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Research on climate change and the distributions of vector-borne diseases in the Hindu-Kush Himalayan region – the case of Nepal

Abstract

In view of increasing concern about the impacts of climate change on vector-borne diseases (VBDs) especially in tropical highlands and temperate regions of our planet, we carried out international collaborative research in Nepal between 2011 and 2015. Nepal is located in the central part of the Hindu-Kush Himalayan (HKH) region where at least seven VBDs (malaria, lymphatic filariasis, Japanese encephalitis, West Nile fever, chikungunya fever, dengue fever and visceral leishmaniasis) are endemic, and threat of Zika virus infection expected. The pathogens causing these diseases are transmitted to or among humans by mosquitoes or sand flies which are sensitive to temperature and thus to climate change. Hydro-meteorological data for the HKH region are scarce, but the available data indicate that its warming trend is more pronounced than the global trend. A shift of disease vectors and disease transmission to higher elevations has been predicted under observed and future climate change scenarios, however, empirical data on the expansion of VBDs in the HKH region was largely lacking. To address this knowledge gap, we carried out entomological, climatological, social and epidemiological studies in Nepal in an integrated eco-bio-social framework and compared our findings with literature on the distribution of VBDs in the HKH region published up to September 2016. Our studies highlight a more pronounced warming in the hills and mountains of Nepal and the HKH region overall compared to other parts of the world. We found a distinct shift of disease vectors and VBD incidence with autochthonous cases to previously non-endemic areas including hills and mountains. Significant relationships between climatic variables and the occurrence of VBDs and their vectors were revealed in short-term studies. The knowledge of people on the prevention and control of VBDs was very low among our study populations in different highland and lowland areas of Nepal. Given the establishment of relevant vectors up to at least 2,000 m above sea level, increasing movement of people and goods between endemic and non-endemic areas, and urbanization and poverty, climate change can intensify the risk of VBD epidemics in the fragile HKH region and its vulnerable populations. The wide distribution of important disease vectors in regions that had previously been considered to be non-endemic calls for regional collaboration in extending and upscaling surveillance and control programs in the HKH region.

Keywords: *Climate change, vector-borne diseases, mountain, Himalaya, poverty*

1 Introduction

The Hindu-Kush Himalayan (HKH) region spans over four million square kilometers, constituting approximately 18% of the world's mountainous areas. This region includes all of Nepal and Bhutan, and the mountains of Afghanistan, Bangladesh, China, India, Myanmar and Pakistan [1]. The HKH region is particularly vulnerable to climate change because the rate of warming in the Himalayas has been much greater (0.06°C yr^{-1}) than the global average in the last three decades [2]. Over 200 million people live in the mountains, valleys, and hills of the HKH region and an estimated 3 billion people benefit from the water and other goods and services that originate in the mountains of this region [1]. As evidence for the varied impacts of climate change on public health is increasing, the published literature continues to focus on the effects of climate change in developed countries and other parts of the world while the effects on mountain populations residing in the HKH region are grossly underreported [3,4].

Vector-borne diseases (VBDs) which are transmitted to or among humans, livestock and wildlife by arthropod animals (in the case of the diseases discussed here: mosquitoes or sandflies) are sensitive to temperature, rainfall and humidity and thus, ultimately, sensitive to climate change [5,6]. Any change in the geographical distribution of a VBD due to climate change, allowing a vector and/or pathogen to shift to new areas, will have a profound effect on the exposure of naïve hosts to those diseases [7]. As VBDs are emerging in highlands and high-latitude regions causing significant morbidity and mortality, the role of climate change on VBDs should be explored as a priority in those areas and countries where disease surveillance systems and reporting efforts are weak [8]. It is estimated that more than half of the world's population is already now at risk of disease from insect-borne pathogens [9] and constitute an important cause of morbidity and mortality, diseases burden and health inequality especially in developing and poor countries [10]. At least seven major VBDs, namely malaria, lymphatic filariasis (LF), Japanese encephalitis

(JE), visceral leishmaniasis (VL, also known as kala-azar), chikungunya fever (CHIK), dengue fever (DF) and West Nile Fever (WNF) are endemic in the HKH region which is now also facing the threat of Zika virus.

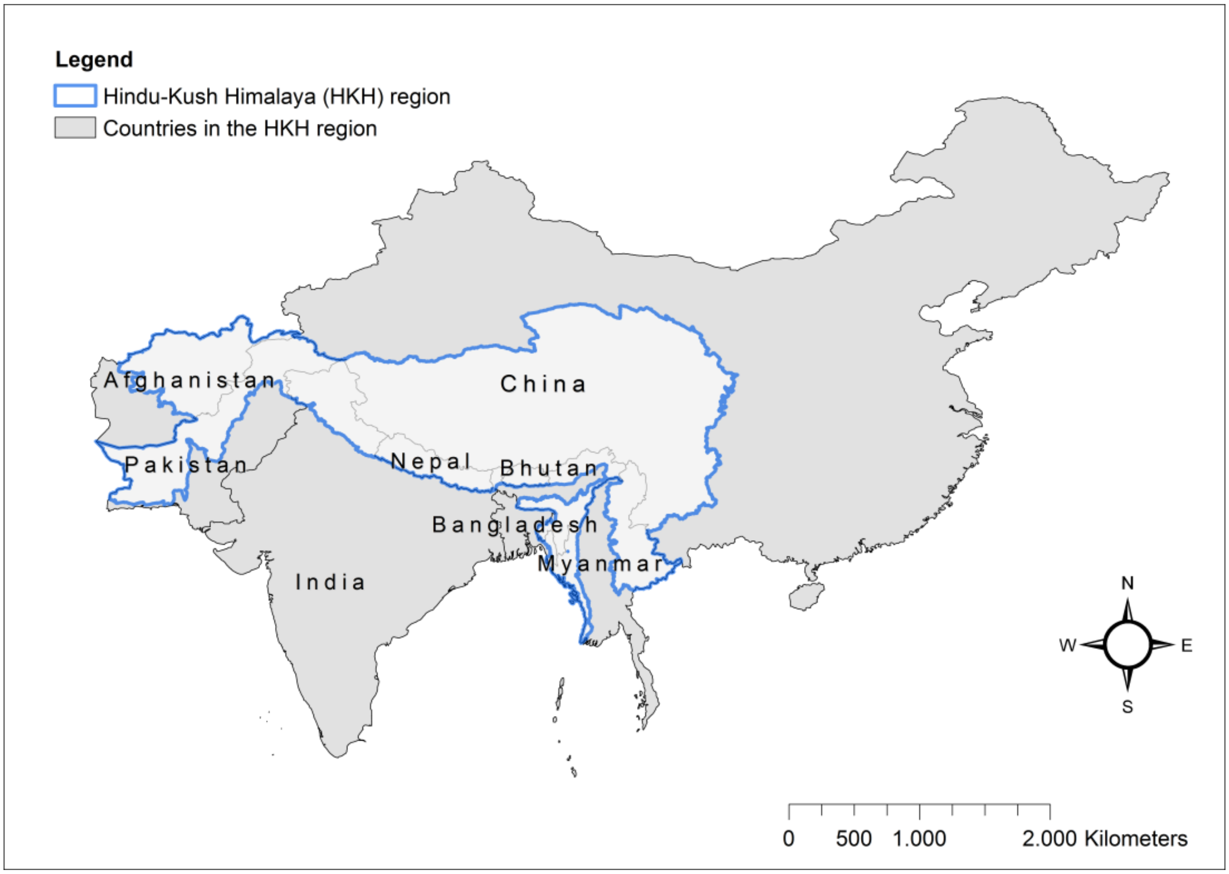

Figure 1. Map of the Hindu-Kush Himalayan region (from Dhimal *et al*., submitted manuscript)

As arthropods are 'cold-blooded' or poikilothermic animals, the period of their life-cycle and the pathogen development in their body is affected by climate change [7,11,12]. The duration of the growth season will increase in many regions with climate change, which means that more generations of vectors may be produced each year in tropical highlands and temperate regions [7]. Therefore, the greatest effect of climate change on VBD transmission is likely to be observed in cooler areas where the minimum temperature is limiting disease transmission, and in warmer areas where temperatures above 34°C have a negative impact on the survival of vectors and pathogens [13-15]. Moreover, as the warming rate is higher closer to the poles and in highlands compared to the tropics and lowlands [16,17], vectors and pathogens are experiencing more differential warming in high latitudes and altitudes compared to lower latitudes and lowlands [18].

Minimum criteria that have been suggested for accepting a causal relationship between climate change and human VBDs are evidence of biological sensitivity to climate, meteorological evidence of climate change, and evidence of entomological and/or epidemiological change in relation to climate change [19]. The first two criteria are obvious, and the third one needs to be explored using empirical data. Changes in the spatiotemporal patterns of climatic variables such as temperature, precipitation and relative humidity under different climate change scenarios based on RCPs, affect the biology and ecology of vectors and intermediate hosts and consequently the risk of disease transmission [14]. However, the local adaptation of disease vectors to micro-climatic variation may modulate the effects of both short- and long-term changes in climate [20]. Moreover, climate, vector ecology, healthcare systems and socio-economic status vary dramatically across geographical regions and countries and therefore demand studies at the local level in each country and region.

Methodology

We used a broad ecological-biological-social conceptual framework which is consistent with the ´One Health´ concept to explore the geographical distribution of VBDs and their associated factors in Nepal. Our international collaborative research project provided a unique opportunity to explore and compare climate change related risks of VBDs with clear eco-socio-medical relevance for people in mountain regions. Both qualitative and quantitative data were collected. We studied the distribution of vectors along an altitudinal transect using standard entomological techniques. We used BG-Sentinel traps, CDC light traps and aspirators with the support of flashlights to capture adult mosquitoes. Immature mosquitoes were collected using locally constructed dippers. Mosquito eggs were collected using ovitraps. We used epidemiological surveillance data collected by the Epidemiology and Diseases Control Division (EDCD) and Health Management Information System (HMIS) of the Ministry of Health, Government of Nepal. Similarly, we used observed meteorological data collected by the Department of Hydrology and Meteorology (DHM), Government of Nepal. Surveys on the knowledge, attitude and practice of people regarding the prevention and control of VBDs were carried out using structured questionnaires. In order to validate and elaborate quantitative data, we assessed local residents' perceptions of the distribution and occurrence of mosquitoes using key informant interview techniques. Quantitative data were analyzed using modeling techniques and qualitative data were analyzed using thematic content analysis techniques.

2 Key Results

Analysis of observed temperature data shows a warming trend in Nepal which is influenced by maximum temperatures with higher warming rates in the mountain regions compared to the lowlands of Nepal [21]. Precipitation does not show a distinct trend in Nepal. However, changes in extreme events such as heavy rainfall, drought, cold days, hot days, consistent with climate change effects, are more significant in Nepal [21]. The review of observed and future projections of climatic data shows a conducive environment for the transmission of VBDs in the HKH region, especially in the highlands (mountains) which had been assumed to be free from these diseases [2,22-24]. However, inter-modal variability and uncertainties in temperature and precipitation have been observed over the region.

The known malaria vectors in Nepal, *Anopheles fluviatilis*, *Anopheles annularis* and *Anopheles maculatus* complex members, currently have established populations at least 1800 m above sea level (asl) [25]. The vectors of chikungunya and dengue viruses (also Zika virus), *Aedes aegypti* and *Aedes albopictus*, the main vector of lymphatic filariasis, *Culex quinquefasciatus*, and the main vector of Japanese encephalitis in Nepal, *Culex tritaeniorhynchus*, have established populations at altitudes of at least 2,000 m asl [25-28]. Larvae of *Anopheles*, *Culex* and *Aedes* species were found up to 2,310 m asl [25,26,28]. We also found significant relationships between climatic variables and the abundance of disease vectors [26,28].

Our systematic review of climate change and the spatiotemporal distributions of VBDs in Nepal and comparison of the results with those of other studies from the HKH region show a consistent trend of VBD expansion in the HKH region [21]. Over the last decade, the distribution of these diseases and their vectors, which were previously believed to be confined to tropical and sub-tropical regions, is now observed to extend to the hills and mountains of the HKH region. For example, the geographical area with autochthonous dengue virus transmission has extended to include Bhutan and Nepal since 2004 and 2006, respectively [29,30] and the primary dengue virus vector *Aedes aegypti* has already expanded its regional range to above 2,000 m altitude in the region [26,31,32]. The first autochthonous cases of chikungunya virus infection (also transmitted by *A. aegypti*) were reported in Bhutan and Nepal in 2012 and 2013, respectively [33,34]. The presence of the principal vector of Japanese encephalitis virus (JEV), *Culex tritaeniorhynchus*, and of JEV circulation itself in the mountain regions of Tibet and Nepal has also been reported [35-37]. Despite significant declining trends of malaria in Nepal [38], malaria hotspots have shifted to new areas which in the past had been regarded as low-risk areas so that vector control interventions were not in place [39]. In addition, we found a significant effect of ambient temperature on the incidence of malaria [39]. The climate and other environmental changes are likely to affect malaria and other parasitic diseases elimination goals of Nepal and other countries of HKH region [8,21,40-42].

The entomological findings are consistent with epidemiological findings from the region [25,26,39]. More importantly, the knowledge of people residing in the highlands on the prevention and control of diseases such as dengue fever is very low [43]. People living in mountain regions reported that mosquito nuisance had started in their communities as recently as 5–10 years ago and increasingly became a problem as mosquito bites started immediately after winter and lasted until the end of autumn. People in the lowlands reported an elongation of the mosquito biting seasons. Participants from highland areas believed that mosquitoes had been carried to the highlands by trucks and buses and that growing mosquito populations breeding in the highlands had been favored by the installation of water supply pipes in communities, domestic water storage and warming temperatures in the last years [25]. They also believed that the replacement of biomass solid fuel by electricity promoted mosquito populations in households because electric lights attract mosquitoes whereas smoke from kerosene lamps and biomass fuels repels mosquitoes. In summary, community people perceived the occurrence and distribution of mosquitoes in their mountain regions to be a recent event which coincided with development and environmental changes including pronounced temperature increases in the latest decade. These reported perceptions are consistent with entomological findings [25,44].

Key publications of our international collaborative study:

1. Dhimal M, Ahrens B, Kuch U (2015) Climate change and spatiotemporal distribution of vector-borne diseases in Nepal - a systematic review of literature. PLoS ONE, 10(6):e0129869. doi:10.1371/journal.pone.0129869

2. Dhimal M, Gautam I, Joshi HD, O'Hara RB, Ahrens B, Kuch U (2015) Risk factors for the presence of chikungunya and dengue virus vectors (*Aedes aegypti* and *Aedes albopictus*), their altitudinal distribution and climatic determinants of their abundance in central Nepal. PLoS Neglected Tropical Diseases, 9(3):e0003545. doi:10.1371/journal.pntd.0003545

3. Dhimal M, Ahrens B, Kuch U (2014) Species composition, seasonal occurrence, habitat preference and altitudinal distribution of malaria and other disease vectors in eastern Nepal. Parasites and Vectors, 7:540. doi:10.1186/s13071-014-0540-4

4. Dhimal M, O'Hara RB, Karki RC, Thakur GD, Kuch U, Ahrens B (2014) Spatiotemporal distribution of malaria and its association with climatic factors and vector control interventions in two high-risk districts of Nepal. Malaria Journal, 13:457. doi:10.1186/1475-2875-13-457

5. Dhimal M, Ahrens B, Kuch U (2014) Altitudinal shift of malaria vectors and malaria elimination in Nepal. Malaria Journal, 13 (Suppl.):P26. doi:10.1186/1475-2875-13-S1-P26

6. Dhimal M, Ahrens B, Kuch U (2014) Malaria control in Nepal 1963-2012: challenges on the path towards elimination. Malaria Journal, 13:241. doi:10.1186/1475-2875-13-241

7. Dhimal M, Gautam I, Kreß A, Müller R, Kuch U (2014) Spatio-temporal distribution of dengue and lymphatic filariasis vectors along an altitudinal transect in central Nepal. PLoS Neglected Tropical Diseases, 8(7):e3035. doi:10.1371/journal.pntd.0003035

8. Dhimal M Aryal KK, Lamichhane Dhimal M, Gautam I, Singh SP, Bhusal CL, Kuch U (2014) Knowledge, attitude and practice regarding dengue fever among the healthy population of highland and lowland communities in central Nepal. PLoS ONE, 9(7):e102028. doi:10.1371/journal.pone.0102028

The available data indicate that the warming trend of the HKH region is more pronounced than that of other parts of the world [2,24]. Climate change, alongside landscape change and population dynamics is resulting in dramatic environmental changes in the HKH region [1]. This drives a shift of disease vectors and disease transmission from tropical regions into temperate regions and highlands, as has been predicted for both observed and future climate change scenarios [45-48]. It has also been reported that the increasing movement of people and imported cases of infection, in the presence of appropriate weather conditions, can initiate epidemics of

VBDs [49,50]. Hence, these factors along with the documented establishment of relevant vectors at altitudes of at least 2,000 m above sea level can intensify the risk of VBD epidemics in the fragile and previously non-endemic areas of HKH region and its vulnerable populations. The wide distribution of important disease vectors in regions that had previously been considered to be non-endemic calls for regional collaboration in extending and upscaling VBD surveillance and control programs in the HKH region.

Challenges faced while conducting study

Multiple challenges exist for conducting research on climate change and health in the mountain regions of developing countries [51]. As a result, research continues to focus on the effects of climate change in developed countries, whereas effects on the most vulnerable populations residing in least developed and developing countries are grossly underreported [3,4]. The Fourth Assessment Report of the IPCC [4] categorized the Himalayan region as a "white spot" and called for global, regional and national responses to fill this gap. In order to study the early effects of climate change on the spatiotemporal distributions of VBDs, environmental and climatic data are needed at finer resolution. However, the application of the general circulation model (GCM) and regional climate model (RCM) data for disease mapping in complex mountain topography is difficult owing to the spatially clustering nature of diseases and high micro-climatic variation within short airline distances. Despite the presently low coverage of meteorological stations in mountain regions, utilizing observed meteorological data provides more reliable information for exploring the relationships between climatic variables and VBD transmission.

Hence, we chose an altitudinal transect where meteorological stations were installed for our study purposes. As the use of CO_2 as an attractant for mosquito collection is difficult to implement in remote mountain regions because of logistic and economic reasons, we collected mosquitoes with CDC light traps without the use of CO_2, and with BG-Sentinel traps using a specific attractant (BG-Lure) designed for *A. aegypti* and *A. albopictus* mosquitoes. Medical entomology data for mapping vector distributions was completely lacking after the 1990s in Nepal except for a few studies of dengue virus vectors. Thus, we also collected qualitative data using interview techniques. Epidemiological data are limited in mountain regions, hence studying the effects of climate on vectors is of interest because such studies can detect responses in vector populations before they cause disease and avoid confounding factors such as changes in diagnosis and treatment regimens or public awareness of the prevention and control of diseases [19]. In addition, entomological transect surveys along an altitudinal gradient can provide direct evidence of the distributional shifts of disease vectors in response to climate change.

Planned Next Steps

We propose to extend such integrative, comparative and interdisciplinary entomological-epidemiological surveys on a broad range of climate change related aspects of VBDs and their vectors to additional areas in the HKH region where uncertainties for the altitudinal distribution of mosquitoes, sand flies and the pathogens they transmit have remained high, and to put the obtained results in a global context by comparing the climate change and health development of the HKH region with that of the Andes as another major mountain region with a high diversity and burden of VBDs. This study will also include analyses of the positive and negative effects that climate change adaptation in other sectors has on VBD transmission, and address possible mitigating measures.

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