வீட்டுக்கு வெளியே வேலை செய்யும் போது கொக்கிரட்டும் மருந்துகளை பயன்படுத்துகிறீர்கள்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
63	எந்தவித கொக்கிரட்டும் மருந்து பயன்படுத்துகிறீர்கள்?		
64	வீட்டிலேயே வெளியேறும் போது காண்கி அணிவதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
65	தூய்மைப்பதற்கு முன் ஆடை மாற்றுவதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
66	வெளியேவை முடித்து வீட்டுக்கு வருவபோது குளிப்பதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
67	திறந்த புல்வெளி / புதர்ச்செடிப்பகுதி / மண்ணில் நீங்கள் படுப்பதே உட்காறுவதே உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
68	ஆம் எனில், வாரத்துக்கு எவ்வளவு நேரம்?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
69	ஆம் எனில், படுப்பதற்கு பாய் அல்லது துணி பயன்படுத்துவது உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
70	வீட்டுக்குள் தளையில் படுப்பதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
71	ஆம் எனில், படுப்பதற்கு பாய் / துணி பயன்படுத்துவது உண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
72	காப்பாடு கையால் பண்ணுவதற்கு கைமுடித்து தளையில் உட்காறுவதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
73	ஆம் எனில், வாரம் எத்தனை மணிநேரம்?		<input type="checkbox"/>
74	உங்கள் துணிகளை, புல்லின்மேல் காப்பப்போடுவதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
75	உங்கள் துணிகளை, வெளியே காப்பப்போடுவதுண்டா?	1. ஆம் 2. இல்லை	<input type="checkbox"/>
76	புதர்ச்செடிகளினிடையில் விளையாட்டுகள் விளையாடுவதுண்டா	1. ஆம் 2. இல்லை	<input type="checkbox"/>
77	ஆம் எனில், வாரம் எத்தனை மணி நேரம்?		<input type="checkbox"/>
78	பகலில் புதர்ச்செடியிலிருந்து 5 மீட்டர் தொலைவில் செல்லுவதுண்டா	1. ஆம் 2. இல்லை	<input type="checkbox"/>
79	ஆம் எனில், ஒரு தளர் எத்தனை தடவை?		<input type="checkbox"/>
80	மக்களுக்கு விக்கிரம் எப்படி வரக்கிறது என்று தெரியுமா?		<input type="checkbox"/>

TELEGU QUESTIONNAIRE

శ్రీ	సంసారాలు	
21.	మీరు ఏ విధమైన గృహములో నివసిస్తున్నారు?	<ol style="list-style-type: none"> 1. కాంక్రీటు గృహము 2. ఇటుక ఇల్లు 3. మట్టి ఇల్లు 4. గుడిసె ఇల్లు 5. ఇతరవిధములు.
22.	మీ గృహములో ఎన్ని గదులు ఉన్నాయి?	<ol style="list-style-type: none"> 1. ఒకటి 2. రెండు 3. మూడు 4. మూడు కంటే ఎక్కువ
23.	మీ గృహములో ఎంత మంది నివసిస్తున్నారు?	_____
24.	మీ గృహములో మరుగుదొడ్డి ఉన్నదా?	<ol style="list-style-type: none"> 1. ఉంది 2. లేదు
25.	మీ గృహములో మరుగు దొడ్డి చేతపోతే మీరు తులత్ర విస్తరణ ఎక్కడ చేస్తారు?	<ol style="list-style-type: none"> 1. ఇంటి బయట 2. భూలే స్థానము 3. ఇతరులు.
26.	పై ప్రశ్నకు జవాబు 1 కి 2 లుంటే మీ ఆ ప్రాంతములో నెడల ఉన్నాయి?	<ol style="list-style-type: none"> 1. ఉంది 2. లేదు.
27.	దీని లంటి మీరు ఆ పాఠశాల ఎంద మారంలో వెళ్ళారు?	_____ మీ.

28.	24వ ప్రశ్నకు మీ జవాబు తెలు అని అంటే మీరు స్థానం ఎక్కడ చేస్తారు?	1. గయకు 2. కాటవలె 3. పంప్ హెట్ కుగ్గర 4. సరస్వ 5. ఇవేరూ.
29.	మీరు స్థానం చేసి రోజు వారాలు ఉన్నాయా?	1. అంత 2. లేదు
30.	శ్రీ అంతి అంటే ఎంత దూరంలో ఉంది?	_____ మీ.
31.	మీ గృహానికి సమీపంలో వందలు ఉన్నాయా?	1. అంత 2. లేదు
32.	అంతి అంటే ఎంత దూరంలో ఉంది?	_____ మీ
33.	మీ గృహములో వంటచెరుకు కుప్పగా ఉన్నాయా?	1. అంత 2. లేదు
34.	మీ గృహము చిరుకు వంటచెరుకు కుప్పలు ఉన్నాయా ఉన్నవి?	1. అంత 2. లేదు.
35.	అంతి అంటే మీ గృహానికి ఎంత దూరంలో ఉన్నది ఉన్నది?	_____ మీ.
36.	మీ గృహములో ఎలకు ఉన్నది?	1. అంత 2. లేదు.

37	మీ గృహములో పశువులు ఉన్నవా?	1. ఓం 2. వేరు.
38	మీ గృహము లయల పశువులు ఉన్నవా?	1. ఓం 2. వేరు
39	మీ గృహముకి ఎవరే దూరంలో పశువులు ఉంచుతారు?	_____ మీ
40	మీరు పాపము పని చేస్తారా?	1. ఔను 2. కాదు
41	ఔను అయితే, మీరు ఏవి ఉంటున్నాయి?	1. పండ్లు 2. గోధుమలు 3. మొక్కజొన్న 4. పండ్లు 5. ఓం 6. రుచులు 7. ఇతరులు పై పేర్లన్నవి కాకపోతే వివరించండి.
42	మీరు నాడులో ఎన్ని గంటలు పాపం పని చేస్తారు?	_____
43	మీరు వార్షికము నాడు పని చేస్తారా?	1. ఔను 2. కాదు
44	ఔను అయితే నాడులో ఎన్ని గంటలు చేస్తారు?	_____
45	మీరు పాపం తప్పి పని చేస్తారా?	1. ఔను 2. కాదు
46	ఔను అయితే నాడులో ఎన్ని గంటలు చేస్తారు?	_____
47	మీరు పండ్లకొర/కలుపు తీసి పని చేస్తారా?	1. ఔను 2. కాదు

48.	ఓరు అబుతే వారంతో ఎన్ని గంటలు చేస్తారు?	_____
49.	మీరు మీ తోడుతో సెలవులకి వెళ్ళుచోస్తారా?	1. ఓను 2. కాదు
50.	ఓరు అబుతే వారంతో ఎన్ని గంటలు చేస్తారు?	_____
51.	మీరు మీ తోడుతో రోజు నాటంతో స్వయంసేవలు చేస్తుంటారా?	1. ఓను 2. కాదు
52.	ఓరు అబుతే ఏ స్వయంసేవలు చేస్తారు?	_____
53.	ఓరు అబుతే వారంతో ఎన్ని గంటలు చేస్తారు?	_____
54.	మీరు వాడుకలు మార్చుకోవడం రోజు ఆలస్యంకీ విద్యార్థుల పని మీద వెళ్ళుతారా?	1. ఓను 2. కాదు
55.	ఓరు అబుతే ఏ పని మీద వెళ్ళుతారు?	1. పండ్లచెరువు తీయడం లేదా రోజువారీ 2. పుచ్చు పండ్లు తీయడం రోజువారీ 3. పనులకు వెళ్ళి రోజువారీ 4. ఇవరమైనవి.
56.	వైన చేసే పని కొరకు వారంతో ఎన్ని గంటలు పని చేస్తారు?	_____
57.	మీరు పనులతో పని చేస్తారా?	1. ఓను 2. కాదు
58.	ఓరు అబుతే ఏమి పని చేస్తారు?	1. పైచేరి తీయడం 2. పైచేరి తీయడం 3. పుచ్చు పండ్లు తీయడం 4. ఇవరమైనవి.

59. మీ వారలతో ఎన్ని గంటలు చేస్తారు?

60. మైనున్న 41 to 56 ప్రశ్నలకు లెసులు
లవాట యిచ్చినట్లుంటే మీరు ఏ
విధమైన దుస్తులు ధరిస్తారు ఆ
పనులు చేసేటప్పుడు ?

1. స్వల్ప చేతులచొక్క
2. సగం చేతులచొక్క
3. చేతులు తని చొక్క
4. చొక్కా కేకుండా
5. సగం పొట
6. స్వల్ప వరకు
7. ~~క్లి~~ మోకాళ్ళపైకి
వదులిన చీర
8. ముందు
9. ఇవేరమైనవి

~~పరిచేసేటప్పుడు~~
61. మీరు ఏమంటే పరిచేసేటప్పుడు ఏమంటే పరిచేసే
టప్పుడు చేతులకి తోడుగులు వేసుకొని
పరి చేస్తారా?

1. లెసు
2. కాదు

62. మీరు బయట పరి చేసేటప్పుడు
క్రిములు కట్టకండ విదైనా వాడుకారా?

1. లెసు
2. కాదు

63. లెసు లుంటే ఏది వాడుకారు?

64. మీరు గృహము నుండి బయటకి వెళ్ళే
టప్పుడు చేష్టలు వేసుకొని వెళ్ళువారా?

1. లెసు
2. కాదు

65. మీరు పడుకొనేటప్పుడు మీ బట్టలు
మార్చుకుంటారా?

1. లెసు
2. కాదు

66. మీరు బయట నుండి స్ట్రాప్ దర్భావ
స్థానం చేస్తారా?

1. లెసు
2. కాదు

67. మీరు ~~కా~~ గట్టి/ నోరు/ మన్ను మీద
కూర్చోవడం చేక పడుకేవడం చేస్తారా?

1. లెసు
2. కాదు

68. లెసు లుంటే వారుతో ఎన్ని గంటలు
చేస్తారు? పడుకుంటారు?

69.	శైను అయితే మీ పడుకునేప్పుడు చాస్ వెకి వస్త్రము పెట్టాడు వాడుతాడా?	1. శైను 2. కాదు
70.	మీరు రృహములో వెల మీద పడుకుంటాడా?	1. శైను 2. కాదు
71.	శైను అయితే పడుకునేప్పుడు చాస్ వెకి వస్త్రము మీద పడుకుంటాడా?	1. శైను 2. కాదు
72.	మీరు 3 సెల మీద కూర్చొని వంట చేస్తాడా?	1. శైను 2. కాదు
73.	శైను అయితే వారులో ఎన్ని గంటలు చేస్తాడు?	_____
74.	మీరు మీ వస్త్రములు గడ్డి మీద తరిచెట్టుతాడా?	1. శైను 2. కాదు
75.	మీరు మీ వస్త్రములు బయట తరిచెట్టుతాడా?	1. శైను 2. కాదు
76.	మీరు వెనక ప్రక్కన ఆటాడుతాడా?	1. శైను 2. కాదు
77.	శైను అయితే ఎన్ని 3 వారులో ఎన్ని గంటలు ఆడుతాడు?	_____
78.	మీరు దినంలో ఏడు మీ దూరంలో పాదలు ప్రక్కన వెళ్ళతాడా?	1. శైను 2. కాదు
79.	శైను అయితే ఎన్నిసార్లు వెళ్ళతాడు?	_____
80.	మీకు ప్రజలకు ప్రజాకే ట్రైఫ్స్ అనే యోధి ఎలా వస్తుంటే తెలుసా?	1. శైను 2. కాదు
	వివరముల ప్రకారం నిజమైన వారు - _____	
	తేది _____	
	వివరముల ప్రకారం దనిఖి చేసినవారు - _____	
	తేది _____	

HINDI QUESTIONNAIRE

पर्यावरण

21	आप किस तरह के मकान में रहते हैं ?	1) सीमेंट 2) ईंट 3) गारा 4) झोंपड़ा 5) अन्य (यदि अन्य विस्तार दें)
22	आप के मकान में कितने कमरे हैं	1) एक 2) दो 3) तीन 4) तीन से अधिक
23	आप के मकान में कितने लोग रहते हैं	_____
24	क्या शौचालय आप के मकान में ही है	1) हाँ 2) नहीं
25	यदि नहीं तो मल मूत्र के लिए आप कहाँ जाते हैं	1) शौचालय मकान के बाहर 2) खुली जगह पर 3) अन्य यदि अन्य तो विस्तार दें
26	यदि उपर वाले प्रश्न का उत्तर 1 या 2 है तो क्या वहाँ पर झाड़ियाँ हैं।	1) हाँ 2) नहीं
27	यदि हाँ तो आप झाड़ी के कितने पास बैठते हैं	_____ (मीटर में)
28	यदि 25 प्रश्न का उत्तर नहीं है तो आप कहाँ स्नान करते हैं	1) बाहर स्नान घर में 2) खुले तालाब में 3) हैंड पम्प के पास 4) तालाब 5) अन्य यदि अन्य तो विस्तार दें
29	क्या उस जगह झाड़ी है	1) हाँ 2) नहीं
30	यदि हाँ तो झाड़ी घर के कितने पास है	_____ (मीटर में)
31	क्या आप के घर के पास झाड़ी है	1) हाँ 2) नहीं
32	यदि हाँ तो सबसे पास की झाड़ी घर से कितनी दूर है	_____ (मीटर में)
33	क्या आप के घर के अन्दर इंधन एकाग्रित है	1) हाँ 2) नहीं
34	यदि नहीं तो क्या घर के बाहर इंधन एकाग्रित है	1) हाँ 2) नहीं
35	यदि हाँ तो घर से कितनी दूरी पर रखा है	_____ (मीटर में)
36	क्या घर में खुतर कर खाने वाले जीव हैं	1) हाँ 2) नहीं
37	क्या आप के मकान में दूध देने वाले पशु हैं	1) हाँ 2) नहीं
38	क्या आप के मकान के बाहर दूध देने वाले पशु हैं	1) हाँ 2) नहीं
39	मकान से कितनी दूरी पर दूध देने वाले पशु रखे हैं	_____ (मीटर में)

दिया

40	क्या आप छोटी गाड़ी में शामिल हैं	1) हाँ 2) नहीं
41	यदि हाँ तो आप किस प्रकार की छोटी कारों में	1) हार्वल /गान 2) गेबू 3) बजरा 4) कल 5) छान 6) रवड 7) अन्य आप का विकार एक से अधिक उत्तर दे सकते हैं
42	आपका में किसने घण्टे आप इस विषय में सीप करते हैं	
43	क्या आप सीप सीप में शामिल होते हैं	1) हाँ 2) नहीं
44	यदि हाँ तो आपका में किसने घण्टे	
45	क्या आप गुड्डा व गुड्डा में भाग लेते हैं	1) हाँ 2) नहीं
46	यदि हाँ तो आपका में किसने घण्टे	
47	क्या आप छोटी गाड़ी की कारवाई व विन्दाई में शामिल होते हैं	1) हाँ 2) नहीं
48	यदि हाँ तो आपका में किसने घण्टे	
49	क्या आप अपने कारोब को चाली लेते हैं	1) हाँ 2) नहीं
50	यदि हाँ तो आपका में किसने घण्टे	
51	क्या आप अपने लेत या कारोब में बीटागुनराक टकाइ चिडकारते हैं	1) हाँ 2) नहीं
52	यदि हाँ तो बीटागुनराक का विकार तो	
53	यदि हाँ तो आपका में किसने घण्टे	
54	क्या आप गाड़ी में टिप को समझ पाते हैं	1) हाँ 2) नहीं
55	यदि हाँ तो किस कारण से	1) इंपेन जुटाने के लिए 2) कल सोडने के लिए 3) पदु का कारा लाने के लिए 4) अन्य
56	यदि हाँ तो आपका में किसने घण्टे आप उत्तर सिटी किया करते हैं।	
57	क्या आप पदुओं को साथ काम करते हैं।	1) हाँ 2) नहीं
58	यदि हाँ तो क्या काम करते हैं।	1) बराना 2) डिपारना 3) सफा करना 4) अन्य आप का विकार एक से अधिक उत्तर दे सकते हैं
59	आपका में किसने घण्टे को लिए उत्तर सिटी किया करते हैं	
60	यदि कल नं 41 से 58 तक आपका उत्तर हाँ है तो आप किस प्रकार को बल पडन कर काम करते हैं	1) भूरी मानुकी कमीन /साउल 2) लाली मानु कमीन /साउल 3) गिना मानु कमीन /साउल 4) कोई कमीन नहीं

		5) नीकर 6) पतनपुन 7) कुटने तक की लाठी 8) आम बिक्रार से
61	क्या आम खेती लाठी व नगु टैडभास से तामर पत्रक पत्रकते है	1) हाँ 2) नहीं
62	क्या आम बाहर काम करते तामर बीटागुरोमक का प्रयोग करते है	1) हाँ 2) नहीं
63	प्रति हाँ तो खीन की रोमक टकाई	_____
64	क्या आम घर टाँडते तामर नुई पत्रकते है	1) हाँ 2) नहीं
65	क्या आम खीन से पत्रकते कपडे बदलते है	1) हाँ 2) नहीं
66	क्या आम बाहर काम कर के घर जाने से बाद तामर करते है	1) हाँ 2) नहीं
67	क्या आम घाल/काठी/सिंदरी से वेडने/संदते है	1) हाँ 2) नहीं
68	प्रति हाँ तो तामरक से किलनी टेर को रिंग	_____
69	प्रति हाँ तो क्या आम बटाई एवं कपडे पर संदते है	1) हाँ 2) नहीं
70	क्या आम को तामरक से आम जमीन पर संदते है	1) हाँ 2) नहीं
71	प्रति हाँ तो क्या आम बटाई एवं कपडे पर संदते है	1) हाँ 2) नहीं
72	क्या आम जमीन पर वेड कर टागा पत्रकते है	1) हाँ 2) नहीं
73	प्रति हाँ तो तामरक से किलने घाटे	_____
74	क्या आम जमने कपडे घाल पर नुटाते है	1) हाँ 2) नहीं
75	क्या आम जमने कपडे बाहर नुटाते है	1) हाँ 2) नहीं
76	क्या आम काठीदार जंगल को घाल खेन बूट करते है	1) हाँ 2) नहीं
77	प्रति हाँ तो तामरक से किलने घाटे तक	_____
78	क्या आम काठीदार जंगल को 5 मीटर को भीतर से नुटाते है	1) हाँ 2) नहीं
79	प्रति हाँ तो दिम से किलनी वार	_____
80	क्या आम जमने है कि खीन को तामर टाडकत कोने होता है	1) हाँ 2) नहीं

ANNEXURE 2

TAMIL CONSENT FORM

ஒப்புதல் படிவம்

ஆய்வு தலைப்பு - தேய்ப்பான் எடீபக ரேயின் ஆபத்து காரணிகளை கண்டறிவும் ஆய்வு. இது ஒரு மருத்துவமனை சார்ந்த வழக்கு கட்டுப்பாட்டு ஆய்வு.

ஆய்வு எண்-

பங்கேற்பாளர் பெயர் -

பிறந்த தேதி . வயது (ஆண்டுகள்) -

-----மகன் / மகள் -----

பெட்டிகளை தயவு செய்து டிக் செய்யவும்

- இந்த தகவல் தானை முழுவதாக படித்துவிட்டேன். மேலும் இந்த படிவத்தில் உள்ள அனைத்து சந்தேகங்களையும் தெளிவு படுத்திக் கொண்டேன்.
- இந்த ஆய்வில் நான் தன்னிகழையாக பங்கு பெறுகிறேன். இந்த ஆய்வில் இருந்து நான் விலகினால் என் மருத்துவ முறையில் எந்த பாதிப்பு இருக்காது என்பதையும் அறிவேன்.
- இந்த ஆய்வினால் ஏற்படும் விளைவுகளுக்கு எந்த ஒரு நிதி இழப்பீடு கிடையாது என்பதை அறிவேன்.
- இந்த ஆய்வின்போது என் மருத்துவ ஏடுகளை ஆய்வாளர்கள் மற்றும் நிறுவன நெறிமுறைகள் குழு பார்ப்பார்கள் என்பதை அறிவேன்.
- இந்த ஆய்வில் என் பெயரோ அல்லது என்னை பற்றிய அடையாளங்களோ வெளியிடப்படார்கள் என்பதை அறிவேன்.
- இந்த ஆய்வில் நான் முழுமத்தத்தோடு பங்குபெறுகிறேன்.

பெயர் -

கையொப்பம் -

கைரேகை -

தேதி -

சாட்சியின் பெயர் -

உறவு முறை -

கையொப்பம் -

கைரேகை -

தேதி -

ENGLISH CONSENT FORM

CONSENT TO TAKE PART IN A CLINICAL TRIAL

Study Title: Risk factors for acquiring scrub typhus in an adult population in South India, a hospital based Case control study.

Study Number:

Participant's name:

Date of Birth / Age (in years):

I _____
_____, son/daughter of _____

(Please tick boxes)

- Declare that I have read the information sheet provide to me regarding this study and have clarified any doubts that I had
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights
- I understand that I will receive free treatment for any study related injury or adverse event but I will not receive anyother financial compensation
- I understand that the study staff and institutional ethics committee will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access
- I understand that my identity will not be revealed in any information released to third parties or published
- I voluntarily agree to take part in this study

Name:

Signature:

Thumb impression(answer to query 4)

Date:

Name of witness:

Relation to participant:

Signature :

Thumb impression(answer to query 4)

Date:

TELEGU CONSENT FORM

వైద్య పరీక్షలలో పాల్గొనడానికి సమ్మతి పత్రము

స్టడీ కేర్షిక: ఒక వయోజన అనాథాలో స్ట్రబ్ లైఫిస్ అను వ్యాధి ప్రమాద కారకాలను కనుగొనుటకు దక్షిణ భారతదేశంలోని ఒక ఆసుపత్రి ఆధారిత కేస్ కంట్రోల్ అధ్యయనం.

స్టడీ సంఖ్య:

పాల్గొనివంట యుక్త్య పేరు:

వయ (సంవత్సరాలలో):

నేను _____

నా తండ్రి పేరు _____

(దయచేసి తీక పెట్టండి)

- ఈ సమాచారం పేజీ ఈ అధ్యయనం గురించి నాకు కలిగి ఉన్న అనుమానాలను వివరించింది అని నేను అంగీకరిస్తున్నాను. []
- నేను కూడా ఈ అధ్యయనంలో పాల్గొనడం, ఘోరంగా నా స్వచ్ఛంద నిర్ణయం అని ప్రకటిస్తున్నాను. మరియు నా సాధారణ చికిత్స లేదా నా దట్టమరమైన చికిత్సలకు ఈవిధమైన ప్రభావితం లేకుండా ఏ సమయంలోనైనా అనుమతి ఉపసంహరించుకోవచ్చునని అర్థం చేసుకున్నాను []
- నేను ఏ అధ్యయనం సంబంధిత గాయం లేదా ఫలితాల సంఘటన కోసం ఉచిత చికిత్స అందుకుంటాను అని అర్థం, కానీ మరి ఏ ఇతర ఆర్థిక పరిహారం లేదు. []
- నేను చెదారణ నుండి వెనక్కివెళ్ళినా కూడా, అధ్యయన సేబ్బంది మరియు ఎదిక్య కమిటీ సభ్యులు, సంస్థాగతమైన నా ఆరోగ్య రికార్డులను నా అనుమతి అవసరం లేకుండా యాడవచ్చునని అర్థం. నేను దీనికి అంగీకరిస్తున్నాను []
- నా గుర్తింపు సమాచారాన్ని ఎటువంటి వేరే వాళ్ళకు లేదా ప్రయోగంలో కానీ బహిష్కరణ చెయ్యబడదు అని అర్థం చేసుకున్నాను. []
- నేను స్వచ్ఛందంగా ఈ అధ్యయనంలో పాల్గొనేందుకు అంగీకరిస్తున్నాను []

పేరు _____
 సంకేతం _____
 తేదీ: _____
 THUMB IMPRESSION

సాక్షి పేరు: _____
 అధ్యర్థి వింటుండం: _____
 తేదీ: _____
 THUMB IMPRESSION

HINDI CONSENT FORM

अनुमति पत्र

दक्षिण भारत के एक मेडिकल कालेज
में किया अध्ययन, डॉ. डॉ. " स्कूल
टाइपस के जोरिम काश्क",

अध्ययन No :

नाम :

जन्म तिथि :

मे _____, _____ का/कं

बेटा/बेटी

TICK करें

- घोषित करता/करती हूँ कि मैं इस अध्ययन के बारे में पढ़ा है और मैं अपनी स्वयं इच्छा से इस अध्ययन में भाग लेना चाहती/चाहता हूँ।
- मुझे मेरी बीमारी के बारे में और इस बीमारी सम्बंधित अध्ययन के बारे में सारी जानकारी विस्तृत था से समझाई गई है। मुझे यह भी बताया गया है कि किसी भी वक्त मैं इस अध्ययन से निकल सकती/सकता हूँ, और जिस पर मेरे वर्तमान या भविष्य ईलाज में किसी भी प्रकार का असर नहीं पड़ेगा।
- मुझे यह भी समझाया गया है कि अध्ययन सम्बंधित मैडिकल कर्मचारियों को मेरे मैडिकल रेकॉर्ड की जांच करनी होगी और इस बात के लिए मेरी दोबारा अनुमति की जरूरत नहीं है। मुझे इस बात से सहमति है।

□ मेरी पहचान को गोपनीय रखा जाएगा।
इस बात को मुझे समझाया गया है।

□ मेरे सभी जानकारी समेत मैं अपनी
स्वयं इच्छा से, बिना कोई अतिरिक्त दबाव,
और पूरी संवृद्धि के साथ, इस
अवकाश में भाग लेने के लिए अपनी
पूरी अनुमति देता/देती हूँ।

नाम :

हस्ताक्षर:

(अंगूठे का निशान)

दिनांक :

गवाह का नाम

भागीवारी से संबंध

दिनांक :

हस्ताक्षर

अंगूठे का निशान

MODIFIED KUPPUSWAMY SCALE FOR SOCIOECONOMIC STATUS
AND INCOME GROUPS 2012

(A)	Education	Score
1.	Profession or honours	7
2.	Graduate or post graduate	6
3.	Intermediate or post high school diploma	5
4.	High school certificate	4
5.	Middle school certificate	3
6.	Primary school certificate	2
7.	Illiterate	1
(B)	Occupation	Score
1.	Profession	10
2.	Semi-profession	6
3.	Clerical, shop-owner, farmer	5
4.	Skilled worker	4
5.	Semi-skilled worker	3
6.	Unskilled worker	2
7.	Unemployed	1
(C)	Family income per month (in Rs, (1976)	Score
1.	=2000	12
2.	1000-1999	10
3.	750-999	6
4.	500-749	4
5.	300-499	3
6.	101-299	2
7.	=100	1
Total score		Socioeconomic class
26-29		Upper(I)
16-25	Middle	Upper middle (II)
11-15		Lower middle (III)
5-10	Lower	Upper lower (IV)
<5		Lower(V)

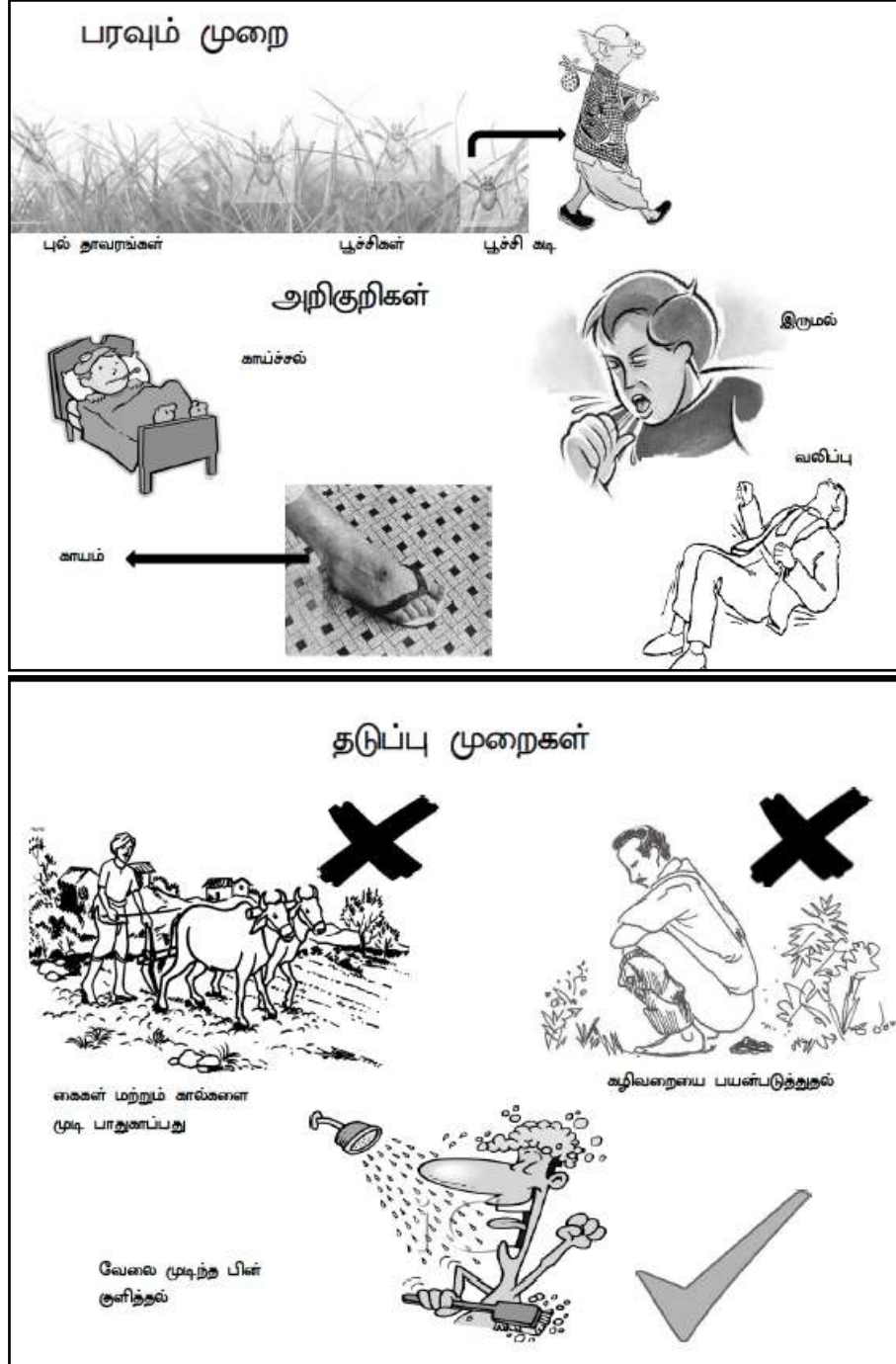
1976	Years		
	1998	2007	2012 (June) (current price index ⁽⁴⁾)
≥2000	≥ 13,408	≥ 19,844	≥ 31,507
1000-1999	6704-13,407	9922-19,843	15,754-31,506
750-999	5028-6703	7441-9921	11,817-15,753
500-749	3352-5027	4961-7440	7878-11,816
300-499	2011-3351	2976-4960	4727-7877
101-299	677-2010	1002-2975	1590-4726
≤100	≤ 676	≤ 1001	≤ 1589

ANNEXURE 4 SOFA SCORE

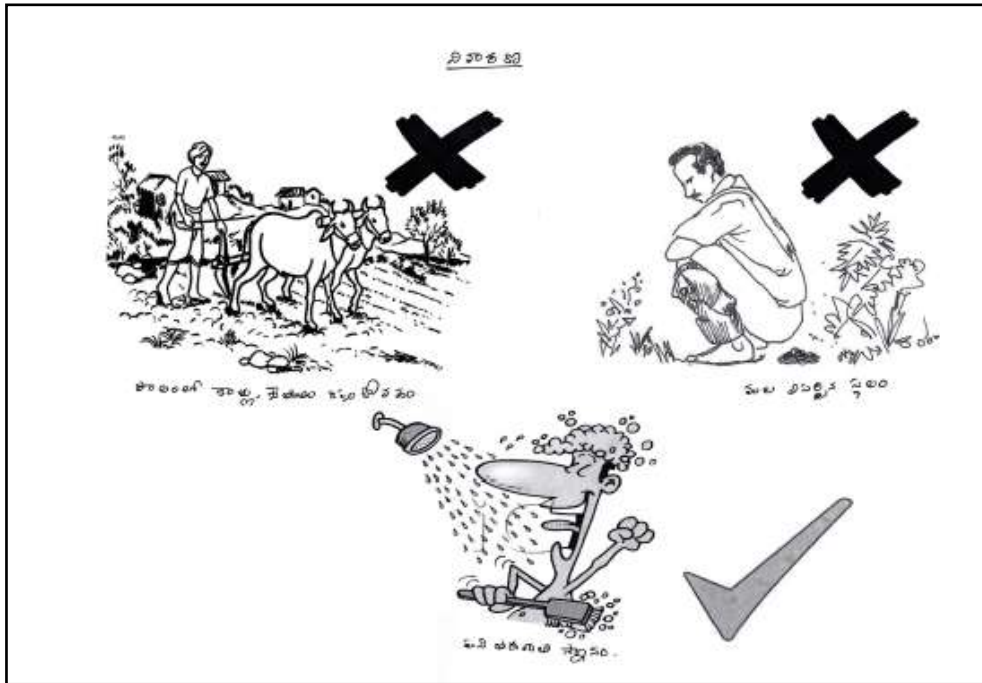
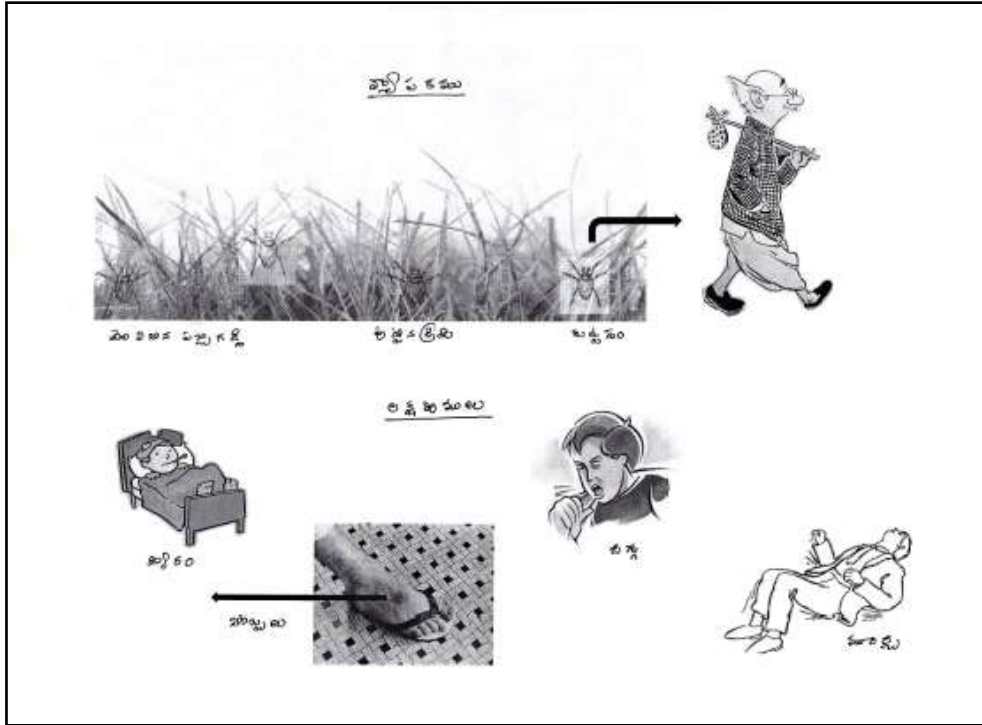
SOFA score	0	1	2	3	4
Respirationa PaO ₂ /FIO ₂ (mm Hg) SaO ₂ /FIO ₂	>400	<400 221– 301	<300 142–220	<200 67–141	<100 <67
Coagulation Platelets 10 ³ /mm ³	>150	<150	<100	<50	<20
Liver Bilirubin (mg/dL)	<1.2	1.2– 1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular^b Hypotension	No hypoten sion	MAP <70	Dopamine </=5 or dobutamine (any)	Dopamine >5 or norepinephrine </=0.1	Dopamine >15 or norepinephrine >0.1
CNS Glasgow Coma Score	15	13– 14	10–12	6–9	<6
Renal Creatinine (mg/dL) or urine output(ml/d)	<1.2	1.2– 1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200

Annexure 4 -Patient health education pamphlets

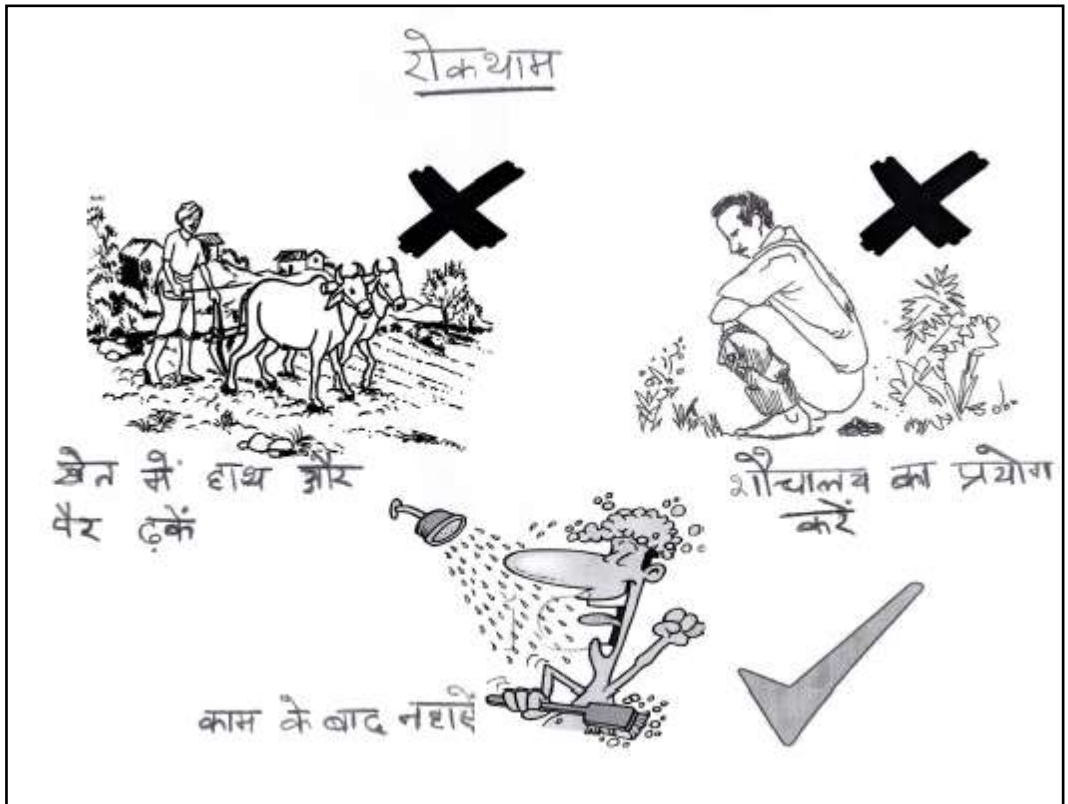
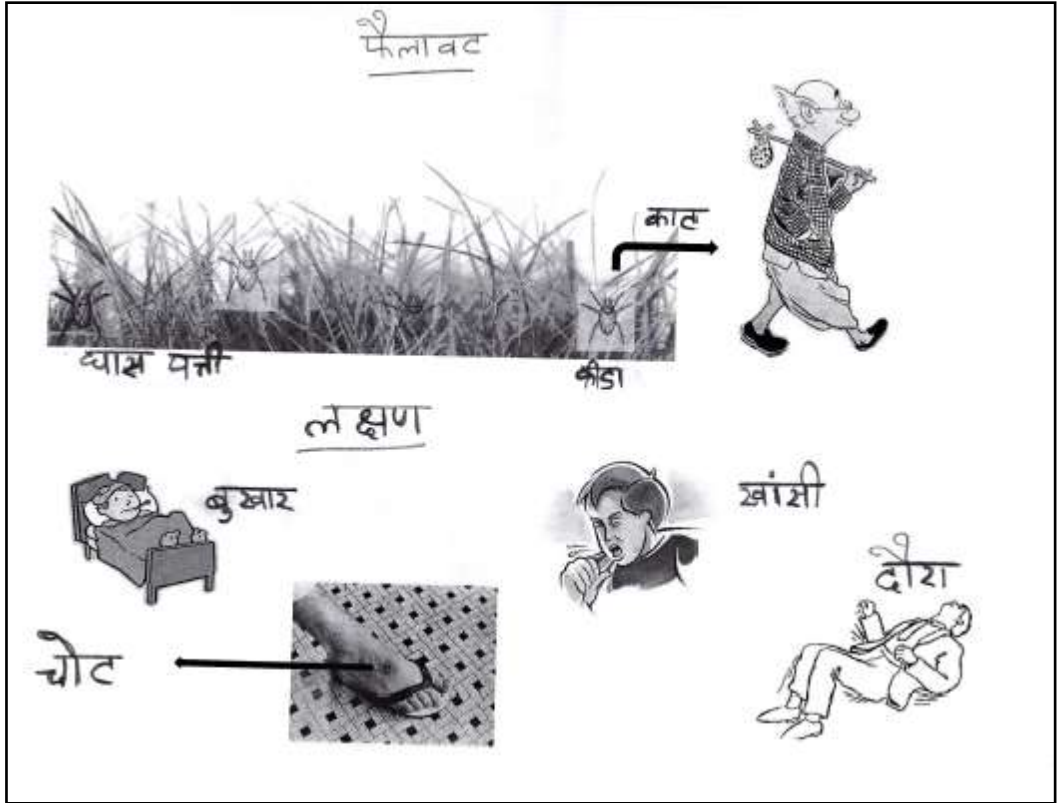
Tamil

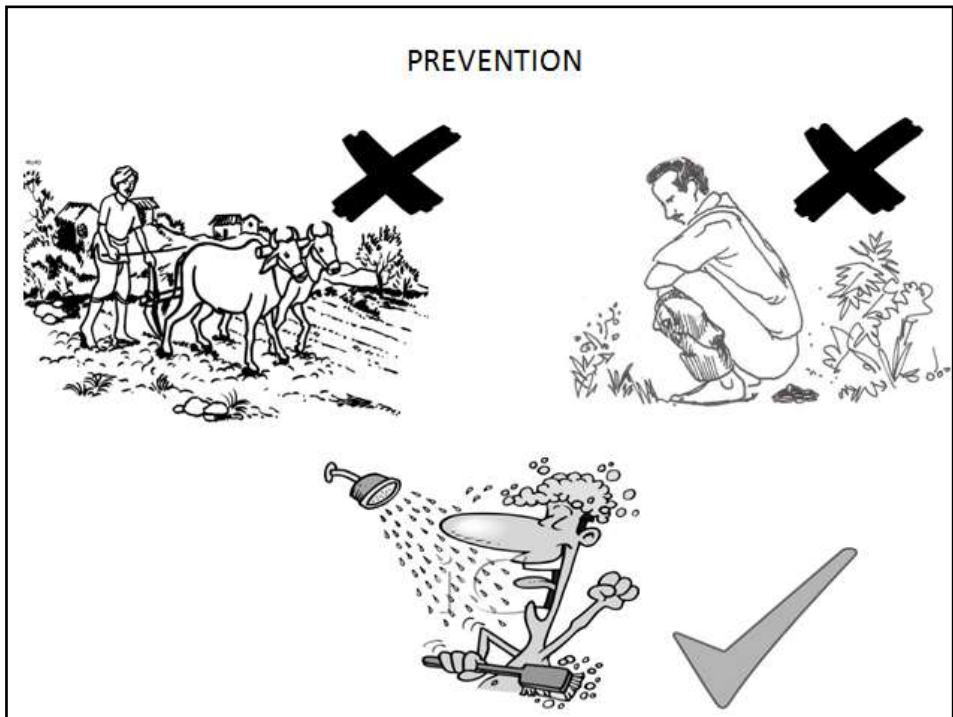
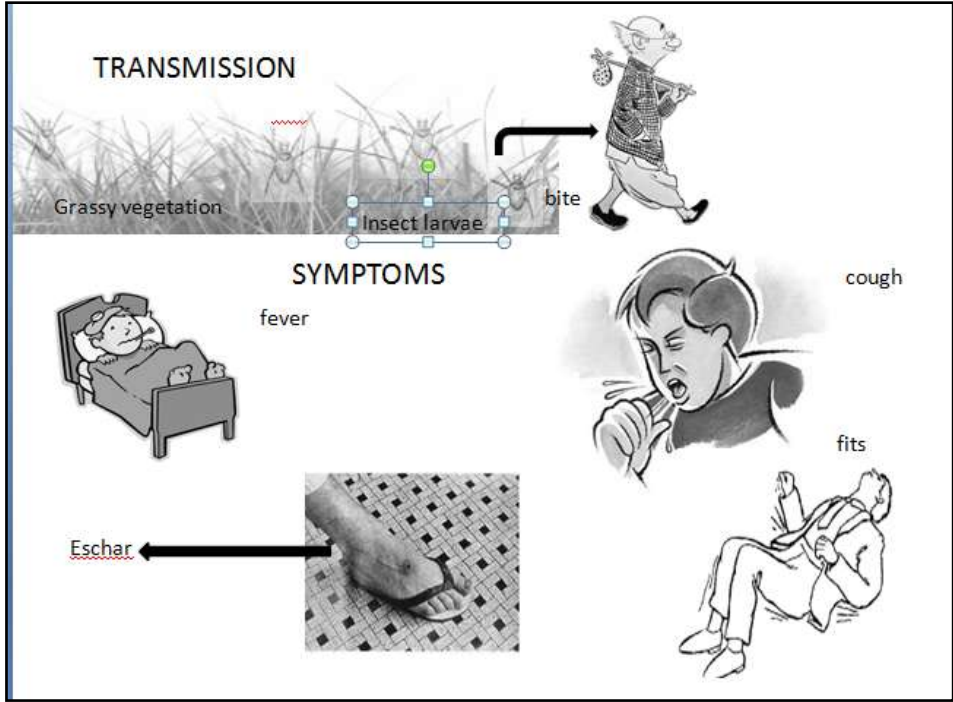


Telegu



Hindi





217	72	daughter	64	1		1	unemploye	6	10	4	20	2	2	1	3	2		2	2	1	3	1	1		
218	73	self	31	1		2	unemploye	5	2	12	19	2	1	1	4	2		2	2	2		2			
219	73	self	25	1		2	lecturer	7	10	10	27	1	2	1	14	2		2	2	2		2			
220	73	self	32	1		2	lab technic	6	10	3	19	2	3												
221	74	self	42	1		1	farmer	5	5	2	12	2	1	1	8	1	2	2		2		2			
222	74	self	27	1		1	beedi mak	5	3	2	10	3	3												
223	74	wife	38	1		2	unemploye	3	5	3	11	2	2	1	3	1	3	2		2		2	1	1	
224	75	self	64	2	2	2	housewife	5	10	10	25	1	1	1	14	2		1	10	2	1	5	2		
225	75	self	32	2	2	2	house wife	5	10	10	25	2	3												
226	75	daughter	60	2	2	1	housewife	5	3	4	12	2	2	1	9	2		2		2		1	2	1	9

q12g	q12gdur	q12h	q12hdur	q12i	q12idur	q12j	q12jdur	q12k	q12kdur	q12l	q12ldur	q12m	q12mdur	q12n	q12ndur	q13a	q13g	q13m	q13b	q13h	q13n	q13c	q13i	q13o	q13d	q13ja	n13jb	q13p
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2	2	2	2	2	2	2	2	2	2	2	2	126	2	2	95	2	2	66	2	2	80	60	2
2	2	2	2	2	2	2	2	2	2	2	2	140	2	1	94	2	2	28	2	1	130	70	2
2	2	2	1	10	2	2	2	2	2	2	2	108	2	2	100	2	2	20	2	2	90	60	2
2	2	2	2	2	2	2	2	2	2	2	2	98	2	2	92	2	2	42	2	2	170	100	1
2	2	2	2	2	2	2	2	2	2	2	2	128	2	2	80	2	2	44	1	2	80	60	2
2	2	2	2	2	2	2	2	2	2	2	2	108	2	2	92	2	2	24	2	2	120	80	2
2	2	2	2	2	2	2	2	2	2	2	2	116	2	2	95	2	2	18	2	2	100	60	1
2	2	2	2	2	2	2	2	2	2	2	2	126	2	2	92	2	2	30	2	1	100	60	2
2	2	2	2	1	1	2	2	2	2	2	2	112	2	2	85	2	2	32	2	2	80	60	2
2	2	2	2	2	2	2	2	2	2	2	2	84	2	2	100	2	2	22	2	2	120	70	2
2	2	2	2	1	7	2	2	2	2	2	2	110	2	2	88	2	2	50	2	2	110	70	2
2	1	3	2	2	2	2	2	2	2	2	2	99	2	2	100	2	2	24	2	2	120	80	2
2	2	2	2	2	2	2	2	2	2	2	2	46	2	1	92	2	2	30	1	2	100	80	2

2	2	2	2	2	2	2	2	2	2	160	2	2	98	2	2	40	2	2	140	90	1	
2	2	2	2	1	3	2	2	2	2	2	124	2	1	35	2	2	54	1	2	110	60	2
2	2	2	2	2	2	1	14	2	2	1	70	1	1	98	2	2	16	2	2	110	70	2
2	2	2	2	2	2	2	2	2	2	2	116	2	2	94	2	2	26	2	2	130	80	2
2	2	2	2	2	2	2	2	2	2	2	140	2	2	86	2	2	28	2	2	110	80	1
2	2	2	2	2	2	2	2	2	2	1	110	2	2	90	2	2	20	1	2	86	66	2
2	2	2	2	2	2	2	2	2	2	2	148	2	2	94	2	2	24	2	2	100	60	1

q13e	q13k	q13q	q13f	q13l	q13r	q13f2	q13f2oth	q14a	q14h	q14n	q14b	q14i	q14o	q14c	q14j	q14p	q14d	q14k	q14q	q14e	q14l	q14r	q14f	q14m	q14s	q14g	q14h1	q15a
2	100	2	2	1	2	99		8.6	5.5		8500	21.7	6.4	76		77000	1.24	15	1.24	0.5	70	123				2		0
2	100	2	2	1	2	5		13	3.3		7200	16		60		78000	5.5		1.9	4.5	220	141				1		2
2	104.4	2	2	2	2			15.4	4		24300	19		88		150000	3.3		3.14	1		137				2		3
2	2	2	2	1	1	2	5	13.2	4.1	6.3	13700	11.5	3.1	87		69	90000	5.3	110	3.04	4.6	195	141	2	1	1		0
2		2	2	2	2			15.4	4.8		9000	34.2		82		214000	2.9		1.6	0.9		139						4
2	105	2	2	1	2	6		14.2	4.3	7.9	4400	16	3.7	59	43	570	50000	0.5	189	2.94	0.1	37	157	2	2	1		0
2	99	2	2	2	2	2		12.5	3.4	7.5	22700	25.7	3.8	88		68	465000	1.5	114	0.8	0.6	129	142	2	2	2		4
2	98	2	2	2	1	2		12.4	3.2	5.6	5900	21	2.5	81		133	38000	1.1	67	1.54	0.7	129	133	2	1	2		0
2	103	1	2	2	2			13.1	4.3	7.5	5500	25	3.9	74		70	167000	0.5	25	1.03	0.2	65	131	2	2	2		0
2	100	1	2	2	2			13.2	3.3	6.8	11500	23	3.7	86		53	273000	0.4	55	0.95	0.1	110	137	2	1	1		0
2	99	2	2	2	2			11.9	3.7	7.3	3400		4	54		30	19000	1.1	19	0.9	0.4	95	138	1	2	2		0
2	104	2	2	1	2	6		8.8	3.3	6.1	10000	17	2.5	74		85	126000	0.7	55	1.32	0.5	153	136	1	1			0
2	100	2	2	2	2			15.5	3.4	6.7	5500	25	3.9	62		122	23000	0.6	66	1.54	0.3	59	138	2	2	2		1
2	2	2	2	1	2	6		8.5	3.4	6.2	10000	23	2.4	85		152	67000	3.5	62	0.99	2.9	162	134	2	1	1		0
2	98	2	2	2	2			11.9	3.5	6.8	11300	18	3.1	76		16	342000	0.8	6	1.04	0.8	110	139	2	1	2		1
2	101	2	2	2	2			9.7	3.7	5.2	6200	20	1.9	76	5313	604	23000	3.5	181	1.23	2.8	270	140	2	1	1		0
2	102	2	2	1	2			11.2	4.1	7.4	14500	18	2.9	90		503	49000	4.9	125	1.11	2.9	336	136	2	2	2		0
2	104.2	2	2	1	2	5		12.6	4.3	6.9	10000	17	2.8	73		113	33000	0.3	61	1.51	0.2	109	123	2	1	1		0
2	99.8	2	2	2	2			15.7		6.7	1600		3.9	38		66	33000	1	36		0.4	58		1	2	2		0
2	100	2	2	1	2	6		10.4		7	10400		3.9	46		43	8000	0.4	34	0.83	0.2	100		2	2	1		0
2	100.4	2	2	2	2			7.6	3.6	5.8	7600	25	2.5	68		67	37000	2.1	15	0.57	1.3	97	133	2	2	2		0
2	100	2	2	1	2	5		11.8	3	8.3	11500	16	3.2	83		91	62000	6.4	27	0.92	4.5	408	137	2	1	1		3
2	98.4	2	2	2	2			8.9	4.3	5.9	11000	19.5	3.2	86		33	151000	14.14	10	5.08	6.6	76	139	2	1	2		0
2	99	2	2	1	2	9 labia major		10	2.5	7.1	14500	18.7	2.9	66		159	9000	1	159	1.78	0.6	120	118	2	1	1		0
2	2	2	2	2	2	2		8.9		7.1	13000		3.2	79		21		0.3	19	0.86	0.1	209						0
2	103	2	2	2	2			9.5	2.9	6.7	8100	26	1.9	66		136	95000	1.8	134	0.69	0.9	189	129	2	1	1		0
2	101	2	2	2	2			11.8	3.7	8.8	18500	26	4.6	71		11	52800	0.23	6	0.78	0.1	60	136					0
2	100	2	2	1	1	6		14.6	4.2	5.3	6600	18.3	3	63	16	233	38000	4.3	113	0.89	2.9	617	135	2	1	1		0
2	103	2	2	2	2			15.7	3.8	5.8	20300	19	2.6	78		203	77000	1.5	66	1.52	1.4	296	136	2	2	2		3
2	102	2	2	1	2	9 back		11.8	5.6	7.1	15600	18.6	3.2	60		144	68000	0.8	92	0.8	0.3	186	127		1	1		0
2	98	2	2	2	2			13.3	3.6	6.5	18000	19	3.4	63		79	46000	0.4	20	1.04	0.1	68	130	1	2	2		2
2	98.4	2	2	2	2			12.8	4.5	5.7	16600	21	2.7	63		180	45000	7	146	2.82	5.7	191	125	2	1	1		0
2	102	2	2	1	2	5		11	5	6.7	5300	29	3.3	69		49	172000	1.2	39	1.6	0.6	94	136	2		2		0
2	98.6	2	2	2	2			11.6	2.8	7.1	9100	27	2.6	78		213	98000	0.8	130	0.8	0.5	231	128		1			0
2	100	2	2	2	2			11.8	6.7	6.7	7600	15	3.4	61		34	179000	0.4	19	3.31	0.2	130	137					0
2	98.4	2	2	2	2			12.8	4.7	6.4	9600	24	2.7	72		101	60000	4	55	1.03	3.4	304	130	2	1	1		0
2	100	2	2	2	2			12.1	3.7	6.4	3900	19	3.5	84		40	35000	0.4	16	0.6	0.2	56	133	2	2	2		0
2	2	2	2	1	1	9 behind ear		11	3.7	6.1	11300	25	2.6	73		161	38000	1.5	118	1.22	1.2	209	130	2	1	1		0
2	99	2	2	2	2			9.5	4.1	8.1	13200	24	3.6	75		21	317000	0.3	13	1.66	0.2	231	118	2	2	2		0
2	102	2	2	1	2	6		9.9	3.5	5.9	9300	19	2.5	58		206	85000	2.9	180	0.71	2.5	294	130	2	2	1		0
2	102	2	2	2	2			11.6		6	14300		3.5	83		42	229000	0.6	144	0.58	0.3	144			2			0
2	98.4	2	2	2	2			11	4.3	7.8	7400	14	3.6	72		405	163000	1.1	316	1.85	0.9	179	126	2	2	1		0
2	100	2	2	2	2			12.8	3.3	8.1	6200	22	4	67		51	97000	0.4	38	0.7	0.2	138	128					0
2	98.6	2	2	2	2	9 axilla		14	4	6.6	7600	17	2.7	59		204	90000	0.8	94	1.29	0.4	96	135	2	2	1		1
2	100	2	2	2	2			14	4	6.2	12700	15.2	2.6	87	23	39	321000	0.6	13	1.03	0.2	53	121	2	1	2		3
2	2	2	2	2	2			12.7	3.7	5.6	18300	19	2.4	78		114	169000	1	106	1.5	0.9	154	135	2	2	1		0

2	102	2	2	2	2		12.8	3.9	8.1	12800	29.9	4.6	90	14	287000	0.25	14	0.72	0.1	50	135	2	2	2	3	
2	98.6	2	2	2	2	9 right axilla	15.2	3.7	7.7	12800	24	3.8	80	57	120000	1.2	51	1.18	0.1	101	130	2	2	1	0	
2	100	2	2	2	2	2	9.3	4.2	5.1	10700	17	2.3	70	75	21000	5.5	50	1.1	3.6	98	136	2	2	2	0	
2	2	2	1	2	2	9 right supra	11.1	3.6	5.7	7300	19	2.7	84	154	18000	5.2	81	1.25	4.8	163	135	2	1	1	0	
2	100	2	2	2	2	2	9.1	4	6.9	10200	19	3.6	81	89	128000	3.8	108	1.79	2.6	473	123	2	2	2	0	
2	101.8	2	1	2	2	9 axilla left	16.1	4.2	6.9	8700	21	3.6	61	149	123000	0.9	197	1.28	0.6	152	134	2	2	1	0	
2	103	2	2	2	2	2	15.4	4	6.6	7400	22.4	3.5	72	22	67000	4.29	23	1.63	1.8	86	129	2	2	2	0	
2	99.5	2	1	2	2	9 axilla	10.4	3.1	5.5	20400	20.2	2.2	87	71	24000	0.63	29	0.86	0.3	115	134	2	1	1	3	
2	2	2	2	2	2	2	11.2	4.4	8.2	8500	24	3.5	92	18	205000	0.4	12	0.85	0.2	58	135	2	2	2	0	
2	100.6	2	2	2	2	2	8.4	4.2	5.8	4700	29	2.2	57	110	10000	0.4	66	1.46	0.3	168	140	2	1	1	2	
1	99	2	2	2	2	2	9	2.4	6.7	15500	28	2.7	83	55	86	290000	0.9	57	0.9	0.3	213	134	2	1	0	
2	99	2	1	2	2	2	10.6	3.5	7.8	19800	22	3	66	49	11000	0.4	30	0.72	0.2	90	132	2	2	1	0	
2	98.6	2	1	2	2	3	11.4	4.2	6.7		26.3	3.5	82	53	105000	0.52	41	1	0.3	59	136	2	2	1	4	
2	99.4	2	1	2	2	9 left infra m	11.2	2.9	6	10600	26	2.9	73	61	10000	0.4	87	0.95	0.2	87	133	2	2	1	0	
2	98.4	2	2	2	2	2	14	3.9	7.2	8300	22	3.1	59	1158	218000	10.4	362	0.54	9.3	362	124	2	2	1	0	
2	104	2	2	2	2	2	11.4	3.4	6.7	9500	21	2.9	78	177	134000	0.9	120	0.6	98	119				0		
1	97	2	2	2	2	6	12	3.3	5.7	11600	18.1	2.4	57	55	44	74000	5.79	18	1.99	4.7	239	138	2	2	0	
2	2	2	1	2	2	6	9.6	3.5	5.5	11100	22	2.4	65	47	118000	0.4	10	1	0.2	181	134	2	2	1	4	
1	100.5	2	2	2	2	5	6.9	4.4	6.5	18900	18	2.5	80	35	546000	0.3	59	1.41	0.2	183	127	2	2	2	0	
2	96	1	1	1	2	5	8	3.4	5.9	10100	23.7	2.6	92	549	111	69000	3.4	7.3	2.3	3.1	473	136	1	2	1	3
2	101	2	2	2	2		12.7		9	11100		4.4	76	19	340000	0.44	13	0.76	0.2	135					0	
2	99.8	2	2	2	2		13.8	3.5	6.7	8100	15	3.2	67	129	107000	1.04	121	0.9	0.5	121	133	2	2	1	0	
2	99	2	2	1	2	9 right breast	11.5	3.1	6.5	11400	25.8	3.2	83	21	109000	3.93	12	1.28	3	48	134		1		0	
2	102	2	1	2	1	9 right breast	8	3.5	6.5	18500	16	2.7	48	57	109000	0.6	71	1.12	0.5	233	137	2	2	1	2	
2	100	2	2	2	2	8 inner thigh	10.8	4.1	6.4	11400	16	2.5	88	17	141000	0.8	12	1.04	0.4	231	124		1		0	
2	96	2	1	2	2	8 inner thigh	10.6	3.8	6.6	13500	11.6	3.1	86	162	80000	0.6	77	2.45	0.5	77	125	2	2	1	2	
2	102	2	2	2	2		7.1	3.1	6.5	21300	28	2.5	65	99	100000	0.5	31	0.85	0.3	290	129		1	1	0	
2	102	2	2	2	2		12.7	3.9	6.5	5000	17.6	3.3	87	97	79000	0.79	45	1.15	0.3	57	131	2	2	1	0	
2	98.6	2	2	1	2		15.9	3.8	7.7	3800	29.3	4.8	33	67	86000	0.57	47	1.15	0.2	48	141		2		0	
2	99	2	2	2	2		10	3.6	6.6	11200	21.8	2.5	66	52	31000	0.9	51	0.76	0.7	161	135	2	2	1	2	
2	98.2	2	2	2	2	5	8	3.6		29100			96		183000	0.5		3.6	0.3		151		2	2	0	
2	99	2	1	2	2	5	13.7	3	8.3	5300	22	3.8	74	162	125000	0.9	129	1.5	0.7	138	128	2	2	1	0	
2	99	2	2	2	2		17.4	5.2	7.2	5400	17	4	29	1076	62000	0.8	398	1.13	0.8	311	143	1	2	2	0	
2	105	2	2	2	2		11.9	3.7	7	7800	17	3.7	82	1500	100	129000	0.7	68	1.6	0.4	122	136	2	2	1	0
2	104	1	2	2	2	6 right flank	14.5	3.9	6.8	10200	24	3.7	87	53	178000	0.6	29	1.42	0.2	79	131				0	
2	98.6	2	1	2	2	6 right flank	11.4	4	6.6	19800	12	2.6	91	91	87000	1.2	35	1.45	0.8	183	129	1	2	1	3	
2	99	2	2	1	2		10.4		4.6	14400	14		76		187000			5.84			129		2		0	
2	98.6	2	2	2	2		14.4	3.9	6.6	13500	20	3.7	66	63	243000	0.7	102	1.64	0.4	131	130	1	2	1	0	
2	2	1	2	1	2		12.1	3.5	6.8	13500	21	2.6	83	317	251000	1.9	133	0.97	1.7	113	131	2	2	1	0	
1	99	2	2	2	2		11.3	3.3	6.1	16100	22	2.3	60	335	91000	11.4	160	0.61	9.8	445	137	1	1	1	0	
2	102	2	2	1	2		11.3	3.8	5.9	14700	18.7	2.3	83	117	85000	1.1	40	0.84	0.4	115	129	2	2	2	0	
2	101	2	2	2	2		13.3	3.6	8.3	9300	16.3	3.9	85	351	167000	0.57	199	2.33	0.2	187	134	2	2	1	0	
2	98.4	2	2	2	2	2	13.9	4.5	6.9	9700	21.7	4	66	13	82000	0.3	6	0.72	0.2	71	137				0	
2	97.6	2	1	2	2	2	12.5	4	6.7	9700	22	2.6	82	123	51000	0.77	41	1.02	0.6	225	138	2	1	1	2	
2	98.6	2	2	2	2	9 left breast	8.2	4.6	7.1	30200	19	3.3	85	14		0.4	7	2.65	0.4	139	122		2		0	
2	103	2	1	2	2	9 left breast	13.9	4.5	7.2	11000	20	3.2	89	46	7000	0.8	23	1.04	0.4	133	120	2	2	1	0	
2	98.4	2	2	1	2	5 penis	6.1	4.8	5.9	36000	16	3.5	98	22	500000	0.5	9	1.69	0.3	53	125		2		0	
2	104.5	2	1	2	2	5 penis	12.5	3.5	6	10500	19	2.8	84	104	89000	0.6	60	1.11	0.5	136	133	2	1	1	3	

2	106.4	2	2	2	2		9.3	4.2	6.8	12100	15	3.8	90	20	457000	0.5	10	1.9	0.2	59	116		1			0
2	98.4	2	1	2	2	9 left axilla	16.5	3.8	6	22700	18	2.6	75	505	10000	3.7	200	1.2	2.8	251	131			1		4
2	100.6	2	2	1	2		4.2	4.2	7	1000	21.7	4.3		72	20000	7.12	19	0.68	0.6	45	136					0
2	102.2	1	1	2	2	9 right axilla	14.2	3.8	6.7	7200	25.8	2.9	47	182	124000	2.58	372	0.87	2	312	133	2	2	1		1
2	105	1	2	2	2		18.2	4	8.6	11200	15	4.3	82	43	12900	0.4	8	1.23	0.2	84	128					0
1	101.6	2	1	2	2	9 suprapubic	10.8	5	5.4	8100	18	2.1	93	242	84000	8.2	50	1.12	6.9	302	128	2	1	1		2
2	100.8	2	2	2	2		8.5	4.7	5.4	15200	15.7	2.8	77	24	296000	0.5	11	0.95	0.3	71	127		1			0

0	0	0	0	0	1	5			1	4	2	1	1						1	0.1	1	1		
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0	0	0	0	0	1	5			1	3	2	1	1					2	1	1	2	2	
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									1	1	4	2	1	1	1	0.1			1	1	1	2	1
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0	3	3	2	4	1	1	4 doxy, ceftri	1	1	4	6	1	1					1	1	1	2	2	
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3	0	0	1	1	1	2			1	3	5	2	2	1	2		1	2	2	1	5	2	1
2	0	0	1	0	1	1	1	1	1	3	3	1	1					2	1	3	2	2	1
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0	0	1	0	0	2	5			1	4	6	1	1						1	2	2	2	1
3	0	0	2	0	1	1	3	2 192 hours	2	3	5	1	1						1	0.1	2	2	1
									1	3	5	2	2	2	1	0.1	1	2	2	1	2	2	1
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4	0	0	3	0	1	1	1	1	1	3	7	2	1	1	2				1	0.1	2	2	1
									1	4	5	2	1	2	1	0.1				1	1	2	2
0	0	0	0	0	2	5			1	3	4	1	1						1	1	2	2	2
2	0	0	1	1	1	1	4 doxy, merc	2 5	1	4	4	1	1						1	10	2	2	1
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0	0	0	0	1	1	5			4	1	2	2	2	2	1	0.5	1	2	2	2	2	2	1
3	0	0	0	0	1	1	4 doxy, azith	2 4	2	2	2	2	2	2	1	1	0.1	1	2	1	2	2	2
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4	4	0	2	1	1	1	4 doxy, pipta	1	1	2	3	2	2	1	1	2	1	2	2	2	2	1	2
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0	0	0	0	0	2	5			1	1	5	2	2	2	1	1	1	2	1	10	2	2	1
0	0	0	0	0	1	1	2 both	2 72	1	3	4	1	2	2	1	1	1	1	1	1	1	2	2
									1	3	1	1							1	2.5	2	2	2
0	0	0	1	2	2	5			1	3	10	2	1	2	1	0.1	1	2	1	0.1	1	2	2
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q35	q36	q37	q38	q39	q40	q41	q41a	q41b	q41c	q41othspe	q42	q43	q44	q45	q46	q47	q48	q49	q50	q51	q52	q53	q54	q55	q55a	q55b	q55c	q55othspe
		1	2	1	20	2									1	2			1	3.5	2			2				
		1	2	1	20	1	1			beans, gro	42	1	42	2	2	2	2		1	1	2			1	1	1	2	2
	1	2	2	2		2						2	2	2	2	2	2		2	2	2		2					
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	1	1	2	2		1	1					70	1	20	1	20	2		1	30	1 dont know		25	1	4			forest guar
	3	2	2	1	10	2							2	2	2	2	2		2	2	2		1	4			agrivulture	
		2	2	2		2							2	2	2	2	2		2	2	2		2				passing thr	
		1	2	1		2							2	2	2	2	2		2	2	2		2					
		1	2	1		1							2	2	2	2	2		2	2	2		2					1
		1	2	1		1							2	2	2	2	2		2	2	2		2					
	3	2	2	1	4	2							2	2	2	2	2		2	2	2		2					leisure
	5	1	2	1	2	1			1				15	2	2	1	15		1	5	2		2					
	5	1	2	2	1	1	1			groundnut	35	1	15	2	2	1	15		1	5	2		2		1			
		2	2	2	2	2						2	2	2	2	2	2		2	2	2		2					
	20	2	2	1	10	1	1	1		sugarcane,	20	1	9	1	9	1	3		2	2	2		1					recreation
	20	2	2	1	10	1	1	1		sugarcane,	6	2		2	2	1	3		1	3	1 dont know		1	2				
		1	2	2		2						2	2	2	2	2	2		2	2	2		2					
	2	1	2	2		1	7			sugarcane	30	2		1	15	1	15		1	0.5	2		2					
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	1	2	2	2		2						2	2	2	2	2	2		2	2	2		2					
	10	1	2	2		2						2	2	2	2	2	2		2	2	2		2					temple
	2	1	2	2		2						2	2	2	2	2	2		2	2	2		2					
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	2	2	2	1	2	2						2	2	2	2	2	2		2	2	2		2					
		1	2	2		2						2	2	2	2	2	2		2	2	2		2					
		2	2	2		2						2	2	2	2	2	2		2	2	2		2					
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		2	2	1	15	2						2	2	2	2	2	2		2	2	2		2					
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		1	2	1	10	2	2					2	2	2	2	2	2		2	2	2		2					
		2	2	2		2						2	2	2	2	2	2		2	2	2		2					
		1	2	2		2				sugrcane		2	2	2	2	2	20		2	2	2		2					
	1	2	2	2		2						2	2	2	2	2	2		2	2	2		2					
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		1	2	1		2						2	2	2	2	2	2		2	2	2		2					
	2	2	2	2		2						2	2	2	2	2	2		2	2	2		2					mud collec
		2	2	2		2						2	2	2	2	2	2		2	2	2		2					to clean
	10	1	2	1	10	1	1					2	2	2	2	2	2		2	2	2		2					
	10	1	2	1	10	2						2	2	2	2	2	2		2	2	2		2					
	5	1	2	2		2						2	2	2	2	2	2		2	2	2		2					
	2	1	2	1	5	1	1			sugarcane	9	1	9	2	2	2	2		2	2	2		2					
	2	1	2	1	5	1	1			groundnut:	9	1	9	2	2	2	2		2	2	2		2					
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	10	2	2	2		2						2	2	2	2	2	2		2	2	2		2					
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	0.01	2	2	1	10	2						2	2	2	2	2	2		2	2	2		2					
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	0.1	1	2	2		2						2	2	2	2	2	2		2	2	2		2					
	0.1	1	2	2		2						2	2	2	2	2	2		2	2	2		2		1			

q56	q57	q58	q58othspe	q59	q60a	q60othspe	q60b	q60bothsp	q60c	q61	q62	q63	q64	q65a	q65b	q66	q67	q68	q69	q70	q71	q72	q73	q74	q75	q76	q77	q78	
		2				4		2		2	2	2		1	1	2	2	2		1	2	2	2	2	1	2			
8		2				3		2		2	2	2		1	2		2	1	1	2	1	1	2	2	2	1	2		
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4.6		2				4		2		2	2	2		1	2	2	2				1	1	2	2	2	1	2	2	
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0.5		2				7	nighty	2		2	2	2		2	2	2	2	1	14	2	1	1	2	2	2	1	2		
		1	2 and 3	1.1		3		2		2	2	2		2	2	2	2	1	7	2	1	1	1	7	2	1	2		
2		2				4		2		2	2	2		1	2	2	2	1	7	2	1	1	1	7	2	1	2		
		2				5	burkha	7	burkha	1		2		1	1	1	2	2			2	2	2	2	2	1	2	2	
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		2				nightdress	nightdress	1		2	2	2		1	1	1	2	2			1	1	1	7	2	1	2	2	
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		2	2 4, milking	7		4		2		2	2	2		1	2	2	2	2		1	1	2	2	2	2	1	2	2	
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		2	2,3,milking	7		4		2		2	2	2		1	1	1	1	3.5	2	1	1	2	2	10	2	1	2	2	
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		2				nighty	nighty	2		2	2	2		1	2	2	2	2			2	2	2	2	2	1	2	2	
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14		2				4		2		2	2	2		1	2	2	2	1	21	2	2	2	1	3	2	1	2	2	
0.3		2	2 bullock car	24		6		1		2	2	2		1	2	2	2	2			2	2	2	2	2	1	2	1	
		2				6		1		2	2	2		2	1	1	2	1	14	2	1	1	2	2	2	1	1	1	
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		2				5	Kurta	2	pyjama	1		2		2	2	2	2	2			1	1	2	2	2	2	1	2	
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