RESEARCH PAPER | Environmental Science | Volume : 5 | Issue : 2 | Feb 2015 | ISSN - 2249-555X

Environmental Awareness and Hygienic Measures Taken Based on a Case Control Study Prevent Further Outbreak of Indian Tick Typhus in and Around Village Deol, Kangra, Himachal Pradesh, India- A Seven Years Follow-Up Study

KEYWORDS: Hygiene, Outbreak, Indian tick typhus, Surveillance Failure

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ABSTRACT *Background: Rickettsial diseases (typhus) is a group of re-emerging infections, which manifests itself as nonspecific febrile illness & pose a serious public health problem when not diagnosed or misdiagnosed. Tick borne disease has been reported among international travelers. An outbreak of tick borne typhus was reported in Botswana among U.S. Soldiers participating in training exercise in Botswana with high attack rates. In a recent study in south India 7.7 % of pediatric patients with fever of unknown origin had spotted fever.*

On 9/7/2007 a pediatrician telephonically informed the Chief Medical Officer Kangra regarding high number of fever cases in Deol Village. Fever presenting with excessive perspiration, headache, chills & rigors. The author was asked to confirm & investigate the outbreak and suggest protective measures to be taken.

Methods: We collected baseline fever data for a period of 5 years. We talked to local people, local service providers to verify if similar disease had occurred in the past & we confirmed that it was an unusual event. We defined a suspected case as occurrence of fever with or without chills or headache with onset from Mid April– Mid August 2007, in a resident of village Deol with no established alternative diagnosis & conducted house to house searches and enumerated the village population. We also collected blood slides for malarial parasite, serum samples for serology for typhus & blood stool samples for salmonella culture. We conducted in depth interviews of key informants regarding the occupation, common activities in the area, obtained data on temperature humidity & rainfall for the last five years to correlate the environmental variables with the outbreak. We inspected the water source & collected water samples for examination for coliform bacteria. We examined animals for the presence of ticks & sent tick samples for identification.

We then conducted a case control study with all 25 lab confirmed cases & 25 age sex & neighborhood matched controls. We collected information on socio- demographic variables, various suspected exposures using a pre tested structured questionnaire to find out the risk factors and take preventive measures.

Results : We found 332 cases (over 17 weeks) from Deol. The incidence of fever in July 2007 was in excess of the expected frequency by more than 2 standard deviations & confirmed to the definition of an outbreak. The common clinical features were fever with chills in 86% followed by fever with headache in 83% & Fever with cough 24%: One case showed 2 eschars. The first case was on 15th April the epi-curve peaked in the week ending 7th July & then declined. The attack rate was 26 % & more in females (32%) than in males (20%). The attack rate was highest in age group of 5-14 (38%), followed by 15-29 yrs (29%). Geographic distribution shows that attack rates were highest among areas close to forest.

No pathogens were isolated in the 3 Stool cultures or 6 blood cultures. Blood film examination for malaria was negative. According to the lab reports of CRI Kasauli, 12 cases of 19 had a titer of >1:80 on Weil Felix.

IgM ELISA done at NCDC, Delhi reported 10 of 16 samples positive for Indian tick typhus R. conorri. 2 cases had a significant rise in titers from 1: 80 to 1:1240. A total of 25 cases had IgM Elisa positive or Weil Felix titer > 1: 80.

The comparison of various exposures among case patients & healthy controls showed that those changing clothes weekly or less frequently had 29 times higher risk of getting the disease, whereas for exposure to tall grass in the neighborhoods it was 14 times higher risk. Travel to forest, bathing animals frequently, less than thrice weekly; personal bathing frequency more than weekly, farming & having tick infested animal in the house were associated with a higher risk of getting disease. Having a household contact with fever case was associated with a 4 times higher risk of getting the diseases. Other factors like having a mud house, ownership of animals in family were not significantly associated with risk of illness.

The village people go to the forest/ grasslands to collect grass or graze the cattle The in depth interviews of key informants revealed that tick paralysis is common among the sheep in spring when crossing forest to grazing pastures.. Riphicephalus ticks which are associated with Indian tick typhus were physically found on the animals.

Conclusions: The high risk associated with poor personal hygiene is corroborated with the life cycle of the tick. The larval stage of the ticks will get washed off the body with good personal hygiene like frequent changing of clothes and bathing. The spurt in rainfall & humidity in beginning of June corresponds to increase in vegetation height & increased propagation of ticks.

Recommendation: The people were advised to bathe daily & change clothes frequently. Exposure to forest & farm activity needs alert behaviour and people need to get the animals treated for the tick infestation regularly. We sensitized the local medical officer & a system was put in place for regular surveillance of the disease based on case definition of fever. No cases have been reported in last more than seven years as a system of effective surveillance is in place for detection of any such cases and people are continuously sensitized to maintain hygiene and be vigilant during rainy season and de-tick the animals regularly.

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Background:
Rickettsial diseases (typhus) is a group of re-emerging infections[1,2] which manifests itself as nonspecific febrile illness; and pose a serious public health problem when not diagnosed or misdiagnosed. The public health importance of rickettsioses remains ill-defined[3] but increasing trends have been reported worldwide[4, 5].

The most prevalent spotted fever rickettsiosis in Europe and Africa is boutonneuse fever (Mediterraneann spotted fever) which is spread by tick bite. Over the past two decades, the incidence of tick-borne diseases (TBDs) increased and poses a major public health problem in Europe[6]. *Rickettsia conorii* has also been isolated in South Africa, Kenya, Morocco, India, Spain, France, Croatia, Georgia, Russia, Ukraine, Pakistan and Ethiopia. The incidence of boutonneuse fever has increased dramatically in Spain, France, Italy and Portugal during the last 15 years[3]. The disease was first observed in India by Megaw (1917) in the foothills of the Himalayas[7]. The investigations of Kalra, Rao, Soman, Helig and Naidu had established that the disease is found in many parts of India[8]. Indian Tick typhus has been reported in Pune in 1984[9]. In a recent study in south India, 7.7 % of pediatric patients with fever of unknown origin (FUO) had spotted fever[10].

Typhus fever is known in Himachal Pradesh but Indian Tick Typhus was not heard of. A pediatrician telephonically informed the Chief Medical Officer regarding high number of fever cases from Deol Village, suspected to be typhoid. On 9/7/2007 the Chief Medical Officer Kangra directed the author to confirm and investigate the outbreak and suggest preventive measures. The typical pattern was fever with excessive perspiration, headache, chills and rigors which had not responded to ofloxacin or cefixime.

We conducted an investigation with the objectives of finding the cause and taking appropriate control and preventive measures.

Setting: The village Deol is located. 8 km from Baijnath (the Tehsil Headquarter and a pilgrim town in eastern part of district Kangra, located in the western Himalayas) It is at a latitude of 76°40′ 37.8″ E to 76 °39′47.3″ E and 32°05′20.2″ N to 32°05′39.5″ N; at an altitude of 1193 -1355 meters above mean sea level and connected by a motorable single lane road in hilly terrain. The population of the village was 1223 as per 2001[11] census. The time of the year was monsoon season with high rainfall. The village is bound by the river at the south and east, forest line in the north and a stream in the west.

Methods: We followed the ten steps recommended by WHO/CDC for the investigations of the outbreak.

Step 1: Determine the existence of an outbreak:
We collected baseline fever data from outpatient records and reports of Ayurvedic health centre Deol for last 5 years and analyzed for seasonal trends and seasonal averages. We also talked to local people, local service providers to verify if similar disease had occurred in the past and if there are any changes in surveillance or population movements.

Step 2: Confirm the diagnosis:
We examined the initial cases and assessed the clinical features to arrive at a diagnosis. We also prepared blood smears for malaria, did blood culture, serology for typhoid and typhus and brucellosis to arrive at possible diagnosis for the fever.

Step 3: Define a case:
We developed a suspected case definition on the basis of presenting clinical features of the initial cases.

Step 4 Search for cases:
We constituted a rapid response team consisting of local health workers, medical officers and conducted a house to house search (on 11/7/2007) enumerated the population, and did the search using three teams (each consisting of a doctor, health workers and local volunteer) and prepared a line list of fever cases using a structured performa. We also prepared a spot map.

Step 5 Generate hypotheses using descriptive:
We administered a trawling questionnaire to a subset of the cases to identify possible exposures.

Step 6 Analytical study:
We then confirmed the hypothesis regarding these exposures by a case control study. We collected information on exposure of fever cases to suspected risk factors- ownership of animals, history of tick infestation in animals, animal handling- milking, bathing, playing with dogs; visit to forest for grazing cattle; grass or forage collection, working in farms, visit to fields for open air defecation, rats seen in house in last 3 months, personal bathing frequency, animal bathing frequency. All 25 lab confirmed cases (IgM ELISA or Weil-Felix positive) and an equal number of age sex matched neighborhood controls were interviewed using a interview schedule.

Step 7, 8. Draw conclusions and comparison with established facts:
We also conducted environmental investigations animal survey for ticks and collected information on rainfall, humidity and temperature to corroborate our findings. We compared our findings with findings of environmental investigation and established facts in literature.

Step 9. We made recommendations based on our conclusions derived, to implement control measures and prevent future outbreaks.

Step 10. We communicated the findings along with the recommendations to the district and state health authorities, who executed prevention measures.

Results:
Step 1: Determine the existence of an outbreak:
Review of records revealed that there were 113 fever cases in June and 497 in Deol Ayurvedic health centre in July. Baseline for July (5 yrs average) was: 38.2 ± 19.3 fever cases. Thus the present event was clearly in excess of the expected average cases and confirmed to the definition of an outbreak. There was no population movement, no change in surveillance. Informal discussion with local health authorities revealed that Integrated Disease Surveillance Project (IDSP) report was not being sent as health workers in that block were not trained. IDSP was functional in only one third of the district and only those persons were trained.

Step 2: Confirmation of diagnosis:
The clinical picture was fever with headache in 86%, fever with chills in 83%, fever with cough in 21%. There was no rash. Typical Eschar was seen in one case. As the cases (95%) had fever more than 7 days therefore typhoid was

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also kept as a differential diagnosis.

Blood smears for malarial parasite were negative. 15 of the 16 Serum samples were negative for brucellosis by the blot method. Blood culture and stool culture did not yield any pathogenic organism. Weil Felix was positive which turned out to be Indian tick typhus (R. conorii) by IgM ELISA. Rising titers were seen in Weil Felix in 2 samples which are diagnostic.

According to the lab reports of CRI Kasauli, 12 cases out of 19 had a titer of >1:80 on Weil Felix. 12 cases out of 19 had a titer of >1:80 OX2 and 4 had positive for OX 19 on Weil Felix. IgM ELISA done at NCDC, Delhi report 10 of 16 samples tested positive for Indian tick typhus R. cornori. 22 of 26 patients have Weil Felix (≥ 1:80). 2 cases demonstrated a rise in titer. A total of 25 cases were confirmed by lab (IGM ELISA or Weil Felix)

Step 3: Defining a case:
We defined a case as occurrence of fever with or without chills or headache with onset from Mid April 2007 – Mid August 2007, in a resident of village Deol with no established alternative diagnosis.

Step 4: Search for cases:
The house to house search yielded 232 cases which confirmed to the case definition among the 1287 enumerated population having an attack rate of 25.8%.

Time distribution: The epidemic curve shows that first case was on 15/4/07 and the curve peaked in the week ending 7th July and is then declining [Figure -II].

Place distribution: The geographic distribution shows that attack rates are highest among resident of village Phata (41.3%), followed by village Dhogri (31.6%) where animal ownership and proximity to forest are factors. The attack rates in village Dharwal and village Bhatt Basti were 30.4% and 27.8% respectively, higher than the average. The age wise attack rates are shown in Table I.

Person distribution: The 5-14 age group had highest attack rates (38.4%), followed by 15-29 years age group (29.2%).

Step 5 Generate hypotheses using descriptive findings:
The risk factors were identified by the analysis of time place person characteristics, and trawling questionnaire and information was collected on possible exposures of fever cases and non cases in the population e.g. ownership of animals, history of tick infestation in animals, animal handling- milking, bathing, playing with dogs, removing ticks with bare hands, use of tick repellents and protective clothing; visit to forest for grazing cattle; grass or forage collection, working in farms, visit to fields for open air defecation, rats seen in house in last 3 months, personal bathing frequency, animal bathing frequency.

Step 6: Analytic epidemiology:
The analytic study results showed that the odds of getting tick typhus is 29.3 times more among those who changed clothes weekly or less frequently compared those who changed them frequently.

In addition the following exposures were also associated with having the disease: Bathing animal less than thrice weekly, personal bathing frequency more than weekly. Having a household contact with fever case was associated with a four times higher risk of getting the diseases. Other factors as having a mud house, ownership of animals in family were not significantly associated with risk of illness. (Table II).

Step 7: Comparing the findings with established facts and environmental:
Hypotheses on the following exposures was thus verified- Travel to forest, farming & having tick infested animal in the house was associated with a higher risk. The animals were examined for the presence of ticks, and tick samples were sent for identification, which were confirmed to be Riphicepalus, brown dog tick, the vector of Indian tick typhus.

We correlated the data on environmental variables - we tried to explore the environmental relationship with the outbreak. Temperature, humidity and rainfall for the last five years obtained from the agro metrology lab of HP Agriculture University Palampur were correlated with the outbreak. The relation of environmental variables to epidemic curve shows a spurt in rainfall and humidity around the 4th June, which is conducive for growth of ticks. The spurt in rainfall and humidity in beginning of June corresponds to increase in vegetation height. The ticks require vegetation to hook themselves for attaching to the host when the host passes by the grass. Higher the grass more it increases the accessibility and likelihood of attachment to the hosts. Also the ticks require moisture for survival, and humid conditions are favorable for propagation of the ticks.

Communicating findings and prevention measures:
We managed all case patients with doxycycline. We shared the report with District Surveillance Officer (DSO) and State Surveillance officer (SSO) for further action. We also shared the findings with other teams that arrived in the area for outbreak investigation including College of Veterinary and Animal Sciences Palampur and National Centre for Disease Control, NCDC, Delhi.

We advised people to bathe daily and observe better hygiene, de-tick the animals regularly. We also asked the resident to be more vigilant during rainy season. We established a surveillance system for the disease based on the case definition of fever.

Discussion:
Rickettsial diseases are a group of emerging/ re emerging infectious disease. This outbreak was detected late, primarily due to failure of surveillance system, IDSP. Since IDSP is already operative since last 2 years in the district, early warning signals of this outbreak should have been recognized by health system. No cases were recognized by the health system until outbreak reached its peak. Integrated disease surveillance project is established in the district, but only one thirds of health workers were trained and people in this affected area were not trained. No weekly surveillance reports were generated or sent. The first report came from a private practitioner who had seen a large number of fever cases.

It is for the first time that such a large outbreak occurred, and there was not enough awareness or facility for diagnosis at the local level. Though outbreaks of scrub typhus were reported in the state earlier, the district hospital and even medical college did not have facilities for Weil Felix at the time of outbreak and samples had to be sent to Central Research Institute (CRI) Kasauli, which delayed the early diagnosis. Confirmatory serologic test is available

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only at the National reference lab. Culture facilities are not available in the county.

Clinically the features of typhus are non specific and resemble typhoid fever. As it was the monsoon season when enteric fever is common, all doctors were treating the cases for typhoid and they were not responding even to third generation medicines. The clinical features of fever with headache and chills suggested malaria or rickettsial disease. The absence of rash though goes in favour of typhoid and lead to misdiagnosis, absence of rash is known in Indian populations. The presence of eschar in one patient favors diagnosis of rickettsial infection.

Recommendations:

No cases were recognized by the health system until outbreak reached its peak. Surveillance needs to be strengthened and training of health functionaries needs to be done. Lab capacity needs to be strengthened. The first report came from a private practitioner who had seen a large number of cases, hence we need to forge partnerships with the private sector and other disciplines including veterinarians as per IDSP recommendations

We recommended health education regarding periodic deticking of livestock and personal protection in handling animals.

As lack of local lab capacity was a major constraint in this investigation, which led to delay in diagnosis, we recommend strengthening of Lab capacity at local level including procurement of ELISA Kits at least at District level.

Action Taken:

We managed all case patients with doxycycline. We advised people to bathe daily and observe better hygiene, de-tick the animals regularly. We established a surveillance system for the disease based on the case definition of fever. Regular monitoring of fever cases from the area through the IDSP is done to keep a tab on the happenings in the village and no unusual surge of cases with fever has been reported from the village Deol and around till date.

Acknowledgements:

We acknowledge with gratitude the timely lab support received from Central Research Institute Kasauli & Microbiologist of Medical College Kangra, Microbiology Division of NCDC & Dr Rina Tilak of AFMC for entomology support, & support of the local health staff of Mahakal Block and agro metrology lab of HP Agriculture University, Palampur.

Figure I: FEVER TRENDS IN DEOL AYURVEDIC HOSPITAL DIST. KANGRA, HP, INDIA SINCE JAN 2002

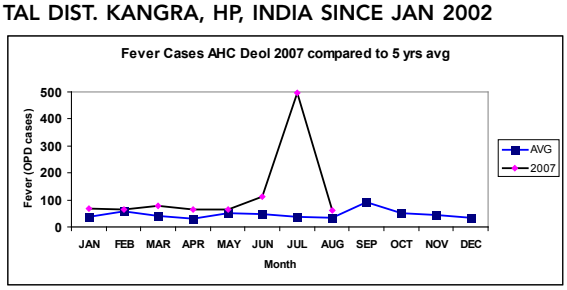


Figure II: Epidemic curve of probable tick typhus cases in Vill Deol, district Kangra, Himachal Pradesh, India, June- July 2007.

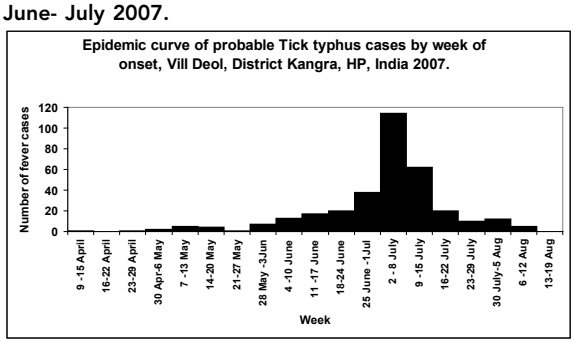
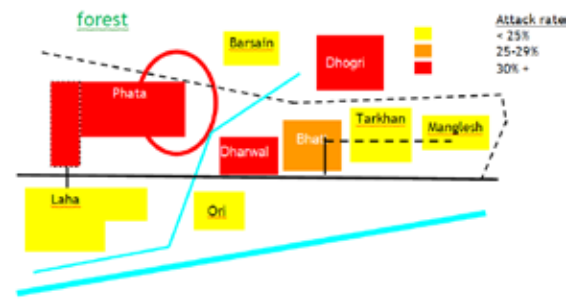


Figure III: Outline Map of Deol village, district Kangra, Himachal Pradesh, India, June- July 2007 showing geographic distribution of fever cases in outbreak.



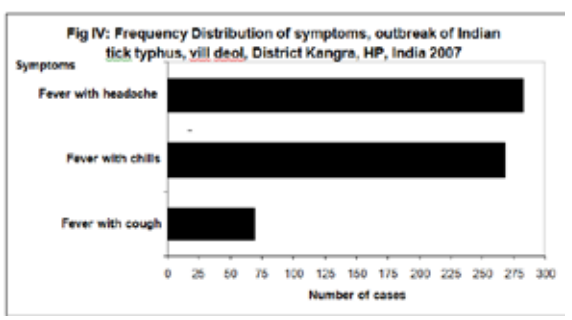


Figure V: Eschar found in a case of fever, outbreak of Indian Tick typhus at Village Deol, District Kangra, Himachal Pradesh, India 2007

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Fig VI: Environmental variables in relation to epidemic curve, Vill Deol, District Kangra, HP India 2007

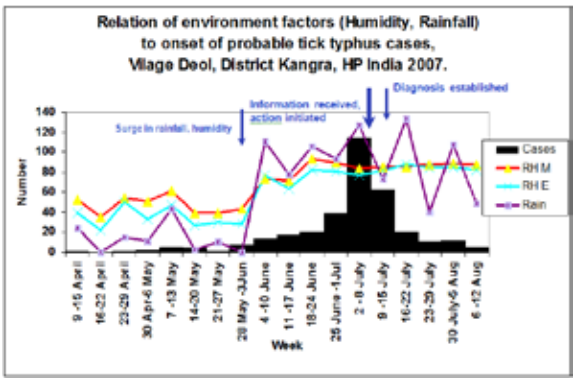

Table I: Age sex distribution of fever cases and attack rates.

	Cases	Popn at risk	Attack rates
	n=332	n= 1287	%
Age			
<4	17	84	20.24
5-14	91	237	38.40
15-29	114	391	29.16
30-44	59	272	21.69
45-59	37	202	18.32
>60	14	101	13.86
TOTAL	332	1287	25.80
Sex			
M	136	675	20.15
F	196	612	32.03

Table II: Case control study to know the significant exposures/ Risk factors to the patients of Indian Tick Typhus.

	Cases N = 25		Controls N = 25		OR	95% C.I.	
Exposures	N	(%)	N	(%)			
Changing clothes weekly or less frequently	20	80	3	12	29.33*	5.17	199.97
Tall grass in neighborhood	24	96	16	64	13.50*	1.46	312.96
Travel to forest for grazing/ forage collection/	15	60	3	12	11.00*	2.22	62.77
Bathing frequency Less than thrice weekly	11	44	3	12	5.76*	1.17	31.99
Animals infested with ticks	16	64	5	20	7.11*	1.7	31.7
Handling tick infected animal	14	56	5	20	5.09*	1.24	22.06
Farming	12	48	4	16	4.85*	1.1	22.8
House hold contact with fever case	18	72	10	40	3.96*	1.02	15.17
Type of house Temporary (Mud)	18	72	12	48	2.79	0.74	10.74
Ownership of animals in family	16	64	12	48	1.93	0.54	7.02

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