Original Article

Seasonal, Regional and Demographic Trends in Patients with Acute Undifferentiated Fever in Northern India

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Introduction : Acute Undifferentiated Fever (AUF) has a myriad of etiologies most common of which are Vector Borne Diseases in a country like India. The etiology and diagnosis of AUF is driven by the regional disease burden, seasonality of infectious diseases, spectrum and severity of disease, availability of diagnostics and access to health care facilities.

Methods : A twelve-month prospective study was conducted at our centre to determine the commonly occurring causes of AUF. Monthly incidence of each of the common etiologies was noted and a graph was plotted to understand the seasonal distribution of each disease. Other parameters including age, gender, occupation and regional distribution were also studied.

Results : The mean age (±SD) of the population in the present study was 33.16 (±15.88) years. Our study established that Scrub Typhus, Dengue fever and malaria were the most common reasons for AUF. The maximum incidence of AUF was between the months of June to October, peaking in the month of August. Urban population, younger age and males were more affected by AUF. Haryana followed by Punjab and Chandigarh had the highest regional burden of disease.

Conclusion : It is imperative that we understand the seasonal and regional trends of AUF so that we can plan the resource allocation. Identifying the population at risk and timely intervention at Community level may help to reduce disease transmission.

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***Key words* : Acute undifferentiated fever, demography, seasonal trends.**

Fever disproportionately affects the most vulnerable human communities of the tropical regions. Populations that live in poverty, without adequate hygiene and sanitation become more prone to febrile illnesses due to the abundance and relentless propagation of mosquitoes, ticks, mites and other disease-transmitting vectors. In India, the population is expanding exponentially outpacing the existing infrastructure and overwhelming our sanitation and disposal facilities. Urbanisation, deforestation and human migration has led to encroachment into the habitat of the various organisms leading to a disruption in the ecological balance with consequent increase in the incidence of tropical illnesses.

A vast number of organisms can cause Acute Undifferentiated Fever (AUF) ranging from bacteria to viruses to protozoa to fungi and account for many preventable deaths in developing countries. In the Western World, AUF is mainly due to viral illness, but in underdeveloped countries including India it is mostly due to avertable illnesses such as Malaria, Dengue Fever, Scrub Typhus, Leptospirosis, Chikungunya and Enteric fever[1].

India, being a tropical country, sees a diverse variation in the climatic condition ranging from extreme summers and harsh winters to torrential rains.The monsoon season in particular is responsible for a rise in AUF as it provides fertile grounds for the transmission of Arthropod Borne Diseases like Dengue Fever and Malaria[2]. Dengue fever and malaria epidemics have been reported from various parts of India during the monsoon season. Leptospirosis and Scrub Typhus are zoonotic infections which have slowly engulfed many regions of the country in the last decade. Chikungunya has been on the rise in the Northern and

Editor's Comment :
- Most AUF in India are due to vector borne diseases.
- The monsoon and post-monsoon season sees the largest number of tropical fevers.
- Demographics of AUF is widening and susceptible population is increasing.
- Understanding the seasonal and regional variations of AUF is crucial.

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Eastern parts of India. Enteric fever is endemic throughout India. There is greater focus on Non-malarial AUF with the decline of Malaria in many regions of India.

Being aware of the occurrence of diseases during a particular season can help us to understand these diseases better so that the can be identified at the earliest and thereby effectively controlled. Improving our understanding of how Environmental factors affect Tropical diseases can help us chalk out life-saving management strategies.

Materials and Methods

Study Design and Setting :

This observational study was conducted at Government Medical College and Hospital, Chandigarh from January to December 2019. The study was aimed at observing the common etiologies of AUF in Northern India and the seasonal distribution along with age, gender, occupation and the regional burden of these fevers. The study was approved by the Research and Ethics Committees of the Medical College.

Study Participants and Sampling :

A total of 200 patients with AUF were included in the study. Hospitalised patients older than 12 years of age with fever of $\leq$14 days were included in the study. Localized infection was ruled out by History, Physical Examination, Complete Blood Counts, Urine Analysis and Chest Radiography at the time of initial presentation. Immunocompromised patients and those who had received prior antibiotics or hospitalisation were not included.

Data collection Tool and Technique :

A written and informed consent of all the participants was taken. A descriptive analysis was done to characterize the participant population by socio-demographic data (eg, Age, Gender, Place of residence and Occupation). All Non-parametric variables were compared using Chi-square and Kruskal Wallis. Mean (SD) or median (range) were calculated for the parametric variables and they were analysed using Student's t-test. All data was expressed as mean ±SD. Empirical therapy was started as per clinical suspicion and preliminary investigations. It was subsequently modified after a diagnosis was established.

Methodology :

Diagnosis was confirmed by suitable laboratory tests after clinical examination. Relevant investigations included Complete Blood Counts, Urinalysis, Renal Function Tests, Liver Function Tests and Chest Radiography. Abdominal Ultrasonography, Electrocardiography, Echocardiography, Arterial Blood Gas, Coagulogram, CT scan and Fluid analysis were done as per the clinical suspicion.

Suspected Malaria was diagnosed based on Rapid Diagnostic Tests for antigen detection and peripheral blood smear for malarial parasite (trophozoite of Plasmodium falciparum, Plasmodium vivax or mixed). Thick smears were used to screen for the presence or absence of parasites while thin smears will be used for species identification. Dengue fever was confirmed by the detection of NS1 antigen or IgM antibody, leptospirosis by IgM ELISA and Scrub typhus by IgM antibody detection by ELISA for *O tsutsugamushi*. Blood cultures were sent for suspected cases of enteric Fever. For Chikungunya, IgM ELISA serology for detection of Anti-Chikungunya virus antibodies was done. The distribution of varied etiologies of AUF was noted for every month over the course of the study.

Results

Out of 340 total cases of acute fever who visited the emergency during the study period, 200 AUF were included in the study after appropriate exclusions. Fig 1 depicts the distribution of fever in our study population. 53 (26%) patients were confirmed cases of Scrub Typhus, 49 (24%) patients were proven to have Dengue fever, 28 (14%) patients established to be Malaria, 22 (11%) patients had mixed infections, 7 (4%) patients had Acute Viral Hepatitis, 5 patient had Leptospirosis, 5 patients diagnosed to be Enteric Fever, 1 patient confirmed Acute Myeloid Leukemia, 2 patients had Infective Endocarditis and one patient had Tubercular Meningitis. 27 (13.5%) patients remained undiagnosed despite a complete analysis for fever. Our study did not find any patients with isolated Chikungunya infection. However, Chikungunya was

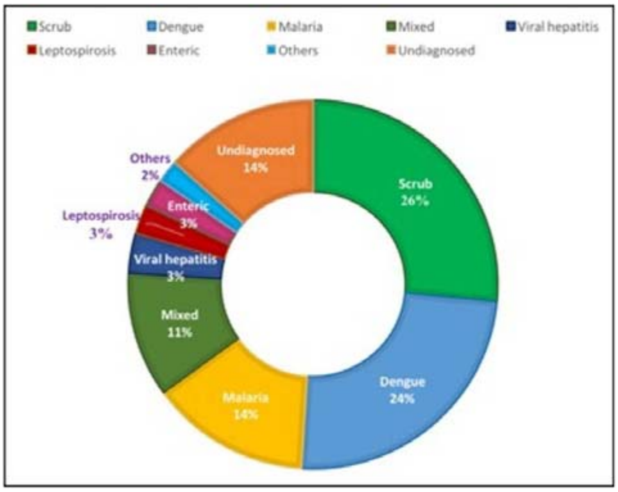

Fig 1 — Graphical representation of distribution of AUF in total study population found as a co- infection with Dengue fever in 1 patient.

The maximum incidence of AUF was between the months of June to October, peaking in the month of August as shown in Fig 2. Out of the total 200 patients, 48 patients of AUF were admitted in August with 39, 20, 18 and 16 in the months of September, October, June and July, respectively.

Demographics of the Study Population :

The mean age (±SD) of the population in the present study was 33.16 (±15.88) years. The age ranged from 12 to 85 years. The mean age in patients of Scrub Typhus, Dengue Fever, Malaria and Mixed Infections was 34.47 (±13.65), 36.63 (±18.79), 24.78 (±11.34) and 30.13 (± 17.38) years, respectively. The number of males outnumbered the females, 118 (59%) being males and 82 (41%) being females. Out of the total 200 patients, 150 were less than 40 years of age. Similar results were seen in established cases of Scrub Typhus, dengue fever and malaria with 38, 35, 26 patients below 40 years. Only 17 patients of the total 200 study population were above 60 years of age. Gender wise distribution of fever among various febrile illnesses in our study population is shown in Fig 3.

Occupation :

In 67 (33%) patients were students, 56 (28%) were engaged in a private job and only 9 (5%) patients had an agricultural background. This is illustrated in Fig 4.

Residence :

All the participants were residents of Chandigarh and the adjoining states. Fig 5 shows the state wise distribution of fever in our study population. The contribution from Haryana (45%) was maximum followed closely by Punjab (33%). The contribution from

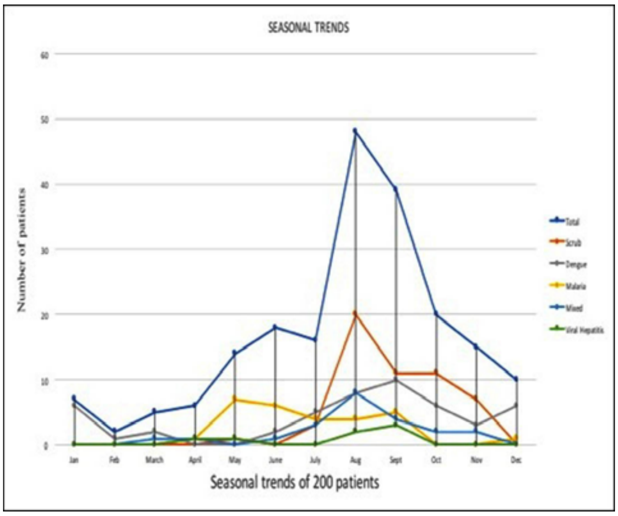

Fig 2 — Monthly distribution of various detected acute febrile illnesses

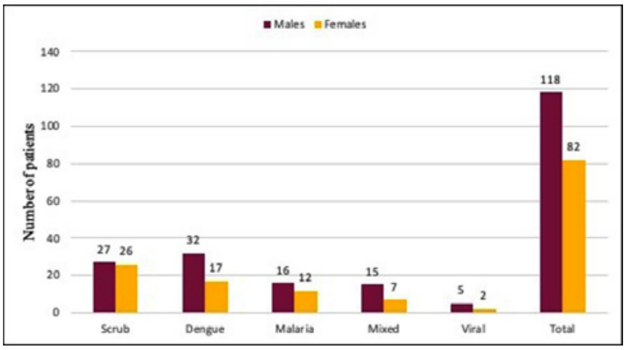

Fig 3 — Gender-wise distribution of fever

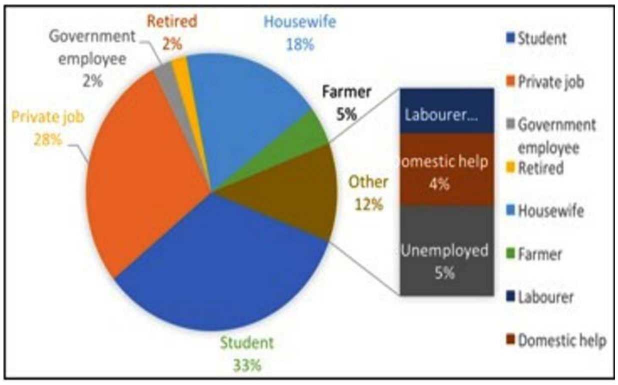

Fig 4 — Graphical representation of various occupations of study population

Chandigarh was on the lower side, however, at 9% with Himachal Pradesh and Uttar Pradesh contributing only 7% and 6%, respectively. In our study more patients belonged to an Urban background, 54.5%, rather than a Rural one, 45.5%. Fig 6 depicts the distribution of various febrile illnesses in our study population based on rural and urban backgrounds. Although with Scrub Typhus, patients with a rural background (50.9%) took a marginal lead than patients dwelling in Urban areas (49%), the other patients with Dengue Fever, Malaria, Mixed Infection or Viral

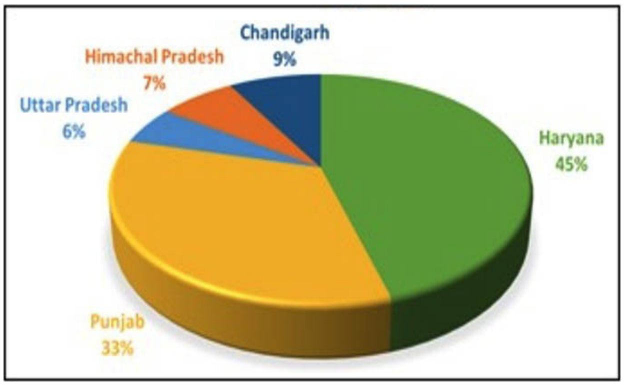

Fig 5 — Geographical distribution of study population

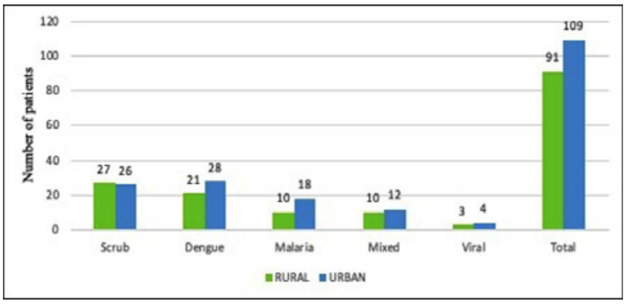

Fig 6 — Distribution of fever in rural and urban areas

Hepatitis had a higher urban to rural ratio.

Discussion

Out of the 200 patients, the maximum participants with AUF turned out to be Scrub Typhus followed by dengue fever. Remarkably, 18% of the AUF still remained undiagnosed despite all relevant investigations. Another element was the presence of 11% of the study population with mixed infections. Scrub typhus has become the leading of AUF not only in India but also in other South Asian countries like Nepal, Bangladesh and Thailand although the relative incidence of the pathogens varies from region to region[3]. A study conducted by Abhilash *et al* in South India also found Scrub, Dengue Fever and Malaria to be the main culprits of AUF[4]. The overall incidence of malaria and its impact on health in India and the neighbouring Countries, however, is declining similar to what was observed in our study[5]. In a recent study conducted in Karnataka, Scrub typhus was identified as the most common causes of Acute fever, followed by dengue fever[6]. Leptospirosis, Malaria, Scrub Typhus, Murine Typhus and Dengue Fever have been identified as major causes of AUF in various studies conducted in Thailand, Malaysia, and Nepal[7-11]. Dengue fever was found to cause one third of all cases of acute undifferentiated non-malarial fever in a similar study conducted in Vietnam[12]. In a study conducted at a Tertiary Hospital in North India, most common causes of AUF consisted of Dengue (37.54%), Enteric Fever (16.5%), Scrub Typhus (14.42%) and Bacterial Sepsis (10.3%)[13].

The peak month recorded for admissions for AUF in our study was August with maximum distribution between the months of June to October. With the onset of monsoon season, the cases with AUF start to rise and this trend continues till the end of the year. This can be ascribed to the humid climate during that season along with immense rainfall. This is in accordance with the reported patterns of disease transmission of Scrub and Dengue Fever[14,15]. However, no significant seasonal variation was found for malaria in our study. Changes in temperature and rainfall are the most critical factors responsible for an increase in the transmission of Vector Borne Diseases. Climate change has had a huge impact on the rate of vector growth and as well as virus amplification rates. Warm humid temperatures help increase the population size of mosquitoes, mosquito life cycle length as well as the rate of reproduction. Increased rainfall and rising sea levels because of global warming provide breeding sites for vectors thereby increasing disease risk[16,17].

Most of the patients in our study were from Haryana (45%) followed by Punjab (33%). Chandigarh only showed a 9% incidence of acute fever. Himachal Pradesh, which was previously the epicentre of Scrub Typhus, showed a lesser incidence of acute fever than previous studies suggesting a shift in the main belt affected with tropical fevers and thereby reflecting the changing demographics. Scrub typhus has been reported in Southern India as well as the Himalayan Region for many years. In the past decade, scrub typhus has started to emerge in the Sub-Himalayan belt as well as parts of Central and Western India. Haryana, Punjab, Himachal Pradesh, Delhi and Chandigarh have emerged as one of the hotspots of Scrub Typhus in recent times[18]. In a South Korean study, squatting in the grass for defecation, working with bare hands and short sleeved clothes are reasons for cases of Scrub Typhus, reasons which are quite applicable to India as well[19]. Our results are consistent with most studies in Northern, Western, and North East India, all of which report cases from July to November[20,21]. This does not apply to studies from the Southern States which report cases from October to February mostly[22].

In our study, Dengue fever cases began to rise in June with a progressive upward slope and finally peaking in September followed by a decline in October and November. This is similar to most studies conducted in India which report peak dengue fever cases in August and September[23]. All 4 Dengue fever virus serotypes are prevalent in various parts of the country. For the past 2 decades, the Dengue fever cases have exponential increased in India with Southern States of Karnataka, Tamil Nadu, Maharashtra and the Northern belt of Delhi, Haryana, Punjab, Chandigarh and Rajasthan showing a meteoric rise.[24] El Nino effect which is a warm climate pattern leading to warming of the Pacific Ocean and causing climate variation has been found to affect the Indian monsoon with a positive Association in terms of Malaria and Dengue fever cases[25].

Our study did not find a discernible trend in the cases of malaria nor any significant peaks. This may be attributable to a smaller figure of Malaria cases reported. However, the cases were more evidently seen in the monsoon months. According to one study conducted in India, the season with the highest average total Malaria cases occurrence was June to August and the minimum Malaria cases were observed during the winter[26]. Both *P.vivax* and *P.falciparum* cases were observed.In the Northern States of India, with extremes of summer and winters, malaria transmission rate remains subpar for most of the year. It is only with the advent of monsoon that the transmission rates pick up. This is in contrast to the Southern States where a stable Malaria Transmission sustains due to minimal temperature variation throughout the year and considerable rainfall. As we move from the west to the east, the rainfall improves tremendously leading to more stable malarial transmission.

Acute Viral Hepatitis has been reported throughout the year. Though HEV is found all year round, according to one study maximum cases were seen from July to October. HAV was highest in the summer[27]. Hepatitis B and C did not show any seasonal variation. Warmer and wetter climates significantly worsen the transmission of Salmonella. A study conducted in Gujarat established that Enteric Fever cases started to rise from March to May due to increasing warm climate leading to Salmonella replication, peaking in the monsoon due to transmission of Salmonella via unhygienic food and water and then declining at the end of the season with a low incidence in the winter months[28].

It is difficult to ascertain a seasonal trend for Leptospirosis in our study as there were only 5 cases of Leptospirosis in our study. Leptospirosis has usually been reported in the Southern and Western states which receive torrential rainfall associated with a predominant agrarian life[29]. Leptospirosis has previously been considered as Non- endemic in North India. However, over the last 2 decades it has slowly gained prominence. This has usually been seen in the months from July to October which sees a good amount of rain during monsoon clubbed with a farming background in the Gangetic belt. In a 5 year study in North India, Leptospirosis was reported from the states of Punjab, Haryana, Himachal Pradesh and Uttar Pradesh[30].

The predominant age group affected by AUF in our study was the younger population rather than the elderly. The mean age in all the febrile illnesses in our study including Scrub Typhus, Dengue fever and malaria was less than 40 years with an overall mean age of 33.16±15.88 years. This is similar to a study conducted in 200 patients of AUF in Thailand where the mean age was 41 years.[3] Males were more affected than the females. Similar results were seen in a multi centre trial in India where the mean age was 34 years with a range of 5-105 years with a predominant male population (57%)[31]. A possible explanation for a higher male involvement could be related to more outdoor activities and, thus, a higher risk of mosquito bites amongst the males.

Reflecting a shift from the previous studies, our study depicted a higher number of Urban population affected by Acute Febrile Illness than the Rural areas. This might be due to increased urbanization of rural areas. The main limitation of our study was that it was a limited period study and therefore, may not translate into longer duration trends. A recent paper discusses the seasonal prevalence, epidemiology and management of six seasonal acute febrile illnesses with high prevalence and burdens in India[32]. A thorough enquiry into the seasonal and epidemiologically relevant contextual history and meticulous general examination can guide the Clinician to identify the etiological diagnosis and initiate management[33].

Conclusion

Fever remains a crucial cause for which patients are hospitalized in India. Determining the etiologies would help and guide Physicians on formulating the most appropriate treatment especially in places where infrastructure and access to facilities is difficult. Establishing diagnostic test for all the possible disease is impractical. Our study found sCrub Typhus, Dengue Fever and Malaria to be the most common causes of acute fever. The demographics of these acute febrile illnesses are widening and it is no longer restricted only to the Rural areas. Appropriate facilities may not be readily available at all centres and in those scenarios suspected cases of various acute febrile illnesses should not be denied targeted Antimicrobial Therapy. Thankfully, the outcome is expected to improve since the medical fraternity is becoming more aware about these diseases and its associated complication profile.

References

1 Chrispal A, Boorugu H, Gopinath KG, Chandy S, Prakash JA, Thomas EM, *et al* — Acute undifferentiated febrile illness in adult hospitalized patients: the disease spectrum and diagnostic predictors - an experience from a tertiary care hospital in South India. *Trop Doct* 2010; **40:** 230-4. doi: 10.1258/td.2010.100132.

2 Salagre KD, Sahay RN, Pazare AR, Dubey A, Marathe KK — A study of clinical profile of patients presenting with complications of acute febrile illnesses during monsoon. *J*

Assoc Physicians India 2017; **65:** 37-42.

3 Wangrangsimakul T, Althaus T, Mukaka M, Kantipong P, Wuthiekanun V, Chierakul W, *et al* — Causes of acute undifferentiated fever and the utility of biomarkers in Chiangrai, northern Thailand. *PLoSNegl Trop Dis* 2018; **12**: e0006477. doi: 10.1371/journal.pntd.0006477.

4 Abhilash KP, Jeevan JA, Mitra S, Paul N, Murugan TP, Rangaraj A, *et al* — Acute undifferentiated febrile illness in patients presenting to a tertiary care hospital in South India: clinical spectrum and outcome. *J Global Infect Dis* 2016; 147-54. doi: 10.4103/0974-777X.192966.

5 Murray CJ, Ortblad KF, Guinovart C, Lim SS, Wolock TM, Roberts DA, *et al* — Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384:** 1005-70. doi: 10.1016/S0140-6736(14)60844-8.

6 Kashinkunti M, Gundikeri S, Dhananjaya M. Acute undifferentiated febrile illness- clinical spectrum and outcome from a tertiary care teaching hospital of north Karnataka. *Int J Biol Med Res* 2013; **4:** 3399-402.

7 Murdoch DR, Woods CW, Zimmerman MD, Dull PM, Belbase RH, Keenan AJ, *et al* — The etiology of febrile illness in adults presenting to Patan Hospital in Kathmandu, Nepal. *Am J Trop Med Hyg* 2004; **70:** 670-5.

8 McGready R, Ashley EA, Wuthiekanun V, Tan SO, Pimanpanarak M, Viladpai-Nguen SJ, *et al* — Arthropod borne disease: The leading cause of fever in pregnancy on the Thai-Burmese border. *PLoS Negl Trop Dis* 2010; **4:** e888.doi: 10.1371/journal.pntd.0000888.

9 Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S — Etiologies of acute undifferentiated febrile illness in Thailand. *J Med Assoc Thai* 2004; **87:** 464-72.

10 Blacksell SD, Sharma NP, Phumratanaprapin W, Jenjaroen K, Peacock SJ, White NJ, *et al* — Serological and blood culture investigations of Nepalese fever patients. *Trans R Soc Trop Med Hyg* 2007; **101:** 686-90. doi: 10.1016/j.trstmh.2007.02.015.

11 Ellis RD, Fukuda MM, McDaniel P, Welch K, Nisalak A, Murray CK, *et al* — Causes of fever in adults on the Thai-Myanmar border. *Am J Trop Med Hyg* 2006; **74:** 108-13.

12 Tran HP, Adams J, Jeffery JA, Nguyen YT, Vu NS, Kutcher SC, *et al* — Householder perspectives and preferences on water storage and use, with reference to dengue, in the Mekong Delta, southern Vietnam. *Int Health* 2010; **2:** 136-42. doi: 10.1016/j.inhe.2009.12.007.

13 Mittal G, Ahmad S, Agarwal RK, Dhar M, Mittal M, Sharma S — Aetiologies of Acute Undifferentiated Febrile Illness in Adult Patients- an Experience from a Tertiary Care Hospital in Northern India. *J Clin Diagn Res* 2015; **9:** DC22-4. doi:10.7860/JCDR/2015/11168.6990.

14 Gurung S, Pradhan J, Bhutia PY — Outbreak of scrub typhus in the North East Himalayan region-Sikkim: an emerging threat. *Indian J Med Microbiol* 2013; **31:** 72-4. doi: 10.4103/0255-0857.108729.

15 Chrispal A, Boorugu H, Gopinath KG, Prakash JA, Chandy S, Abraham OC, et al — Scrub typhus: An unrecognized threat in South India- Clinical profile and predictors of mortality. *Trop Doct* 2010; **40:** 129-33. doi: 10.1258/td.2010.090452.

16 Chakraborty S, Sarma N — Scrub Typhus: An Emerging Threat. *Indian J Dermatol* 2017; **62:** 478-85. doi: 10.4103/ijd.IJD_388_17.

17 Sarkar S, Gangare V, Singh P, Dhiman RC — Shift in Potential Malaria Transmission Areas in India, Using the Fuzzy-Based Climate Suitability Malaria Transmission (FCSMT) Model under Changing Climatic Conditions. *Int J Environ Res Public Health* 2019; **16:** 3474. doi: 10.3390/ijerph16183474.

18 Sharma N, Biswal M, Kumar A, Zaman K, Jain S, Bhalla A — Scrub Typhus in a Tertiary Care Hospital in North India. *Am J Trop Med Hyg* 2016; **95:** 447-51. doi: 10.4269/ajtmh.16-0086.

19 Kweon SS, Choi JS, Lim HS, Kim JR, Kim KY, Ryu SY, *et al* — A community-based case-control study of behavioral factors associated with scrub typhus during the autumn epidemic season in South Korea. *Am J Trop Med Hyg* 2009; **80:** 442-6.

20 Narvencar KP, Rodrigues S, Nevrekar RP, Dias L, Dias A, Vaz M, *et al* — Scrub typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa. *Indian J Med Res* 2012; **136:** 1020-4.

21 Sharma PK, Ramakrishnan R, Hutin YJ, Barui AK, Manickam P, Kakkar M, *et al* — Scrub typhus in Darjeeling, India: opportunities for simple, practical prevention measures. *Trans R Soc Trop Med Hyg* 2009; **103:** 1153-8. doi: 10.1016/j.trstmh.2009.02.006.

22 Mathai E, Rolain JM, Verghese GM, Abraham OC, Mathai D, Mathai M, *et al* — Outbreak of scrub typhus in Southern India during the cooler months. *Ann N Y Acad Sci* 2003; **990:** 359-64. doi: 10.1111/j.1749-6632.2003.tb07391.x

23 Sathish J V, Naik TB, Krishna PVM, Biradar A — Dengue Infection - prevalence and seasonal variation among patients attending a tertiary care hospital at Chamarajanagar, Karnataka. *Indian J Microbiol Res* 2018; **5:** 275-9. doi: 10.18231/2394-5478.2018.0057

24 Chakravarti A, Arora R, Luxemburger C — Fifty years of dengue in India. *Trans R Soc Trop Med Hyg* 2012; **106:** 273-82. doi: 10.1016/j.trstmh.2011.12.007.

25 Kakarla SG, Caminade C, Mutheneni SR, Morse AP, Upadhyayula SM, Kadiri MR, Kumaraswamy S — Lag effect of climatic variables on dengue burden in India. *Epidemiol Infect* 2019; **147:** e170. doi: 10.1017/S0950268819000608.

26 Srimath-Tirumula-Peddinti RCPK, Neelapu NRR, Sidagam N — Association of Climatic Variability, Vector Population and Malarial Disease in District of Visakhapatnam, India: A Modeling and Prediction Analysis. *Plos One* 2015; **10:** e0128377.https://doi.org/10.1371/journal.pone.0128377

27 Barde PV, Chouksey VK, Shivlata L, Sahare LK, Thakur AK — Viral hepatitis among acute hepatitis patients attending tertiary care hospital in central India. *Virus disease* 2019; **30:** 367-372. doi: 10.1007/s13337-019-00541-6.

28 Iyer V, Sharma A, Nair D, Solanki B, Umrigar P, Murtugudde R, *et al* — Role of extreme weather events and El Niño Southern Oscillation on incidence of Enteric Fever in Ahmedabad and Surat, Gujarat, India. *Environ Res* 2021; **196:** 110417. doi: 10.1016/j.envres.2020.110417.

29 Sambasiva RR, Naveen G, Bhalla P, Agarwal SK — Leptospirosis in India and the Rest of the World. *Braz J Infect Dis* 2003; **7:** 178-93. https://doi.org/10.1590/S1413-86702003000300003

30 Sethi S, Sharma N, Kakkar N, Taneja J, Chatterjee SS, Banga SS, Sharma M — Increasing trends of leptospirosis in northern India: a clinico-epidemiological study. *PLoSNegl Trop Dis* 2010; **4:** e579. doi: 10.1371/journal.pntd.0000579.

31 March K, Manoharan A, Chandy S, Chacko N, Alvarez-Uria G, Patil S, *et al* — Acute undifferentiated fever in India: a multicentre study of aetiology and diagnostic accuracy. *BMC Infect Dis* 2017; **17:** 665. doi: 10.1186/s12879-017-2764-3.

32 Aggarwal KK, Pareek KK, Nadkar M, Tiwaskar M, Vora A — Clinical recommendations on the management of seasonal and acute febrile infections. *Journal of the Indian Medical Association* 2020; **118(3):** 13-9.

33 Chandra A, Chakraborty U — Fever: A Case Based Approach for the Clinicians. *Journal of the Indian Medical Association* 2021; **119(1):** 70-5.