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A SYSTEMATIC REVIEW ON THE DISTRIBUTION AND DENSITY OF *AEDES* SPECIES IN THE HINDU-KUSH HIMALAYAN COUNTRIES

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ABSTRACT

***Aedes* mosquitoes are effective carriers of virus pathogens such as chikungunya, dengue, yellow fever, zika, and other viruses, leading to high morbidity and mortality. This review compiles information on the geographical distribution of *Aedes* mosquitoes in the Hindu-Kush Himalayas (HKH). Articles published in SCI-indexed journals from 2000 to 2022 have been reviewed using the key words "*Aedes*", "distribution", and "country name (e.g., Nepal)". A total of 353 articles have been indexed, of which only 52 were ultimately explored. The review highlights a historical prevalence of *Aedes* spp. in the HKH countries, with their distribution gradually shifting along altitude gradients. Surging dengue cases in the HKH region pose a public health threat. Urgent action is required, including comprehensive nationwide surveys mapping *Aedes* spp. across diverse altitudes.**

Key words: Abundance, *Aedes*, *Aedes* distribution, altitudinal gradients, anthropogenic factors, chikungunya, climate change, culicidae, dengue, Hindu-Kush Himalaya, mosquitoes, mosquito-borne diseases, public health, vector control, zika virus

Mosquitoes, belonging to the family Culicidae, are prevalent worldwide, excluding Antarctica (Hawkes and Hopkins, 2022). The global count stands at 113 genera and 3619 species (Harbach, 2022a), with less than 10% known to transmit diseases to humans (Yee, 2022). Among them major disease vectors are the genera *Anopheles*, *Aedes*, and *Culex*, with *Aedes* mosquitoes, such as *Aedes aegypti* and *Aedes albopictus*, transmitting over 20 viruses and filarial worms (Tandina et al., 2018; Tippelt et al., 2020). *A. aegypti* and *A. albopictus*, native to the African continent and Southeast Asian forest, respectively (Russell et al., 1969; Tedjou et al., 2020), have significant global health implications as carriers of pathogens like chikungunya, dengue, yellow fever, and zika viruses (Mordecai et al., 2020). Their breeding preferences and feeding habits contribute to their effectiveness in transmitting diseases and substantially impacting on human health and economies worldwide (Ebi and Nealon, 2016). The Hindu-Kush Himalaya (HKH) region, a complex tapestry of diverse landscapes across Afghanistan, Bangladesh, China, India, Myanmar, Pakistan, Nepal, and Bhutan, faces unique challenges posed by climate change and population growth (Shrestha et al., 2012; ICIMOD, 2019; Chandrashekhar, 2022), raising concerns about the spread of *Aedes*-borne diseases (Rao, 1967; Chen et al., 2011). With a projected population of 300 million by 2030 and temperatures rising faster than the global average (ICIMOD, 2019), understanding the distribution of *Aedes* mosquitoes in this region is particularly crucial for public health. However, a comprehensive review of *Aedes* mosquito distribution across the diverse HKH countries is currently lacking, hindering effective public health planning and implementation of targeted vector control strategies. This study aims to assess *Aedes* distribution and density across diverse geographical locations and climatic scenarios within the HKH countries, including variations in altitude, temperature, and rainfall patterns. This review represents the UN Sustainable Development Goals (Goals 3 and 13), contributing to the global effort to enhance public health and address the impact of climate change (UN, 2015).

MATERIALS AND METHODS

In this review, articles (SCI index journals) published from 2000 to 2022 (23 years) were searched using the keywords "*Aedes*", "distribution", and the names of specific countries (e.g., Nepal) in PubMed (Fig. 1). This

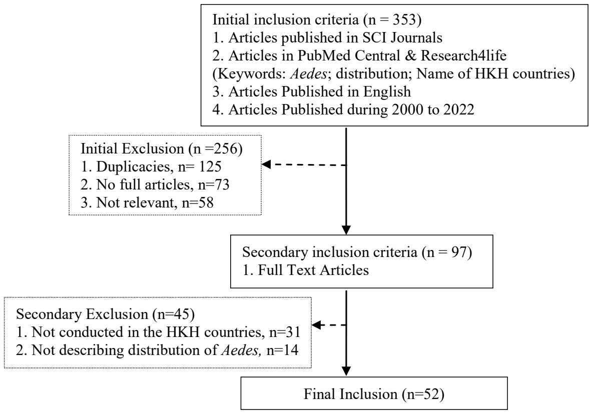

Fig. 1. Flow diagram for publications (PubMed Central and Research4Life)

search yielded 353 articles, from which only 52 were selected for the analysis based on the current objectives. Firstly, the ICIMOD-produced map was utilized to illustrate the geography of the HKH region (ICIMOD, 2019). Subsequently, the selected articles encompassed two from Afghanistan, seven from Bangladesh, thirteen from China, eleven from India, two from Myanmar, eight from Nepal, and nine from Pakistan. Notably, no relevant papers meeting the review's objectives were identified in Bhutan over the past 23 years. Thirdly, the selected articles aligning with the present objectives were reviewed, analyzed, and compared in the context of the distribution and density of the *Aedes* mosquitos within the HKH countries. Descriptive summaries of these papers were then extracted and listed in the tables (Table 1). The density of *Aedes* mosquitoes was analyzed using published metrics such as relative abundance (RA), house index (HI), container index (CI), and Breteau index (BI). Finally, additional information required for this review was sought through Google Scholar and Research4Life. It is important to note that the quality of these articles was not evaluated. Drawing on the methodology outlined by the Institute of Medicine (IOM, 2011), systematic reviews were performed to synthesize information regarding *Aedes* mosquitoes in the HKH countries.

RESULTS AND DISCUSSION

Density and distribution

Density and distribution of *Aedes* spp. in the HKH countries revealed that historically, the HKH countries have been one of the most critical habitats (Table 1). *A. aegypti* has been reported since 1930s in Bangladesh (Rao, 1967). After a long gap, in 2016, the Irish and others listed 26 species of *Aedes* in this country (Irish et al., 2016). In the same year, entomologists reported 11.07% (N=6088) larval prevalence of *Aedes* in semi-urban areas of Dhaka, with a nearly equal prevalence of *A. aegypti* and *A. albopictus*- 5.09% and 5.98%, respectively (Bashar et al., 2016). In the same city, Farhana Ferdousi and colleagues collected the larval and pupal forms of *Aedes* spp. (N=3027867) with 63.5% of *A. aegypti* and 36.5% of *A. albopictus* (Ferdousi et al., 2015). Similar results were obtained from Chattogram, the nearby city, for example, with 64.75% (n=371) of *A. aegypti* and 35.25% (n=202) *A. albopictus* (Rahman et al., 2021). Studies in 2018 found a higher RA of *A. aegypti* than that of *A. albopictus* (82% vs 13%) (Paul et al., 2018). Subsequent research found a similar predilection for the RA of *A. aegypti* and *A. albopictus* (90% vs 8%) (Islam et al., 2019). Except for 2016, all these studies found that *A. aegypti* had higher RA than *A. albopictus* (Ferdousi et al., 2015; Bashar et al., 2016; Paul et al., 2018; Islam et al., 2019; Rahman et al., 2021) (Table 1). Another similarity in the study, except in 2016, was a higher RA of *Aedes* mosquitoes. In 2016, larvae and pupae were collected from all different possible habitats of mosquitoes, including drains and rice fields (Bashar et al., 2016). Drains and rice fields might have increased the density of *Culex* and other mosquitoes and reduced the RA of *Aedes* spp. In contrast, other researchers sampled from *Aedes*-dominant habitats like discarded tires, plastic drums/ containers, and cemented tanks present around human settlements (Ferdousi et al., 2015; Paul et al., 2018; Islam et al., 2019; Rahman et al., 2021) which could enhance the rates of *Aedes* abundance.

Regarding HI, the value decreased from 2011 (25%) (N=884) to 2015 (14.2%) (N=9222) (Ferdousi et al., 2015; Paul et al., 2018) and it was nearly the same in 2019 (14.9%) (Islam et al., 2019) but slightly higher in 2021 (17.35%) (Rahman et al., 2021). The CI followed a similar pattern from 2011 (39%) to 2015 (5.9%) (Ferdousi et al., 2015; Paul et al., 2018). This index was 33.2% (N=674) in 2019 (Islam et al., 2019; Rahman et al., 2021) and then reported to be 7% (N=704) in 2021 (Islam et al., 2019; Rahman et al., 2021). In addition, the BI was reported to be 55.8% (493/ 884) in 2011 and 22.5% (144/639) in 2013, and the data were similar in 2015 (24.6%), 2019 (30.8%) and 2021 (24.49%) (Ferdousi et al., 2015; Islam et al., 2019; Rahman et al., 2021). All HI, CI, and BI were higher in 2011 than in 2021, indicating the distribution of *Aedes* spp. was reduced. However, recent reports suggest the enhanced rates of dengue cases year after year (WHO, 2022a), indicating the necessity for more vector surveillance programs in Bangladesh to control the disease.

Table 1. Density of *Aedes* spp. in the Hindu-Kush Himalayan countries

Species	HI	CI	BI	Relative abundance of *Aedes* spp.	Country (study site)	Citation
A. aegypti, *A. albopictus* (Larva, pupa)	17.35%	7%	24.49%	-	Bangladesh	(Rahman et al., 2021)
A. aegypti, *A. albopictus* (Larva)	14.9%	33.2%	38.8%	98%		(Islam et al., 2019b)
A. aegypti, *A. albopictus* (Larva, pupa)	25%	39%	55.8%	95%		(Paul et al., 2018)
A. aegypti, *A. albopictus* (Larva, pupa)	24.7%	37.4%	28.4%			
A. aegypti, *A. albopictus* (Larva, pupa)	16.6%	24.3%	22.5%			
A. aegypti, *A. albopictus* (Larva)	14.2%	5.9%	24.6%	100%		(Ferdousi et al., 2015)
A. aegypti, *A. albopictus* (Larva)	-	9.37%	17.57%	-	China	(Guo et al., 2016)
A. aegypti *A. albopictus* (Larva)	8.36% to 37.67%	3.96% to 21.34%	8.72% to 39.04%	-		(Devi et al., 2020)
A. aegypti, *A. albopictus*, *A. vittatus* (Larva)	13.08%	13.28%	16.57%	-		(Vijayakumar et al., 2014)
A. aegypti (Larva)	77%	49%	133%	-	Myanmar	(Oo et al., 2011)
A. aegypti (Larva)	26%	16%	34%	-		
A. aegypti (Larva)	2.56% to 56.92%	5.07% to 56.52%	2.67% to 17.56%	-		(Oo et al., 2020)
A. aegypti (Larva)	47.7%	25.2%	70.5%	48.7%	Nepal	(Dhimal et al., 2015)
A. aegypti (Larva)	46.4%	24.8%	66.1%			
A. aegypti (Larva)	22%	11.1%	33.2%			
A. aegypti (Larva)	1.4%	1.8%	1.4%			
A. albopictus (Larva)	7.4%	5.5%	15.3%			
A. albopictus (Larva)	26.8%	12.3%	32.8%			
A. albopictus (Larva)	21.5%	9.1%	27.4%			
A. albopictus (Larva)	2.4%	1.4%	2.4%			
A. aegypti, *A. albopictus* (Larva)	21.2%	41.8%	0.1%	-		(Tuladhar et al., 2019)
A. aegypti, *A. albopictus* (Larva)	20.8%	36%	0.05%	-		
A. aegypti, *A. albopictus* (Larva)	19.7%	24.3%	0.06%	-		
A. aegypti, *A. albopictus* (Larva)	-	-	-	91%		(Kawada et al., 2020)

HI: House Index, CI: Container Index, BI: Breteau Index

Latest Walter Reed Biosystematics Unit (WRBU) study compiled 60 *Aedes* spp. from China (Gaffigan et al., 2022). Guo and team considered *A. albopictus* to be an indigenous mosquito in China (Guo et al., 2018), and it is widely distributed in 16 provinces (Wu et al., 2011; Yang et al., 2021; Yue et al., 2022), although this species has been well reported in other HKH countries. The extensive four-year dengue vector surveillance in 25 Chinese provinces revealed 12.6% of RA for *A. albopictus*. (N=2706) (Yang et al., 2021). In contrast, *A. aegypti* is distributed only in four provinces (Guangdong, Guangxi, Hainan, and Yunnan) in southern China (Guo et al., 2016; Wei et al., 2019; Yue et al., 2022). In Yunnan province, *A. aegypti* was first recorded from Xishuangbanna in 2013 (Zhang et al., 2014). In Jinghong, Yunan, *A. aegypti*-positive containers were double those of *A. albopictus* (56% vs 27%), and importantly, 5.4% of containers were shared by both species, resulting in the BI and CI of 17.6% and 9.4%, respectively (Guo et al., 2016). Yunnan has subtropical and tropical climates, which are ideal for *Aedes* spp., and it is also connected to dengue-endemic neighbors such as Myanmar, Laos, and Vietnam. That might cause high BI and repeated dengue outbreaks in Yunnan since 2004, with a large-scale outbreak occurring in 2013 (Guo et al., 2015, 2016). The detailed entomological surveys of *A. aegypti* from 151m (Hainan) to 501m (Guangxi) before 2013 (Guo et al., 2016) and at 566 m (Yunnan) in 2013 (Zhang et al., 2014) also indicated that the *Aedes* mosquitoes probably began to colonize in new areas inside China. They were gradually adapting to higher altitude. The higher values of BI could be associated with future dengue outbreaks, which would be more likely in many regions of China (Liu and Liu, 2020). Moreover, although Inner Mongolia is far from the HKH region, there are reports of 28 species of *Aedes* (Cao et al., 2011), including *A. caspius*, *A. dorsalis*, *A. flavescens*, *A. flavidorsalis*, *A. caspius*, *A. koreicus*, and *A. vexans* indicating China to be an important region for *Aedes* vectors (Cao et al., 2011; Wang et al., 2012)

The chronological evidence of *Aedes* distribution in India is interesting, and it is one of the best model countries for studying these vectors in HKH. For example, reports of *Aedes* spp. in British India, including present-day Pakistan and Bangladesh, were produced before independence. Barraud recorded 113 *Aedes* spp. in that period (Barraud, 1934); however, 115 *Aedes* spp. have been recorded in different habitats from new Indian geography (Kaur, 2003; Rajavel et al., 2004; Dutta et al., 2010). Notably, *A. aegypti* was densely spread along the Gangetic landscapes of North India. Following the DDT Indoor Residual Spraying Programme in many cities, *Aedes* disappeared for many years (Barraud, 1934). However, the scenarios changed subsequently because of trade, shipping, population density, poor sanitation, travel, and the use of vehicles (Barraud, 1934; Bhat, 1975; Devi and Jauhari, 2004; Aditya et al., 2009), which led to the strong reemergence of *Aedes* all over India, including the high altitudinal and mountainous areas.

Near the 21st century, adults of 10 species of *Aedes*, including *A. aegypti* and *A. albopictus*, have been recorded from 340 m to 1870 m asl in India (Devi and Jauhari, 2004). Then, immature stages of *A. aegypti* were recorded from 2130 m asl (Aditya et al., 2009). A paper published in the Journal of Vector-Borne Diseases quantified 13.08% (n=1750) HI, 13.28% CI, and 16.57% BI in the Thiruvananthapuram district in Kerala (Vijayakumar et al., 2014). Das and colleagues reported adults and pupae of *A. aegypti*, *A. albopictus*, *A. edwardsii*, and *A. vittatus* from Odisha (Das et al., 2015). The adult *Aedes selsiae* was recorded in Himachal Pradesh during an entomological survey (Kumar et al., 2020). Similarly, both *A. aegypti* and *A. albopictus* were recorded from Uttaranchal Pradesh in 2018 with 5% RA (Kaur, 2021), Jammu and Kashmir (Dar et al., 2016) and *A. aegypti*, *A. albolateralis*, *A. albopictus*, *A. pseudotaeniatus*, and *A. vittatus* from Dehradun, Uttarakhand with 18.85% RA (Haq and Singh, 2021). The presence of *Aedes* mosquitoes in northwestern high altitudinal areas of India, like Himachal, Jammu and Kashmir, Uttaranchal, and Uttarakhand, indicates that this vector is well-adapted to the highlands and may cause an *Aedes*-borne disease outbreak in the future.

Interestingly, Shalini and her colleagues reported 22.6% larvae of *A. albopictus* from Tamil Nadu, indicating South India is a major area of *Aedes* spp. (Shalini et al., 2022). The CI of three species of *Aedes*, namely, *A. aegypti*, *A. albopictus*, and *A. vittatus* in 2014 was 13% in Kerala (Vijayakumar et al., 2014), five species of *Aedes* (*A. aegypti*, *A. albopictus*, *A. malayensis*, *A. subalbopictus*, and *A. walbus*) in 2017 was 2.1% in Andaman and Nicobar Islands at 86 m asl (Shriram et al., 2017), and *A. aegypti*, and *A. albopictus* was 8.5% in 2020 in Punjab (Devi et al., 2020). Punjab is bordered by Pakistan, Jammu and Kashmir, Himachal State, Haryana, and Rajasthan and has an alluvial plain with rivers and an extensive irrigation canal system (Devi et al., 2020). The HI, CI, and BI in 2017 ranged from 8.36% to 37.67%, 3.96% to 21.34%, and 8.72% to 39.04%, respectively, in the urban areas of 11 districts in

Punjab (Devi et al., 2020). All these findings suggest the widespread distribution of *Aedes* mosquitoes throughout India, spanning low to high-altitude areas. As a result, *Aedes* shifting in these landscapes may be a constant risk in the dengue outbreak.

In Nepal, 55 species of *Aedes* have been recorded (Darsie and Pradhan, 1990; Darsie et al., 1991, 1992, 1993, 1996) and [WHO, 2006 (Gautam et al., 2009)]. Although *A. albopictus* was reported in 1956 (Peters and Dewar, 1956), *A. aegypti* was discovered in 2006 from low altitudinal areas of Nepal, bordering North India [WHO, 2006 (Gautam et al., 2009)] and in 2009 from Kathmandu, the capital city (Gautam et al., 2009) indicating its predominance both in warm and cold climates. Both species were commonly found in lowland to highlands areas (1,350 m asl) (Gautam et al., 2009; Pandey et al., 2013; Dhimal et al., 2015); however, they were rarely detected up to 2310 m asl in a mountainous region (Dhimal et al., 2015, 2014). Nevertheless, the authors could not provide molecular evidence for the presence of *Aedes* at an altitude of 2310 m asl (Dhimal et al. 2015), suggesting the need for further molecular assessment to understand the distribution ranges of *Aedes* spp. Dhimal's group reported 9.7% (N=2,538) adult and 49.5% (N=188) larval abundance of *Aedes* spp. in Eastern Nepal in 2014 (Dhimal et al., 2014). In the subsequent studies in 2015, they reported a larval abundance of 48.7% (N= 3,241) in Central Nepal (Dhimal et al., 2015), which was roughly comparable. However, in subsequent studies in Kathmandu, Bharatpur, and Pokhara by Kawada and his team, larval RA was recorded as almost double that of Dhimal's studies (91%, N=880) (Kawada et al., 2020). In central Nepal, *Aedes* larval indices during the monsoon season were higher than those in the pre-monsoon and post-monsoon (Tuladhar et al., 2019). All these authors assessed a higher RA of *A. aegypti* than *A. albopictus*. Based on the abundance data, it is evident that the imported *A. aegypti* exhibits better adaptation to the Nepalese Environment than *A. albopictus*, the native species of South Asia (Benedict et al., 2007).

A study reported decreasing values of HI, CI, and BI of the larvae of *A. aegypti* along increasing altitudinal gradients (<90m to 2100m asl) (Dhimal et al., 2015). However, for the larval forms of *A. albopictus*, the values of HI, CI, and BI first increased from <90 masl to 500m asl, then decreased through 1400 m up to 2100 m asl indicating the patterns of both species differ along the low altitude to high mountain areas (Dhimal et al., 2015). In a molecular study, the allele frequencies of genes related to climatic adaptation were compared in the natural *A. aegypti* populations along an altitudinal (200 m vs. 600 m vs. 800 m vs. 1300 m) and temperature gradient in central Nepal. This study proposes local high-altitude adaptation to determine the phenotypic cold adaptation *A. aegypti*, which is not associated with climate tolerance (Kramer et al., 2022). Furthermore, quantifying knockdown resistance (kdr) mutations and the altitude level did not affect the changes in the population (Kramer et al., 2022). This conclusion, however, may not represent other species of *Aedes* of different landscapes with different morphological, physiological, anatomical, and molecular adaptiveness concerning various environmental and geographical factors in HKH countries. In summary, although *Aedes* spp. are reported to occur up to 2310 m asl, the presence of dengue all over 77 districts may indicate that the vectors are distributed in all landscapes of the country. In this context, molecular changes in those insects cannot be ignored, and further molecular-epidemiological evidence is essential. The presence of *Aedes* spp. in Pakistan during the British colony has been well documented (Barraud, 1934). Although 42 species of *Aedes* mosquitoes had been recorded from low to high altitudes in Pakistan before (Aslamkhan, 1971), a recent extensive review published by the National Institute of Health compiled 27 species (Jabeen et al., 2019). Studies suggested that the RA of *Aedes* spp. was increased with the elevation up to 1000 m asl, then decreased above this height, and was absent at 2000 m asl (Fatima et al., 2016). Current studies measured the RA of *Aedes* spp. to be 8% (N=5,505) in 2000 (Ilahi and Suleman, 2013) in Swat, 15% larvae (N=1,684) of *A. aegypti*, *A. albopictus*, *A. unilineatus*, and *A. walbus* in 2014 (Ashfaq et al., 2014) in Panjab and Khyber Pakhtunkhwa, 17% of *A. albopictus* larvae in 2018 (Hira et al., 2018) in Swabi, 19.54% of RA *A. aegypti*, and *A. albopictus* in 2020 (Manzoor et al., 2020) in Lahore, 17% of *A. aegypti*, *A. albopictus*, and *A. vittatus* in 2021 (Attaullah et al., 2021) in Malakand and Dir lower, and 21.53% of *A. aegypti*, and *A. albopictus* in 2022 in Khyber Pakhtunkhwa (Khan et al., 2022). The continuous increase in the RA of *Aedes* mosquitoes from 2000 to 2022 indicates the predominance of *Aedes* spp. in Pakistan, which was also supported by a massive outbreak of dengue in Pakistan in 2022 (WHO, 2022b).

In Afghanistan, the *Aedes* was first recorded in 1972 (Ward, 1972). Interestingly, although *A. albopictus* was recently confirmed in Afghanistan {WHO, 2019 (Sahak, 2020)}, five other species, namely *A. aegypti*, *A. caspius*, *A. dorsalis*, *A. pulcritaris*, and *A. vesans* were well documented previously (Ward, 1972; Kadamov, 2006; Rueda et al., 2008; Gaffigan et al., 2022). Unfortunately, many relevant articles from Afghanistan in PubMed were lacking regarding the objectives of the current review.

An Online portal (www.mosquitocatalog.org) published by Gaffigan compiled 17 species of *Aedes*, including *A. aegypti* and *A. albopictus*, in Myanmar (Gaffigan et al., 2022). In 2011, the respective HI, CI, and BI values of *A. aegypti* larvae ranged from 26-77%, 16-49%, and 34-133%, and the values were higher in the rainy season compared to the dry season (Oo et al., 2011) in Yangon city. Another survey conducted in 2020 reported that the respective ranges of HI, CI, and BI of *A. aegypti* larvae were 4-42%, 5.07%-56.52%, and 35%-230%, and these values were highest in June and least in April (Oo et al., 2020). Such high values of HI, CI, and BI are critical indications of probable dengue outbreaks in the future; however, the distribution ranges throughout Myanmar are poorly identified.

In Bhutan, both *A. aegypti* and *A. albopictus* have been reported (Gaffigan et al., 2022); however, research related to the current objectives of the review was not found in the PubMed in Bhutan during the 23 years. Although dengue and chikungunya outbreaks in Bhutan have been hypothesized as causal associations with *A. aegypti* and *A. albopictus* due to urbanization, industrial growth, and the border with India (Dorji et al., 2009; Wangchuk et al., 2013; Zangmo et al., 2015; Tsheten et al., 2020), there remains a gap in the detailed study of vectors.

Anthropogenic factors and distribution

Studies within the HKH countries have evinced several anthropogenic factors facilitating *Aedes* spp. to propagate; for example, out of 121 factors, the increasing order of reported factors was from Bangladesh (47%), India (31%), Nepal (14%), Pakistan (14%), and Myanmar (3%) (Fig. 2). These factors provide the best environment for success in breeding, dispersal, and overwintering of the immature stages of *Aedes* spp. *Aedes* spp. have been observed breeding in wet containers with water ranging from very low (2 ml) to high amounts (1000 liters) (Shriram et al., 2017). Interestingly, discarded tires, plastic containers, mud pots, drums, tanks, and cemented tanks are highly preferred by *Aedes* spp. for breeding (Dhimal et al., 2015; Ferdousi et al., 2015; Bashar et al., 2016; Shriram et al., 2017; Paul et al., 2018; Islam et al., 2019a; Tuladhar et al., 2019; Devi et al., 2020; Manzoor et al., 2020; Oo et al., 2020; Rahman et al., 2021. Notably, *A. aegypti* and *A. albopictus* could share the same container for breeding (Guo et al., 2016; Shriram et al., 2017; Rahman et al., 2021), usually outdoors and at higher altitudes (Dhimal et al., 2015). Availability of anthropogenic factors plays a crucial role in *Aedes* shifting along the altitudinal gradients where recent development activities have begun; for example, transport services, including motor roads and discarded tires along the motorway. These anthropogenic landscape features will extensively enhance the distribution and development of immature stages of the vectors and may pose the threat of dengue outbreaks in new areas.

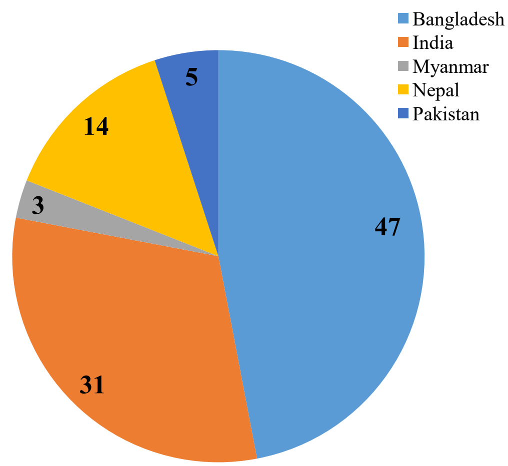

Fig. 2. Anthropogenic factors (N = 121) that influence development of immature forms of *Aedes* spp.

Environmental factors and distribution

It is evident that local climatic factors, *Aedes* vectors, and their disease incidences are associated; therefore, local climate-based early warning systems should be applied (Choi et al., 2016). Similar to other mosquitoes, the successful survival of *Aedes* spp. requires micro-and macroclimates determined by optimum climatic factors such as temperature, rainfall, extremes of flooding or drought, relative humidity, and wind. Rainfall, temperature, and relative humidity have been shown to influence the distribution of *Aedes* spp. in Pakistan (Fatima et al., 2016; Hira et al., 2018; Manzoor et al., 2020; Attaullah et al., 2021), Nepal (Dhimal et al., 2014, 2015; Tuladhar et al., 2019), Myanmar (Oo et al., 2020), and India (Selvan et al., 2020; Borah and Bora, 2022), however, the former two factors have been implicated in China (Wu et al., 2011; Zhou et al., 2021). Temperature is a primary determinant of mosquito population dynamics; for example, it enhances the aging of mosquitoes (Selvan et al., 2020). The enhanced environmental temperature increases the vectors' growth rate, reduces the extrinsic incubation period, and increases pathogen transmission (Selvan et al., 2020). The increased temperature also increases the gonotrophic cycle, thereby increasing the aggressive activities of *Aedes* spp. and the biting frequencies (Teurlai et al., 2015). The temperature that guides the activity of *Aedes* spp. is different in different geographies of HKH. For example, in Pakistan and China, *Aedes* spp. were highly active in the temperature ranges of 22°C to 31°C (Hira et al., 2018; Oo et al., 2020; Kaur, 2021) in contrast to more stenothermal ranges of 19°C to 24°C (Aditya et al., 2009), or 22-26°C (Ramachandran et al., 2016) in India, and 21-23°C in Pakistan (Hira et al., 2018). The study by Ramachandra and colleagues has shown that when the temperature drops below 17°C, the vector stops feeding (Ramachandran et al., 2016). Therefore, the ideal temperature extends the lives of mosquitoes and promotes their spread over geographic areas (Reinhold et al., 2018).

Increased rainfall during the monsoon season induces population growth; however, its excess or flood can destroy breeding sites and kill immature stages (Withanage et al., 2018). This becomes especially serious along an altitudinal gradient in the HKH countries. Similarly, enhanced relative humidity can increase vectors' oviposition and surviving ratio (Ramachandran et al., 2016). Regarding rainfall values, 18 mm to 500 mm was the optimum in India (Devi et al., 2020), Myanmar (Oo et al., 2011, 2020), and China (Wu et al., 2011), and notably with the relative humidity of 64% to 92% in India (Aditya et al., 2009; Borah and Bora, 2022), and Myanmar (Oo et al., 2020). The data were supported by a higher RA of *Aedes* spp. as observed during the monsoon than during the pre-monsoon and post-monsoon seasons in India (Selvan et al., 2020), Myanmar (Oo et al., 2020), and Nepal (Tuladhar et al., 2019), similar to the reports from Ivory Coast (Kpan et al., 2021). In comparison, the RA of *Aedes* spp. in the pre-monsoon season was higher than in the post-monsoon season in Nepal (Dhimal et al., 2014), and this was because of the suitable temperature in the pre-monsoon. Interestingly, the mean temperature, rainfall, and relative humidity were positively correlated with the RA of *A. aegypti* (Dhimal et al., 2015; Tuladhar et al., 2019). In contrast to this species, only mean temperature was positively correlated with the RA of *A. albopictus* (Dhimal et al., 2015; Tuladhar et al., 2019). Although *A. albopictus*, *A. aegypti*, and other *Aedes* species were reported in pre-monsoon and post-monsoon seasons, *A. aegypti* was not reported in pre-monsoon (Dhimal et al., 2015), indicating temperature, rainfall, and other factors control the existence and distribution of different *Aedes* spp. Therefore, temperature, rainfall, or humidity may act together in the mosquito's lifecycle and may be species-specific. In Bangladesh, the mean temperature and relative humidity were positively correlated with the RA of *Aedes* spp. (Ferdousi et al., 2015). The abundance of *Aedes* during monsoon was also associated with the rise in mean temperature, relative humidity, and average rainfall (Islam et al., 2021). The role of temperature and precipitation in *Aedes* spp. distribution in China has been studied in detail (Wu et al., 2011; Zhou et al., 2021) and showed the distribution of *A. albopictus* in areas with an annual mean temperature above 8°C and annual precipitation above 500 mm (Wu et al., 2011), and a higher level of oviposition at around 33°C (Zhou et al., 2021). In India, the distribution of *Aedes* spp. was shown to possess a strong positive correlation between maximum temperature and HI, CI, and BI. However, precipitation and humidity had a moderate positive correlation with these density parameters (Borah and Bora, 2022), indicating that the water temperature of 27-28°C and relative humidity of 84-88% were most appropriate for mosquito breeding (Selvan et al., 2020). Data also show that temperature, rainfall, and relative humidity influence *Aedes* distribution in Myanmar (Oo et al., 2020). Evaluations of temperature, rainfall, humidity, and altitude in the *Aedes* distribution were made in Pakistan; subsequently, the optimum temperature, humidity, and rainfall were 25°C, 80%, and 15 mm, respectively, in Lahore (Manzoor et al., 2020), the best propagation of *A. albopictus* in Swabi occurred at a temperature of 21-23°C and elevation of 250-500 m asl (Hira et al., 2018). In the same way, the optimum temperature range for *A. aegypti* was found 17-19°C and preferred an elevation between 800-1600 m asl in Swat (Fatima et al., 2016).

In addition to temperature, humidity, and rainfall, the physiochemical factors of water and vegetation play an important role in the survival, development, and distribution of *Aedes* spp. Studies from Bangladesh have shown that alkalinity, chemical oxygen demand, dissolved oxygen, total hardness, turbidity, water depth, and water temperature have determining roles in the lifecycle of *Aedes* (Bashar et al., 2016). However, how these factors affect the immature stages of the *Aedes* spp. of different HKH landscapes has been lacking.

Interestingly, various vegetation factors and *Aedes* density in the HKH have been discussed in different studies. For example, the percentage of vegetation

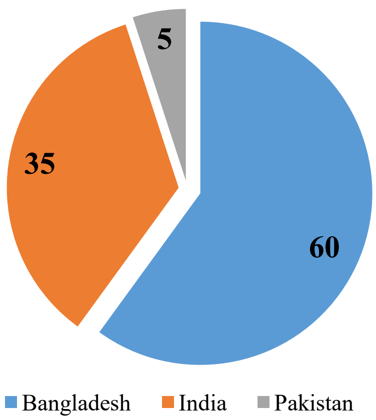

Fig. 3. Vegetation factors (N = 60) that influence development of *Aedes* spp.

factors decreased in the following order: Bangladesh, India, and Pakistan, respectively (Fig. 3). Bamboo stumps, plant axils, tree holes, leaves, shade, and coconut shells were factors commonly reported from Bangladesh (Ferdousi et al., 2015; Bashar et al., 2016; Islam et al., 2019; Rahman et al., 2021) and India (Das et al., 2015; Shriram et al., 2017; Vijayakumar et al., 2014), and only tree holes were reported from Pakistan (Manzoor et al., 2020). Although *Aedes* spp. prefer the breeding area without vegetation (61%, n= 49), the presence of shade had a significant association (96%, n=49) (Rahman et al., 2021), indicating that direct sunlight might not be favorable for immature forms. It was also crucial that immature *Aedes* spp. were recorded inside bamboo stumps (50%, n=42) in Darjeeling (Aditya et al., 2009), the Himalayan part of India at 2130m asl, indicating bamboo to be one of the critical habitats for breeding of these insects (Barraud, 1934; Bhat, 1975; Devi and Jauhari, 2004; Aditya et al., 2008, 2009) not only in India but also throughout all over the HKH regions which are rich in bamboo varieties (IDRC, 1996). Similar situations exist for other vegetation factors, which serve as the best milieu for the *Aedes* lifecycle.

Key questions for future research

Understanding the spatial and temporal dynamics of the density and distribution of *Aedes* vectors and identifying the relationship between *Aedes* vectors and climatic, physiochemical, anthropogenic, vegetation, and altitudinal variables is essential for targeting surveillance and control strategies in HKH countries. In these contexts, the following topics will be critical for further research:

- What is the effect of the change in behavior and survival pattern of the *Aedes* spp. when their mature forms and immature forms like eggs, larvae, and pupae are brought from low to high altitude or high-temperature areas to low-temperature areas?
- What will be the seasonal density of mature and immature forms concerning altitude, seasons, and climatic factors in all HKH countries in situ?
- How do anthropogenic and environmental factors determine the survival, multiplication, and distribution of *Aedes* spp. in the HKH countries?
- What is the evidence-based role of vehicles, planes, or lifters in distributing *Aedes* spp. along roads, air, or rivers within the HKH countries?
- Are vectors modified at molecular levels along the altitudinal gradient? Are there any changes in the microbiota composition, e.g., *Wolbachia* spp. and other species? How does their presence affect the disease-transmitting capacity of *Aedes* spp. along the gradient?
- What is the prediction data regarding the distribution of *Aedes* spp. and their causal association with dengue, chikungunya, and other VBDs in the HKH countries?

In conclusion, climatic, vegetation, and anthropogenic factors are central in regulating *Aedes* distribution in the HKH countries. The situation is critical as the temperature of the HKH countries is increasing by at least 1.8°C with a higher precipitation rate (Singh, 2011; "Global Warming Effects", 2019; ICIMOD, 2019), of the world by at least 1.5°C currently (ICIMOD, 2019), and by 1.0–3.5°C by 2100 (Watson et al., 1996). Besides the direct contributions of anthropogenic, demographic, vegetative, and physiochemical factors, *Aedes* spp. are greatly influenced by climatic factors that are either naturally favorable or regulated by climate change. In these contexts, changes in the climatic pattern can influence vectors and modify their habitat, ecosystem, and behavior; therefore, in the context of the HKH countries, there is a possibility of expansion of the altitudinal distribution ranges of *Aedes* spp. Although *Aedes* surveys in the HKH have a long history, the progress toward their control is naive. Therefore, knowing species-specific behavioral, ecological, and biological factors will help us understand their disease-causing characteristics. Data mining and open-access *Aedes* prediction modeling will best suit this context. Further studies of extensive nationwide seasonal field surveys from low altitude to high altitude or vice versa coupled with molecular taxonomy will generate *Aedes* prediction data. The data will be subsequently critical in the early detection and design of prevention strategies for *Aedes*-borne diseases all over the HKH countries.

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CONFLICT OF INTEREST

No conflict of interest.

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