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Health problems in travellers to Nepal visiting CIWEC clinic in Kathmandu — A GeoSentinel analysis

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Abstract

Background: Nepal has always been a popular international travel destination. There is limited published data, however, on the spectrum of illnesses acquired by travellers to Nepal.

Methods: GeoSentinel is a global data collection network of travel and tropical medicine providers that monitors travel-related morbidity. Records for ill travellers with at least one confirmed or probable diagnosis, were extracted from the GeoSentinel database for the CIWEC Clinic Kathmandu site from January 1, 2009 to December 31, 2017.

Results: A total of 24,271 records were included. The median age was 30 years (range: 0–91); 54% were female. The top 3 system-based diagnoses in travellers were: gastrointestinal (32%), pulmonary (16%), and dermatologic (9%). Altitude illness comprised 9% of all diagnoses. There were 278 vaccine-preventable diseases, most frequently influenza A (41%) and typhoid fever (19%; *S. typhi* 52 and *S. paratyphi* 62). Of 64 vector-borne illnesses, dengue was the most frequent (64%), followed by imported malaria (14%). There was a single traveller with Japanese encephalitis. Six deaths were reported.

Conclusions: Travellers to Nepal face a wide spectrum of illnesses, particularly diarrhoea, respiratory disease, and altitude illness. Pre-travel consultations for travellers to Nepal should

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CDC disclaimer

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CRedit authorship contribution statement

Prativa Pandey: Conceptualization, Methodology, Writing – original draft, preparation, Writing – review & editing, Supervision. **Keun Lee:** Methodology, Data curation, Software, Formal analysis, Writing – original draft, preparation, Writing – review & editing. **Bhawana Amatya:** Writing – original draft, Writing – review & editing, Formal analysis, Visualization. **Kristina M. Angelo:** Conceptualization, Methodology, Writing – original draft, preparation, Writing – review & editing. **David R. Shlim:** Writing – original draft, preparation, Writing – review & editing. **Holly Murphy:** Conceptualization, Writing – original draft, preparation, Writing – review & editing.

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focus on prevention and treatment of diarrhoea and altitude illness, along with appropriate immunizations and travel advice.

Keywords

Altitude sickness; Environmental exposure; Nepal; Sentinel surveillance; Travel

1. Introduction

Nepal is a popular destination for adventure travellers, cultural tourists, wildlife enthusiasts, and pilgrims. An average of 719,117 tourists visited Nepal annually from 2009 to 2017, with a mean duration of stay of 12.6 days [1]. Since 2018, Nepal has hosted over 1 million tourists annually, with an increasing number of travellers coming from within Asia [1,2]. A slight decline in tourism occurred during the earthquake of April 2015; however, tourism rebounded in 2016 [1].

There are 2 seasonal peaks in tourism when the weather is favourable, occurring in the spring (March–April) and the fall (October–November). Previous studies have shown that the risk of enterically-transmitted diseases is increased in the spring relative to all other seasons [3]. Although numerous papers describe individual risks to travellers to Nepal, including altitude illness, diarrhoea, cyclosporiasis, enteric fever, rabies, and hepatitis, a comprehensive analysis of diseases reported among travellers in Nepal has not been published.

The CIWEC Clinic in Kathmandu was founded in 1982 with a mission to provide medical care to expatriates working for the Canadian International Water and Energy Consultants (CIWEC) project in Nepal. The clinic became the first destination travel medicine clinic in the world, and evolved into a hospital [4] providing care to expatriates and travellers to Nepal as well as to the local Nepali population [5]. CIWEC joined the GeoSentinel surveillance network in 1998 [6,7].

The aim of this analysis was to provide a comprehensive summary of diseases acquired by international travellers in Nepal over a 9-year period. Using data from CIWEC, the largest infectious diseases centre catering to travellers in Kathmandu, the findings of this analysis can be used to strengthen pre-travel counselling and recommendations for travellers to Nepal.

2. Methods

2.1. Data source

GeoSentinel is a global, clinician-based sentinel surveillance system that monitors travel-related illnesses among international travellers and migrants. It consists of 68 specialized travel and tropical medicine clinics located in 28 countries. It was established in 1995 as a collaboration between the International Society of Travel Medicine and the Centers for Disease Control and Prevention (CDC) [6,7]. CIWEC joined the GeoSentinel network as the Kathmandu site in 1998 and has been contributing ill traveller records continuously. Information collected includes traveller demographics, trip details, country of exposure,

clinical information, and diagnoses. GeoSentinel's data collection protocol has been reviewed by a human subjects advisor at CDC's National Center for Emerging and Zoonotic Infectious Diseases and is classified as public health surveillance and not human subjects research.

2.2. Inclusion and exclusion criteria

Records of non-migrant travellers (including expatriates), seen during travel, had at least one confirmed or probable diagnosis, entered into the GeoSentinel database from the Kathmandu site (CIWEC) from January 1, 2009 to December 31, 2017 were included. Records of migrant travellers were excluded.

Diagnosis codes were classified by physical exam systems (cardiovascular, dermatologic, head/eyes/ears/nose/throat (HEENT), gastro-intestinal (GI), genitourinary (GU), lymphatic, musculoskeletal, neurologic, pulmonary, and psychiatric). Two additional classifications were developed for systemic febrile syndromes and "other" illnesses that did not correlate to a system. If applicable, diagnoses were further classified as environmental hazards (e.g., altitude-related illness), animal exposures, vector-borne (VBDs), or vaccine-preventable diseases (VPDs).

2.3. Data analysis

Data were managed using Microsoft Access (Redmond, Washington, USA). All analyses were descriptive and performed using SAS Version 9.4 (Cary, NC, USA).

3. Results

There were 24,271 records included (annual mean: 2,662 travellers) with 29,281 diagnoses. The median age was 30 years (range: 0–91); 54% were female. Travellers were most frequently tourists (63%), business travellers (20%), and missionaries, volunteers, or humanitarian aid workers (14%). The median trip duration was 16 days. Eight percent were hospitalized; there were 6 deaths. Travellers were most frequently born in the United States (18%), the United Kingdom (11%), Australia (8%), and Germany (6%). The most common systems-based diagnosis groups included: GI, pulmonary, dermatologic, HEENT, neurologic, musculoskeletal, GU, and febrile syndromes.

Diagnoses among travellers to Nepal seen at CIWEC are in Table 1.

3.1. Gastrointestinal (n = 9,501; 32%)

Approximately one-third of illnesses among travellers to Nepal were related to the GI system. Acute diarrhoea was the most frequently reported diagnosis (72%), followed by acute gastroenteritis (7%). Two cases of cholera were reported; one was imported from Bangladesh in a Bangladeshi traveller and the second was in a volunteer who worked in post-earthquake rural Nepal. The predominant parasitic pathogen was *Giardia* (5%); *Cyclospora*, *Entamoeba histolytica*, and *Cryptosporidium* were reported less frequently. There were 5 liver abscesses; 1 case was caused by *E. histolytica*. Gut nematodes were rare (5 reports of ascariasis and 3 reports of enterobiasis). Acute hepatitis A and E were seen

in 8 and 10 travellers, respectively. *Salmonella enterica* serotypes Typhi and Paratyphi were found in 52 (1%) and 62 (1%) travellers, respectively [antimicrobial susceptibility data for *Salmonella* Typhi is described below].

3.1.1. Paediatric travellers—There were 2,340 ill travellers under 18 years of age; 0–5 years: 45%, 6–11 years: 26%, and 12–17 years: 29%. G.I. diagnoses comprised 35% of all diagnoses and 63% of these were acute diarrhoea. *Salmonella* paratyphi was diagnosed in 10 children. Among the parasitic pathogens, cyclosporiasis (n = 16), giardiasis (n = 15), and dientamoebiasis (*D. Fragilis*) (n = 4) were noted. Five children were diagnosed with acute appendicitis.

3.1.2 Cyclospora—There were 191 cases of Cyclospora included. Between 9 and 38 cases were reported annually, always presenting between May and August (Fig. 1). Sixty percent of travellers with *Cyclospora* were female. Half (53%) were residents of Nepal (expatriates) and 31% percent were among long term travellers (travel for >1 year). The most common reason for travel was business (47%). Among 99 travellers with data available, 55 (55%) had a pretravel consultation with a healthcare provider. Nearly all (99%) were managed as outpatients.

3.2. Respiratory (n = 4,711; 16%)

Most diagnoses in this category were upper respiratory infections (42%) and acute bronchitis (25%). High altitude pulmonary oedema (19%), lobar pneumonia (6%), and asthma or bronchospasm (5%) were less frequently reported. There were 19 cases of pulmonary embolism and a single case of pulmonary tuberculosis.

3.3. Dermatological (n = 2,671; 9%)

Skin and soft tissue infections (cellulitis, abscess, infected wound) accounted for 38% of illnesses in this category. Rates for methicillin-resistant *Staphylococcus aureus* (MRSA) during the time period of the study were 50% as determined by resistance to oxacillin with disk diffusion assay. Laceration (11%), frostbite (9%), dermatitis (7%), urticaria or angioedema (7%), and superficial fungal infection (6%) were less frequently reported. There were only 2 cases of hookworm-related cutaneous larva migrans.

3.4. HEENT (n = 2,456; 8%)

Top 5 diagnoses in this category were pharyngitis, sinusitis, otitis media, conjunctivitis, and tonsillitis. Streptococcal pharyngitis due to group A streptococcus (by rapid test or by culture) accounted for 18% of all pharyngitis diagnoses (5% of total HEENT diagnoses). Head injury was noted in 80 travellers (3%) and epistaxis in 28 (1%). The other conditions in this category were: otitis externa (6%), headache (5%), allergic rhinitis (3%), stye/hordeolum/blepharitis (1%), barotrauma or other eustachian tube dysfunction (1%), dental problem (abscess, caries, other) (1%), poor vision/visual loss (1%), and others.

3.5. Other syndromes

Neurologic diagnoses were predominantly high altitude cerebral oedema (HACE) discussed below. Most musculoskeletal diagnoses were trauma-related: 32% sprain or strain, 22%

fracture, and 4% tendinitis. GU diagnoses were mostly urinary tract infections (UTI) (507; 50%). Febrile illness was predominantly viral or undiagnosed (46% and 15%, respectively) with influenza A (16%) as the most commonly diagnosed aetiology of fever.

Other physical exam classifications and the diagnoses associated with them are in Table 1.

An additional classification of diagnoses, including environmental hazards, animal exposures, vector-borne diseases, and vaccine-preventable diseases among travellers to Nepal seen at CIWEC are in Table 2.

3.6. Altitude-related illness

Among 2,564 travellers seen with an altitude-related diagnosis, the median age was 47 years (range: 1–84); 60% were male. Almost all (99%) travelled to Nepal for tourism; 57% had a pretravel consultation with a healthcare provider. Half the travellers (50%) had acute mountain sickness (AMS) and the remaining 50% had severe high altitude illness: 25% high altitude pulmonary oedema (HAPE), 16% high altitude cerebral oedema (HACE), and 9% due to combination of both HACE and HAPE. Eighty-one percent of travellers were seen as outpatients. The top 5 nationalities among travellers who acquired an altitude-related illness were the United Kingdom (12%), Australia (11%), USA (10%), Japan (7%), and India (5%). Most exposures were in Nepal (96%), but 4% were in Tibet near the border mountains. Among 1920 travellers with exposure data available, altitude illness exposure in Nepal occurred in the Everest region (71%), the Annapurna region (11%), Langtang (3%), Mera peak region (3%), and Manaslu (2%) (Fig. 2).

3.7. Animal exposures

Four hundred forty-six travellers presented to CIWEC for rabies post-exposure prophylaxis. The median age was 22 years (range: 0–75) and the median travel duration was 15 days (range: 0–4035). Three hundred-five travellers presented after a dog bite and 8 after a non-bite exposure; there were also 99 monkey bites (all were offered herpes B prophylaxis with acyclovir 800 mg tablets 5 times a day for 14 days) [8] and 37 with non-bite exposures, 16 cat bites, and 8 bites by other animals (4 rat bites, 1 squirrel bite, and 3 other). Among travellers with dog exposures, 55% were female and all travellers were treated as outpatients. Seventy-two percent travelled for tourism, 16% for business, 8% were volunteers or aid workers, and 2% were visiting friends or relatives (VFRs). Ninety-three percent of dog exposures occurred in Nepal, 2% in India, 2% in Thailand, 1% in Bhutan; 97% of exposures were in South Central Asia. Among travellers with monkey bite and non-bite exposures, 61% were female and 93% travelled for tourism. Ninety-four percent were exposed in Nepal and 5% in India. Among the 16 travellers with a cat bite, 10 were male and 11 travelled for tourism, 3 were business travellers, and 2 were volunteers or aid workers.

3.8. Vector-borne diseases (VBD)

Of 64 travellers with vector-borne illnesses, there were 41 cases of dengue fever (7 [17%] were locally-acquired) and 9 cases of malaria (3 *Plasmodium vivax*: 2 from India and 1 possibly from Nepal; 5 *P. falciparum*: 1 each from Mali, Kenya, Tanzania, Sudan, and 1 from

Sub-Saharan Africa (country not ascertainable); 1 *P. malariae* from India). There were also 4 cases of chikungunya (all imported), 4 cases of *Rickettsia* (unknown species), 2 cases of murine typhus, 1 case of tick-borne typhus, 1 case of Japanese encephalitis (JE), and 1 each of early and late Lyme disease, early one probably imported in Nepal and late one imported from the UK.

3.9. Vaccine-preventable diseases (VPD)

Of 278 VPD's, influenza A was the most frequently reported diagnosis (41%), followed by typhoid fever (19%) (Table 2). Less frequently reported diagnoses included influenza B (14%), herpes zoster (10%), varicella (6%), and measles, mumps, and hepatitis A at 3% each. There were 52 travellers diagnosed with *Salmonella* Typhi and 62 with *Salmonella* Paratyphi. Among these, 54% with *Salmonella* Typhi and 53% with *Salmonella* Paratyphi received any typhoid vaccine (vaccine type unknown). Not all typhoid cases were vaccine preventable as some infections were caused by *Salmonella* paratyphi and the vaccine is not 100% effective against *Salmonella* typhi. Antibiotic susceptibility data were available for 45 isolates (40%) of typhoid fever cases. Susceptibility to azithromycin, ceftriaxone, co-trimoxazole was 60%, 87%, and 85%, respectively. Ciprofloxacin and levofloxacin sensitivity were 89% and 71%, respectively, however, all the isolates were resistant to Nalidixic acid (Fig. 3). No isolates were pan-resistant.

3.10. Deaths

There were 6 deaths among travellers during the study period. All were males with a median age of 63 years (range: 28–71). Deaths were due to out-of-hospital cardiac arrest (n = 3), multi-drug resistant *Klebsiella* pneumonia (n = 1), febrile illness and sepsis (n = 1), and sudden death with unknown aetiology (n = 1). No autopsies were conducted.

4. Discussion

This analysis provides a description of over 24,000 ill travellers who presented to CIWEC in Kathmandu over 9 years. CIWEC has the highest volume of travellers in both the GeoSentinel Network and in Nepal, making it ideal to describe the spectrum of travel-related illnesses. The strengths of this report are in the large number and longitudinal perspective as well as patient care by practitioners experienced in travel medicine which validates the diagnoses. Given increasing travel to Nepal in recent years, knowing the frequency of travel-related illness among travellers to Nepal is necessary to optimally prepare international travellers before arrival.

Gastrointestinal illnesses, including acute diarrhoea, were the most frequently reported diagnoses for which travellers sought healthcare at CIWEC while visiting Nepal. The aetiology of diarrhoea in travellers and expatriates has been studied systematically at CIWEC in various publications [3, 9–11]. Acute diarrhoea accounts for a significant proportion of illnesses faced by travellers to many developing countries and regions of the world [12–15]. Bacterial aetiologies of acute diarrhoea predominate in Nepal, though recent comprehensive molecular analyses demonstrated that the top 3 pathogens are *Campylobacter*, *Norovirus*, and *Shigella* [3, 9–11]. Near-total bacterial resistance to

fluoroquinolones has been documented for nearly a decade in Nepal and azithromycin has become the drug of choice for moderate to severe bacterial diarrhoea [10, 11]. Our study was unable to determine how many travellers self-diagnose and treat travellers' diarrhoea, or whether travellers have failed self-treatment.

Parasitic pathogens are typically less frequent among travellers in Nepal with diarrhoea, however, this analysis demonstrates large numbers of parasitic pathogens, such as giardiasis and cyclosporiasis. Cyclosporiasis infections have remained steady in recent years in Nepal; the coccidian parasite that causes cyclosporiasis is only present in Nepal from May to September, a time of decreased tourism [16], which may explain why approximately one-third of cyclosporiasis infections in this analysis were diagnosed among long-term travellers or expatriates.

Nepal remains one of the highest risk destinations for enteric fever globally, complicated by increasing drug-resistance [17]. Typhoid vaccine is recommended for international travellers visiting Nepal but is not required [18]. A study in Nepal suggested that the typhoid vaccine may have been more protective in travellers than in local people [19]. The authors postulated that travellers taking food and water precautions may experience lower exposure to *S. Typhi*, allowing the vaccine to be more effective. However, typhoid vaccine efficacy studies performed in local populations demonstrate between 48 and 80% protection depending on the population studied, so best practices for prevention of typhoid fever among travellers to Nepal include vaccination in addition to safe food and water precautions [20,21]. A conjugate typhoid vaccine is now available that was found to be 81.6% effective when studied in Nepali children [22] and should be recommended to the paediatric and VFR traveller visiting South Asia including Nepal. Nalidixic acid (NA) resistance is a good marker for fluoroquinolone (FQ) resistance and there is increasing NA resistance in enteric fever cases in Nepal [23,24], hence the use of FQs for treatment of enteric fever in travellers to Nepal ought to be discouraged.

Altitude illness is a preventable condition, but cases continue to occur including deaths due to severe altitude illness [25,26]. Among cases of altitude illness seen at CIWEC during the study period, half were severe (HAPE or HACE). Everest area trekkers and climbers are known to suffer the most from altitude-related conditions, needing helicopter evacuations [27]. Despite resources available to trekkers [28], basic knowledge about altitude illness symptoms, prevention, and treatment remains low and less than 50% of Himalayan trekkers are adequately prepared for prevention prior to their journey [29]. Notably, altitude illnesses were the 2nd (HAPE) and 3rd (AMS) most common aetiology of illness among travellers >70 years of age. This suggests that the elderly may also be prone to altitude-related illness [30] and special consideration should be given to them in pretravel counselling to ensure they are aware of prevention measures, including chemoprophylaxis and gradual ascent.

Frostbite occurs regularly in Nepal when mountain climbers and trekkers get trapped in bad weather conditions. Frostbite occurred exclusively in tourist travellers, as was seen in a previous CIWEC study [31]. The prostacyclin analogue Iloprost has been used in Nepal in Himalayan climbers with severe frostbite with promising results [32]. Tourists who travel to Nepal from warmer climates need pretravel education on frostbite prevention,

including wearing appropriate clothing and footwear, staying hydrated, and limiting their time outdoors in cold weather.

Many travellers in this analysis presented to CIWEC after an animal bite or exposure and required receipt of rabies post-exposure prophylaxis (PEP). Rabies vaccine for PEP is available in Nepal; human rabies immune globulin (RIG) is available in specialty clinics in Kathmandu but it is not widely available throughout the country. This may pose an issue for travellers outside of Kathmandu that have animal exposure if they are unable to travel to a specialty clinic. Since rabies can be found in various mammals in Nepal, travellers involved in outdoor activities, people working with or around animals, and people who are long-term travellers should be offered rabies pre-exposure prophylaxis [18] which negates the need for RIG and simplifies the post-exposure vaccine regimen [33]. Monkeys have also been found to have rabies in the Indian subcontinent and South East Asia [34,35]. It is advisable to provide PEP against rabies after monkey bites [35,36]. With intradermal rabies vaccine becoming more widespread in use and increasing acceptability of the new WHO recommendation [37] of a 2-dose series for rabies pre-exposure (PrEP), the cost of rabies PrEP (seen as a barrier in parts of the world, including the United States) may be more acceptable to travellers.

Recent reports of vector-borne spread and increased vector-borne disease, especially dengue, have been reported among the local population in the face of global warming and increased population mobility [38–40], but few cases of vector-borne diseases were reported in this analysis, especially those that were locally acquired. Almost all malaria cases and most dengue cases were imported, suggesting that these diseases may not be frequently acquired by travellers to Nepal. Travellers typically visit Kathmandu and are less likely to visit the areas of the country, especially the low-lying Terai, that are endemic for JE and dengue. However, with the spread of mosquitoes to higher elevation, this is likely to change, as is evidenced by reports in 2019 of a dengue outbreak in the Kathmandu Valley [41].

Locally-acquired rickettsial infections, especially *R. typhi*, which are a cause of febrile illness among the local population including Kathmandu [42], were rarely reported. Despite 120 reported tick bites, tick-borne rickettsiosis diagnoses were low; just one case of *Rickettsia honei* infection (exposure in Kathmandu) was reported during this period [43]. Scrub typhus and murine typhus have been reported during the evaluation of febrile Nepali patients in a hospital-based setting [44, 45], and scrub typhus in serum samples obtained from febrile patients in a laboratory setting [46]. Travellers to Nepal should maintain awareness of the prevalence of rickettsial diseases in Nepal, especially if planning to work or live among the local population.

This analysis includes the first reported case of JE in a long-term traveller to Nepal [47]. Vero cell vaccine (JE-VC), recombinant chimeric virus vaccine (CV-JE) and live vaccine of SA 14–14-2 (Chengdu) strain (JE-LV) are available in Nepal to international travellers for prevention of JE [48]. This case highlights the importance of JE awareness and vaccination among travellers to Nepal, particularly for those traveling long-term.

It is likely that some travellers diagnosed with undifferentiated febrile syndromes reported in this analysis may have been ill with a vector-borne disease, such as murine typhus [49]; molecular studies are underway to improve fever diagnostics at CIWEC and are expected to help define the frequency of vector-borne disease among travellers with fever in Nepal.

Despite the representativeness of CIWEC's data for travellers to Nepal, this analysis has limitations. These data are not population-based, so rates and risks cannot be determined. Vaccination history is not routinely collected and classification of a diagnosis as confirmed or probable is reliant on case definitions and clinical expertise.

5. Conclusion

Travellers to Nepal may acquire a variety of infectious and non-infectious diseases and conditions during travel in Nepal. Pretravel preparation for travellers to Nepal should include a pretravel consultation with a healthcare provider who can administer appropriate recommended vaccinations and provide education about the unique risks based upon their itinerary. These recommendations should include education about prevention and self-treatment of traveller's diarrhoea; advice about altitude illness including recognition, prevention, and treatment; instructions on how to avoid animal exposures, emphasizing the need for PrEP and PEP; and protection from insect and arthropod bites including available vaccinations.

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Abbreviations:

CIWEC	Canadian International Water and Energy Consultants
CDC	Centers for Disease Control and Prevention
MRSA	methicillin resistant <i>Staphylococcus aureus</i>
HEENT	head/eyes/ears/nose/throat
GI	gastrointestinal
GU	genitourinary
VBD	vector-borne diseases
VPD	vaccine-preventable diseases
SAS	Statistical Analysis Software

HACE	High Altitude Cerebral Oedema
UTI	Urinary Tract Infection
AMS	Acute Mountain Sickness
HAPE	High Altitude Pulmonary Oedema
FQ	fluoroquinolone
VFR	visiting friends or relatives
JE	Japanese Encephalitis
PEP	post-exposure prophylaxis
RIG	rabies immune globulin
PrEP	pre-exposure prophylaxis

References

- [1]. Ministry of Culture, Tourism and Civil Aviation. Nepal tourism statistics 2017. Singha Durbar, Kathmandu: Government of Nepal; 2018.
- [2]. Ministry of Culture, Tourism and Civil Aviation. Nepal tourism statistics 2018. Kathmandu, Nepal: Government of Nepal; 2019.
- [3]. Taylor DN, Houston R, Shlim DR, Bhaibulaya M, Ungar BL, Echeverria P. Etiology of diarrhea among travelers and foreign residents in Nepal. *J Am Med Assoc* 1988; 260(9):1245–8.
- [4]. CIWEC Hospital Travel Medicine Center, Kathmandu, Nepal. Available from: <http://www.ciwec-clinic.com>.
- [5]. CIWEC Hospital Travel Medicine Center. About Us [Internet]. [cited 2019 November 12]. Available from: <http://ciwec-clinic.com/about-us/>.
- [6]. Freedman DO, Kozarsky PE, Weld LH, Cetron MS. GeoSentinel: the global emerging infections sentinel network of the International Society of Travel Medicine. *J Trav Med* 1999;6(2):94–8. 10.1111/j.1708-8305.1999.tb00839.x.
- [7]. Wilder-Smith A, Boggild AK. Sentinel surveillance in travel medicine: 20 Years of GeoSentinel publications (1999–2018). *J Trav Med* 2018;25(1). 10.1093/jtm/tay139.
- [8]. Cohen JI, Davenport DS, Stewart JA, Deitchman S, Hilliard JK, Chapman LE, et al. Recommendations for prevention of and therapy for exposure to B virus (Cercopithecine Herpesvirus 1). *Clin Infect Dis* 2002;35(10):1191–203. 10.1086/344754. [PubMed: 12410479]
- [9]. Hoge CW, Shlim DR, Echeverria P, Rajah R, Herrmann JE, Cross JH. Epidemiology of diarrhea among expatriate residents living in a highly endemic environment. *J Am Med Assoc* 1996;275(7):533–8.
- [10]. Pandey P, Bodhidatta L, Lewis M, Murphy H, Shlim DR, Cave W, et al. Travelers' diarrhea in Nepal: an update on the pathogens and antibiotic resistance. *J Trav Med* 2011;18(2):102–8. 10.1111/j.1708-8305.2010.00475.x.
- [11]. Murphy H, Bodhidatta L, Sornsakrin S, Khadka B, Pokhrel A, Shakya S, et al. Traveler's diarrhea in Nepal-changes in etiology and antimicrobial resistance. *Trav Med* 2019;26(8). 10.1093/jtm/taz054.
- [12]. Olanwijiwong J, Lawpoolsri S, Ponam T, Puengpholpool P, Sharma C, Chatapat L, et al. Incidence and spectrum of health problems among travellers to Myanmar. *J Trav Med* 2018;25(1). 10.1093/jtm/tax077.
- [13]. Wilson ME, Chen LH, Han PV, Keystone JS, Cramer JP, Segurado A, et al. Illness in travelers returned from Brazil: the GeoSentinel experience and implications for the 2014 FIFA world

- cup and the 2016 summer olympics. *Clin Infect Dis* 2014;58(10): 1347–56. 10.1093/cid/ciu122. [PubMed: 24585698]
- [14]. Freedman DO, Weld LH, Kozarsky PE, Fisk T, Robins R, von Sonnenburg F, et al. Spectrum of disease and relation to place of exposure among ill returned travelers. *N Engl J Med* 2006;354(2):119–30. 10.1056/NEJMoa051331. [PubMed: 16407507]
- [15]. Flores-Figueroa J, Okhuysen PC, von Sonnenburg F, DuPont HL, Libman MD, Keystone JS, et al. Patterns of illness in travelers visiting Mexico and Central America: the GeoSentinel experience. *Clin Infect Dis* 2011;53(6):523–31. 10.1093/cid/cir468. [PubMed: 21832261]
- [16]. Hoge CW, Shlim DR, Rajah R, Triplett J, Shear M, Rabold JG, et al. Epidemiology of diarrhoeal illness associated with coccidian-like organism among travellers and foreign residents in Nepal. *Lancet* 1993;341(8854):1175–9. 10.1016/0140-6736(93)91002-4. [PubMed: 8098077]
- [17]. Browne AJ, Kashef Hamadani BH, Kumaran EAP, Rao P, Longbottom J, Harriss E, et al. Drug-resistant enteric fever worldwide, 1990 to 2018: a systematic review and meta-analysis. *BMC Med* 2020;18(1):1. 10.1186/s12916-019-1443-1. [PubMed: 31898501]
- [18]. Centers for Disease Control and Prevention. Nepal [January 18, 2019]. Available from: <https://wwwnc.cdc.gov/travel/destinations/traveler/none/nepal>.
- [19]. Schwartz E, Shlim DR, Eaton M, Jenks N, Houston R. The effect of oral and parenteral typhoid vaccination on the rate of infection with *Salmonella typhi* and *Salmonella paratyphi A* among foreigners in Nepal. *Arch Intern Med* 1990;150(2): 349–51. [PubMed: 2105702]
- [20]. Milligan R, Paul M, Richardson M, Neuberger A. Vaccines for preventing typhoid fever. *Cochrane Database Syst Rev* 2018;5:CD001261. 10.1002/14651858.CD001261.pub4.
- [21]. Centers for Disease Control and Prevention. Updated recommendations for the use of typhoid vaccine — advisory committee on immunization practices, United States. In: *Morbidity and Mortality Weekly Report (MMWR)*. 64; 2015. p. 305–8. 11. [PubMed: 25811680]
- [22]. Shakya M, Colin-Jones R, Theiss-Nyland K, Voysey M, Pant D, Smith N, et al. Phase 3 efficacy analysis of a typhoid conjugate vaccine trial in Nepal. *N Engl J Med* 2019;381(23):2209–18. 10.1056/NEJMoa1905047. [PubMed: 31800986]
- [23]. Karki S, Shakya P, Cheng AC, Dumre SP, Leder K. Trends of etiology and drug resistance in enteric fever in the last two decades in Nepal: a systematic review and meta-analysis. *Clin Infect Dis* 2013;57(10):e167–76. 10.1093/cid/cit563. [PubMed: 23985342]
- [24]. Albayrak F, Cokca F, Erdem B, Aysev AD. Predictive value of nalidixic acid resistance for detecting salmonellae with decreased ciprofloxacin susceptibility. *Int J Antimicrob Agents* 2004;23(4):332–6. 10.1016/j.ijantimicag.2003.09.014. [PubMed: 15081080]
- [25]. Leshem E, Pandey P, Shlim DR, Hiramatsu K, Sidi Y, Schwartz E. Clinical features of patients with severe altitude illness in Nepal. *J Trav Med* 2008;15(5):315–22. 10.1111/j.1708-8305.2008.00229.x.
- [26]. Shlim DR, Houston R. Helicopter rescues and deaths among trekkers in Nepal. *J Am Med Assoc* 1989;261(7):1017–9.
- [27]. Dawadi S, Pandey P, Pradhan R. Helicopter evacuations in the Nepalese Himalayas (2016–2017). *J Trav Med* 2020;27(2). 10.1093/jtm/taz103.
- [28]. Strickland BM, Kanaan NC. Sources for altitude illness information for trekkers in the Himalayas. *Wilderness Environ Med* 2019;30(4):417–20. 10.1016/j.wem.2019.07.003. [PubMed: 31672512]
- [29]. McDevitt M, McIntosh SE, Rodway G, Peelay J, Adams DL, Kayser B. Risk determinants of acute mountain sickness in trekkers in the Nepali Himalaya: a 24- year follow-up. *Wilderness Environ Med* 2014;25(2):152–9. 10.1016/j.wem.2013.12.027. [PubMed: 24864065]
- [30]. Luks AM, Swenson ER, Bärtsch P. Acute high-altitude sickness. *Eur Respir Rev* 2017;26(143):160096. 10.1183/16000617.0096-2016.
- [31]. Boggild AK, Costiniuk C, Kain KC, Pandey P. Environmental hazards in Nepal: altitude illness, environmental exposures, injuries, and bites in travelers and expatriates. *J Trav Med* 2007;14(6):361–8. 10.1111/j.1708-8305.2007.00145.x.
- [32]. Pandey P, Vadlamudi R, Pradhan R, Pandey KR, Kumar A, Hackett P. Case report: severe frostbite in extreme altitude climbers-the Kathmandu Ilprost experience. *Wilderness Environ Med* 2018;29(3):366–74. 10.1016/j.wem.2018.03.003. [PubMed: 29887348]

- [33]. Centers for Disease Control and Prevention. Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the advisory committee on immunization practices. In: *Morbidity and Mortality Weekly Report (MMWR)*. 59; 2010. p. 1–9. RR02. [PubMed: 20075837]
- [34]. Bharti OK. Human rabies in monkey (*Macaca mulatta*) bite patients a reality in India now! *J Trav Med* 2016;23(4). 10.1093/jtm/taw028.
- [35]. Wallace RM, Peterson BW, Shlim DR. Rabies: Centers for disease Control and prevention (CDC). 2019 [cited 2020. Available from: <https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/rabies>.
- [36]. Riesland NJ, Wilde H. Expert review of evidence bases for managing monkey bites in travelers. *J Trav Med* 2015;22(4):259–62. 10.1111/jtm.12214.
- [37]. World Health O Rabies vaccines: WHO position paper, April 2018 - Recommendations. *Vaccine* 2018;36(37):5500–3. 10.1016/j.vaccine.2018.06.061. [PubMed: 30107991]
- [38]. Dash AP, Bhatia R, Sunyoto T, Mourya DT. Emerging and re-emerging arboviral diseases in Southeast Asia. *J Vector Borne Dis* 2013;50(2):77–84. [PubMed: 23995308]
- [39]. Rossati A, Bargiacchi O, Kroumova V, Garavelli PL. [Vector transmitted diseases and climate changes in Europe]. *Inf Med* 2014;22(3):179–92.
- [40]. Zell R Global climate change and the emergence/re-emergence of infectious diseases. *Int J Med Microbiol* 2004;293(Suppl 37):16–26. 10.1016/s1433-1128(04)80005-6. [PubMed: 15146981]
- [41]. Lachish T, Lustig Y, Leshem E, Katz-Likvornik S, Biber A, Nadir E, et al. High incidence of dengue in Israel travelers to Kathmandu, Nepal. *J Trav Med* 2019;27 (1). 10.1093/jtm/taz105.taz105.
- [42]. Pradhan R, Shrestha U, Gautam SC, Thorson S, Shrestha K, Yadav BK, et al. Bloodstream infection among children presenting to a general hospital outpatient clinic in urban Nepal. *PLoS One* 2012;7(10):e47531. 10.1371/journal.pone.0047531.
- [43]. Murphy H, Renvoise A, Pandey P, Parola P, Raoult D. *Rickettsia honei* infection in human, Nepal, 2009. *Emerg Infect Dis* 2011;17(10):1865–7. 10.3201/eid1710.101943. [PubMed: 22000356]
- [44]. 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(6):670–5. 10.4269/ajtmh.2004.70.670. [PubMed: 15211012]
- [45]. Blacksell SD, Sharma NP, Phumratanapapin 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(7):686–90. 10.1016/j.trstmh.2007.02.015. [PubMed: 17433390]
- [46]. Upadhyaya BP, Shakya G, Adhikari S, Rijal N, Acharya J, Maharjan L, et al. Scrub typhus: an emerging neglected tropical disease in Nepal. *J Nepal Health Res Counc* 2016;14(33):122–7. 10.33314/jnhrc.v14i2.801. [PubMed: 27885295]
- [47]. Lagarde S, Lagier JC, Charrel R, Querat G, Vanhomwegen J, Despres P, et al. Japanese encephalitis in a French traveler to Nepal. *J Neurovirol* 2014;20(1): 99–102. 10.1007/s13365-013-0226-2. [PubMed: 24408307]
- [48]. Batchelor P, Petersen K. Japanese encephalitis: a review of clinical guidelines and vaccine availability in Asia. *Trop Dis Travel Med Vaccines* 2015;1:11. 10.1186/s40794-015-0013-6. [PubMed: 28883942]
- [49]. Thompson CN, Blacksell SD, Paris DH, Arjyal A, Karkey A, Dongol S, et al. Undifferentiated febrile illness in Kathmandu, Nepal. *Am J Trop Med Hyg* 2015;92 (4):875–8. 10.4269/ajtmh.14-0709. [PubMed: 25667056]

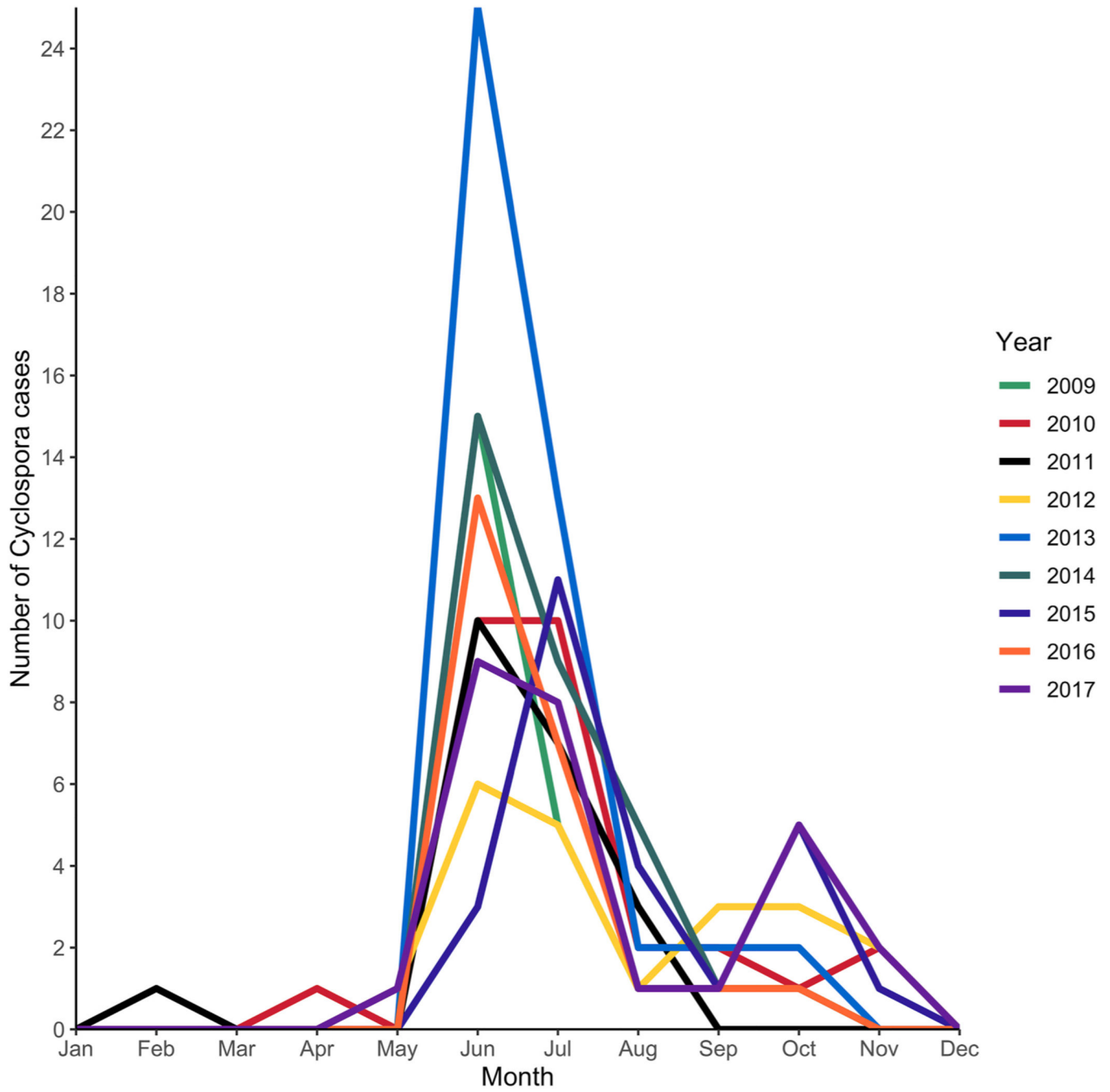


Fig. 1. Distribution of *Cyclospora* cases at CIWEC, 2009–2017 (n = 191).

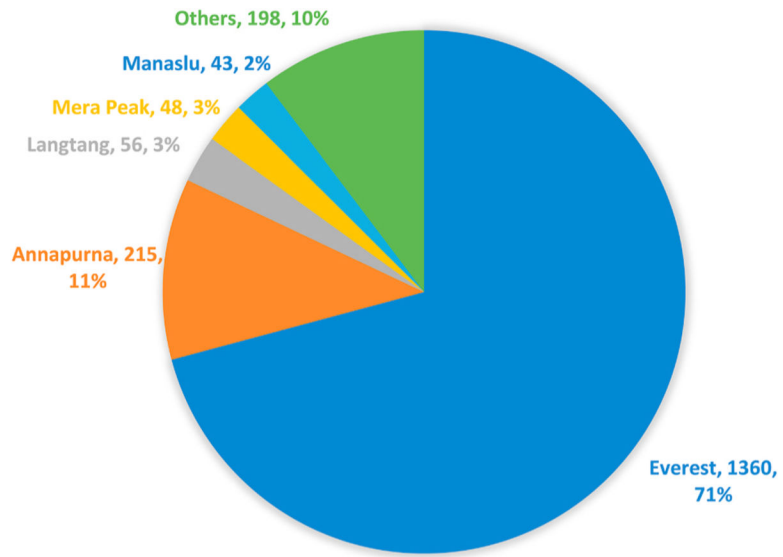


Fig. 2. Altitude illness from various trekking regions of Nepal, 2009–2017 (n = 1920).

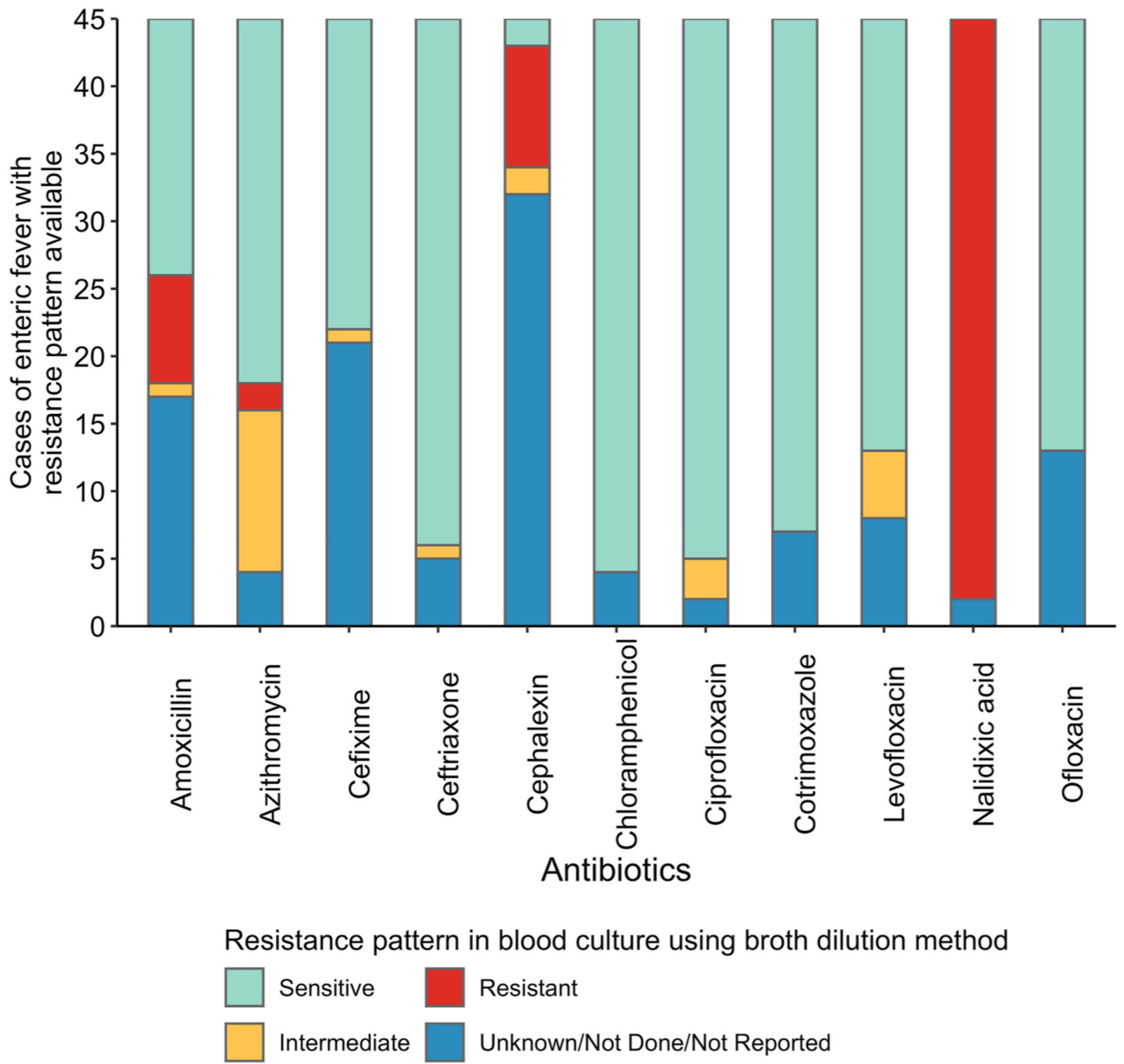


Fig. 3. Antibiotic sensitivity in typhoid fever cases at CIWEC (2009–2017) with resistance patterns available (n = 45).

Table 1

System-based top diagnoses (n = 29,281) among travellers to Nepal seen at the Kathmandu GeoSentinel Clinic (CIWEC), 2009–2017.

System and Diagnoses	n (%)
Gastrointestinal	9501 (32)
Acute diarrhoea	6795 (72)
Acute gastroenteritis	619 (7)
Giardiasis	483 (5)
Abdominal pain	244 (3)
Gastroesophageal reflux disease, esophagitis, or non-specific gastritis	195 (2)
Cyclosporiasis	191 (2)
Pulmonary	4711 (16)
Upper respiratory tract infection	1970 (42)
Acute bronchitis	1158 (25)
High altitude pulmonary oedema	881 (19)
Lobar pneumonia	296 (6)
Asthma or bronchospasm	228 (5)
Dermatologic	2671 (9)
Skin and soft tissue infections ^a	1002 (38)
Laceration	286 (11)
Frostbite	245 (9)
Rash, dermatitis (including contact dermatitis)	193 (7)
Rash, urticaria or angioedema	175 (7)
Head, Eyes, Ears, Nose, Throat	2456 (8)
Pharyngitis	554 (23)
Acute Sinusitis	389 (16)
Acute otitis media	332 (14)
Conjunctivitis	236 (10)
Tonsillitis	220 (9)
Musculoskeletal	2153 (7)
Sprain or strain	683 (32)
Arthralgia	594 (28)
Fracture	474 (22)
Non-cardiac chest pain	160 (7)
Tendinitis	93 (4)
Genitourinary/STDs	1017 (3)
Acute urinary tract infection	507 (50)
Vaginitis	103 (10)
Kidney or urine stone	87 (9)
Non-genital warts	41 (4)
Gynaecological disorder, other	30 (3)

System and Diagnoses	n (%)
Neurologic	786 (3)
High altitude cerebral oedema	631 (80)
Dizziness	52 (7)
Seizure disorder	23 (3)
Cerebrovascular accident	16 (2)
Peripheral neuropathy	12 (2)
Systemic Febrile Syndromes	706 (2)
Viral syndrome, not otherwise specified	322 (46)
Influenza A	113 (16)
Febrile illness, unspecified (<3 weeks)	103 (15)
Dengue (complicated or uncomplicated)	41 (6)
Influenza B	40 (6)

^aSkin and soft tissue infections including abscess, impetigo, folliculitis, furuncle, carbuncle, paronychia, ecthyma, erysipelas, cellulitis, gangrene.

Table 2

Additional classification of top diagnoses as altitude-related, animal bites, vector-borne diseases, and vaccine-preventable diseases among travellers to Nepal seen at the Kathmandu GeoSentinel Clinic (CIWEC), 2009–2017.

Classification	N	n (%)
Altitude-related diseases	2564	
Acute mountain sickness (AMS)		1281 (50)
High altitude pulmonary oedema (HAPE)		652 (25)
High altitude cerebral oedema (HACE)		402 (16)
HAPE and HACE combined		229 (9)
Animal bites	1260	
Rabies post-exposure prophylaxis		446 (35)
Dog bite		305 (24)
Insect or other arthropod bite		206 (16)
Tick bite		119 (9)
Monkey bite		99 (8)
Monkey exposure (scratch, lick, etc.)		37 (3)
Cat bite		16 (1)
Other animal bite ^a		9 (1)
Dog exposure (scratch, lick, etc.)		8 (1)
Vaccine-preventable diseases	278	
Influenza A		113 (41)
<i>Salmonella</i> Typhi (typhoid fever)		52 (19)
Influenza B		40 (14)
Herpes zoster (shingles)		27 (10)
Varicella (chickenpox)		18 (6)
Mumps		8 (3)
Acute hepatitis A		8 (3)
Measles		7 (3)
Chronic hepatitis B		3 (1)
Cholera		2 (1)
Vector-borne diseases	64	
Dengue (complicated or uncomplicated)		41 (64)
Malaria ^b		9 (14)
Chikungunya virus infection		4 (6)
<i>Rickettsia</i> (unknown species)		4 (6)
<i>Rickettsia typhi</i> (flea-borne murine typhus)		2 (3)
<i>Rickettsia</i> , tick-borne spotted fever		1 (2)
Japanese encephalitis		1 (2)
Lyme disease, acute or early disease ^c		1 (2)

Classification	N	n (%)
Lyme disease, late ^d		1 (2)

^aIncludes rat/mouse bite (n = 6), squirrel bite (n = 1), and unspecified other animal bites (n = 2).

^bIncluding *P. falciparum* (n = 4), *P. malariae* (n = 1), *P. vivax* (n = 3), and severe and complicated (n = 1).

^cIncluding erythema chronicum migrans and other early manifestations.

^dIncluding arthritis, neurologic manifestations, and other late manifestations.