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Original article

Prevalence of dengue virus in Haripur district, Khyber Pakhtunkhwa, Pakistan

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ABSTRACT

Dengue virus (DENV) has caused about 12 large outbreaks in Pakistan, resulting in 286,262 morbidities and 1108 deaths. The most affected province is Khyber Pakhtunkhwa (KP). This study was conducted to determine the average DENV prevalence in different areas of the Haripur endemic district of KP and the causing factors of DENV.

Methods: This work was a cross-sectional study that was performed in the DENV endemic district Haripur. A total of 761 individuals were included in this study. The data were categorized according to sex, age and symptoms (like fever, body aches, bleeding, and skin rash). For data analysis, SPSS 23 version was applied. ArcGIS version 10.8 was used to map the study area.

Results: In this study, there were 716 confirmed cases of DENV fever, including 421 males (58.8%) and 295 females (41.2%). The most affected age range, 16–30 years, reported by 301 (42.0%), was followed by 31–45 years, 184 (25.7%), above 46 years, 132 (18.4%), and 0–15 years, 99 (13.8%). The positive IgG cases were 581(81.0%). Those whose age ranges from 1 to 15 years 82 (8.7%) cases, 16–30 years 244 (34.1%), 31–45 years 156 (21.8%), above 46-year age 99 (13.8%) cases. In addition, this suggests that those between the ages of 16 and 30 are at the highest risk for DENV infection. However, this might be the fact that individuals in this age range are more likely to be out in the environment, making them more vulnerable to the virus.

Conclusion: Over the past ten years, DENV fever has become increasingly prevalent in Pakistan. The risk is substantially higher for males. Dengue outbreaks hit those between the ages of 16 and 30 the hardest. The proper monitoring and assessment of DENV are necessary for prevention and controlling the disease. Disease surveillance includes identification and molecular characterization of infected persons and monitoring mosquito populations in high-risk locations for the purpose of vector surveillance. In order to assess the community's willingness to participate in DENV preventive efforts, behavioral impact surveillance is also necessary.

Introduction

Dengue virus (DENV) is a viral infection spread to humans by infected mosquito bites [1–3]. The infection is mostly spread by the Aedes aegypti mosquitos and, to a lesser extent, by the Aedes albopictus mosquitos [4,5]. There are four DENV serotypes [6], and the virus can happen up to four times. Severe dengue is a major factor in serious illness and death in some Latin American and Asian nations [7]. DENV has no specific cure medications [5]. Early detection of the infection and the availability of adequate medical treatment can minimize mortality rates to fewer than 1%. DENV is widespread in tropical and subtropical regions across the globe, mainly in urban and semi-urban areas. The worldwide incidence of infection has grown rapidly, with about half of the world's people at risk. Even though 100–400 million infections are thought to happen every year, the vast majority are mild and cause no symptoms [5].

From September to December 2019, Pakistan had 53498 DENV cases and 95 fatalities. From January 1 to November 25, 2021, 48906 cases, including 183 deaths, were reported in four provinces: Khyber Pakhtunkhwa, Punjab, Balochistan, Sindh, and the federally controlled

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ICT and AJK autonomous regions. Khyber Pakhtunkhwa, a province that shares borders with Afghanistan, had the second most cases, with 10223, or 21% of all cases, and ten deaths occurred [8].

Based on the severity of the symptoms, dengue fever can be divided into three primary stages: mild dengue fever, severe dengue fever, and fatal dengue fever. Recent studies show that dengue virus infection is common in Pakistan after the monsoon [9,10]. From 1994–2011, the DENV disease caused numerous outbreaks in Pakistan. The infection was first testified in Pakistan in 1982 when 12 patients out of 174 were affected [11]. In 1994, the first signs of DENV were seen in Karachi. In August 2013, the first case of DENV in Khyber Pakhtunkhwa was reported in Swat. Travelers spread the DENV from one place to another. Based on data from 2013, Khyber Pakhtunkhwa had the most people with dengue, with 3177 cases reported [12]. In Swat, 5569 people contracted DENV between August 2013 and November 2016, and 37 died [13]. According to research, a humid or warm atmosphere facilitates mosquito vector breeding [12]. Several studies have also identified risk factors for DENV. Vectors' favorite breeding locations have been discovered as little pools of stagnant water in plants, tires, and ditches. Long-sleeved clothes, mosquito repellent, and vector control (residual insecticide spray and thermal fogging) have been found to be the best ways to avoid getting DENV fever [14].

In light of the infection's severity, as mentioned above, the current study is intended to contribute significantly to public health officials' efforts to contain and eradicate the infection. Most of the high-endemic districts in KP province are currently experiencing DENV fever. One of them is the district of Haripur. This study was carried out to determine the average DENV prevalence in different areas of the Haripur district and causing factors of DENV infection.

Methods and materials

Study design, area and period

This was a cross-sectional study that was conducted in the district of Haripur with DENV endemic (Fig. 1). The estimated total study area was 1725 kilometer square. Haripur has a humid subtropical climate with no dry season and is located at an elevation of 509.24 m (1670.7 feet) above sea level. The yearly temperature in the district is 19.6 ºC (67.3 ºF), which is − 1.3% lower than the national average. Haripur gets about 131.7 millimeters (5.2 in.) of rain annually and has 145.5 rainy days (39.9% of the time).

The investigation was carried out throughout August and November 2021, corresponding to the peak transmission season for DENV. Due to inadequate management efforts, the prevalence of dengue fever has increased dramatically in KP, Pakistan. This rise of infections can be attributed to several factors, including floods, largely socioeconomic, a lack of resources, and a lack of information on how dengue transmission occurs [15–17]. Before carrying out this investigation, the appropriate consent was received from the relevant authorities and the patients who engaged in this study; the data from the patients were gathered using a questionnaire.

Sample selection

The main District Headquarters Hospital (DHQ), Haripur, offering dengue laboratory tests, was surveyed. A total of 761 individuals were included in this study. The data were categorized according to sex, age and symptoms (like fever, body aches, bleeding, and skin rash).

Data analysis

For data analysis, SPSS 23 version was used. For continuous variables, means and standard deviations (SD) were calculated, and for categorical variables, frequencies, and percentages were also calculated. The chi-squared test was used to investigate the relationship between categorical variables and the *p*-value smaller than 0.05 was regarded as statistically significant.

Laboratory test

Fresh blood was collected from patients about 2 ml in an Ethylene Diamine Tetraacetic acid (EDTA) tube. Diagnosis of dengue virus infection in the laboratory was based on an immune chromatography technique (ICT) commercially available standard diagnostic (SD ICT) kit. After adding 20ul of whole blood to the sample well, the well was examined after 10 min for the presence of nonstructural protein NS1, immunoglobulin M (IgM), and immunoglobulin G (IgG) in the T test line and the C control line, respectively. This was done to ensure that the testing was carried out correctly. A positive NS1 result indicates the presence of DENV in the body; IgM and IgG are utilized to confirm acute and chronic inflammation in dengue infection.

Ethical considerations

The Institutional Review Board of The University of Haripur, Pakistan, granted ethical approval for the study. The DHQ Hospital in Haripur, Pakistan, granted the permission to perform the research and provided the required information.

Results

This study had 716 confirmed cases of DENV fever, including 421 men (58.8%) and 295 women (41.2%) Fig. 2. The data is reported in terms of frequencies, most prevalent average group, and statistical significance difference at $p < 0.05$ for each variable. The ages of all confirmed cases ranged from 0 to over 60 years old, as shown in Table 1. The age group 16–30 years was the most suffering, accounting for 301 (42.0%), followed by 31–45 years at 184 (25.7%), over 46 years at 132 (18.4%), and 0–15 years at 99 (13.8%) Fig. 3.

Patients with confirmed IgG (the initial antibodies to emerge after primary dengue infection) or IgM-positive findings were tested for the presence of active DENV. The confirmed cases are 716, and 581 (81.0%) have positive IgG. Those aged 1–15 account for 82 (8.7%) instances, those aged 16–30 for 244 (34.1%), those aged 31–45 for 156 (21.8%), and those aged beyond 46 for 99 (13.8%). This suggests that the age range between 16 and 30 years has the most prominent risk for the prevalence of DENV infection.

The fever symptoms in positive dengue cases are 421 (58.8%) in males while 295 (41.2%) are females; body ache symptoms in positive dengue cases are 421 (58.8%) in males while 293 (40.9%) in females. 2 (0.3%) did not show body ache symptom. Skin rashes in dengue infection are 581 (80.0%) cases. Bleeding and skin rashes are not significant in positive cases in both males and females. The correlation of DENV symptoms is more likely in patients with fever and body aches (Table 2).

Discussion

DENV is a rapidly spreading pandemic risk in many parts of the globe. A virus of the Flaviviridae family causes dengue, and there are four different but closely related serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) [18]. This research aims to identify the prevalence of dengue infection throughout the regions that make up the Haripur district and the variables that contribute to its spread. In 1982 DENV was initially detected in Pakistan [19]; nevertheless, DENV has developed into a very critical vector-borne virus since 2006. Humans become the virus's major vectors, multipliers once infected, providing a viral reservoir for uninfected mosquitos. Controlling

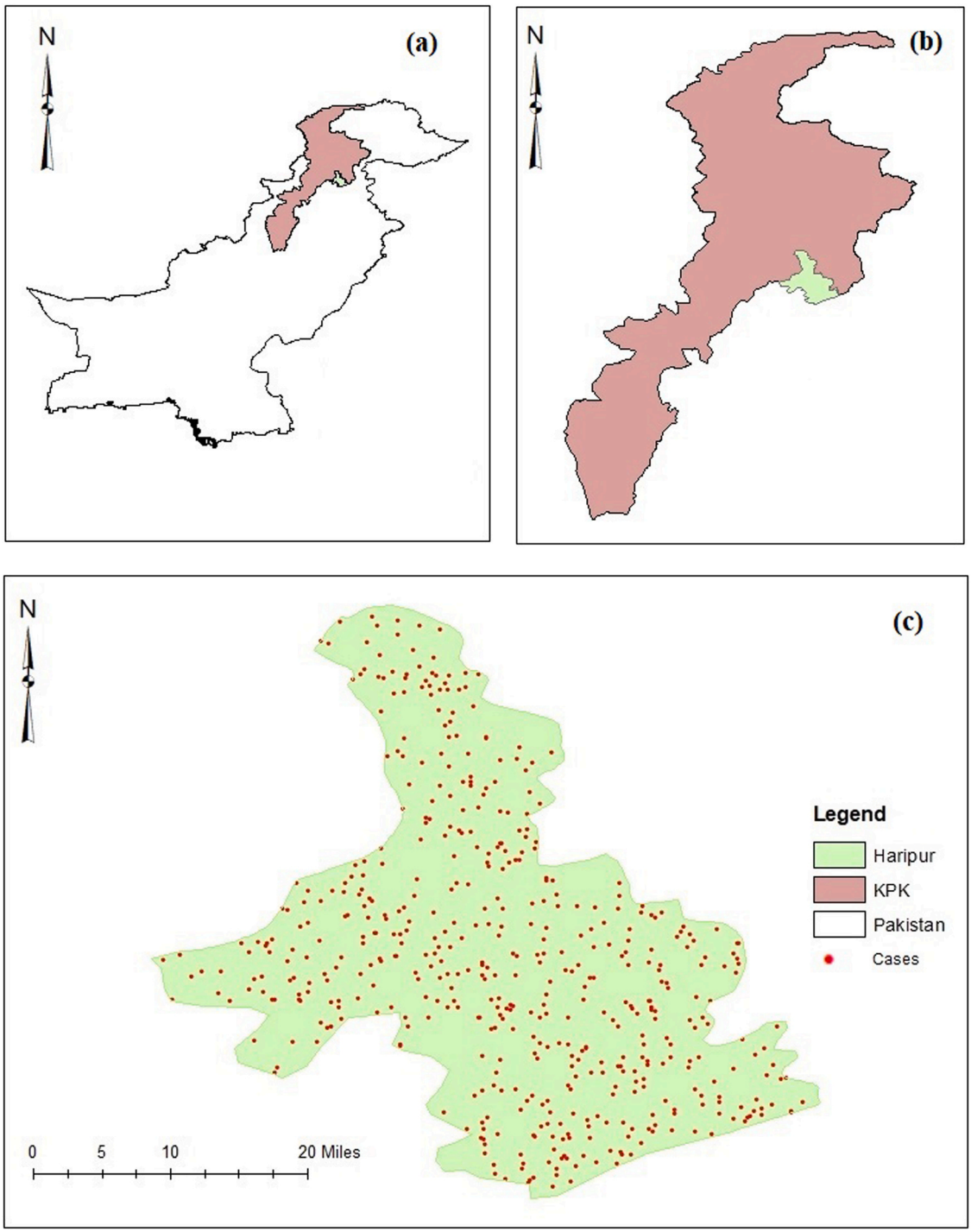

Fig. 1. Study area map.

mosquito populations is the primary strategy for preventing DENV spread [20]. Several outbreaks have occurred in the country over the last decade, infecting thousands of people and killing some parts of them [21–29]. Over 50,000 individuals died due to a severe illness in Punjab in 2011, a populous province with a border with KP. According to the data published by the WHO, the province of KP saw yet another major infection outbreak in the year 2013, with an estimated 8546 cases, including 33 fatalities in the Swat region, with the most common serotypes were 1, 2, and 3 [30–33].

The predominant variant of the dengue virus in Pakistan is identified as DENV-2, as per research findings [24]. However, it is crucial to acknowledge that the prevalence of the virus or its subtypes can shift over time and across different geographical areas within the nation. Another study carried out at the National Institutes of Health (NIH) in Islamabad analyzed 343 human serum samples in 2022, all of which tested positive for the dengue virus NS1. Upon evaluating the serotypes of these samples, it was found that the three most widespread serotypes were DENV-2 (62%; n = 183), DENV-1 (37%; n = 109), and DENV-3 (0.3%; n = 1) [34].

Since Pakistan did not have enough diagnostic and monitoring facilities, it is likely for the virus to be widespread those areas. Real dengue cases might be underreported because most dengue infections are self-managed and either mild or asymptomatic. A significant number of instances are also incorrectly diagnosed as other

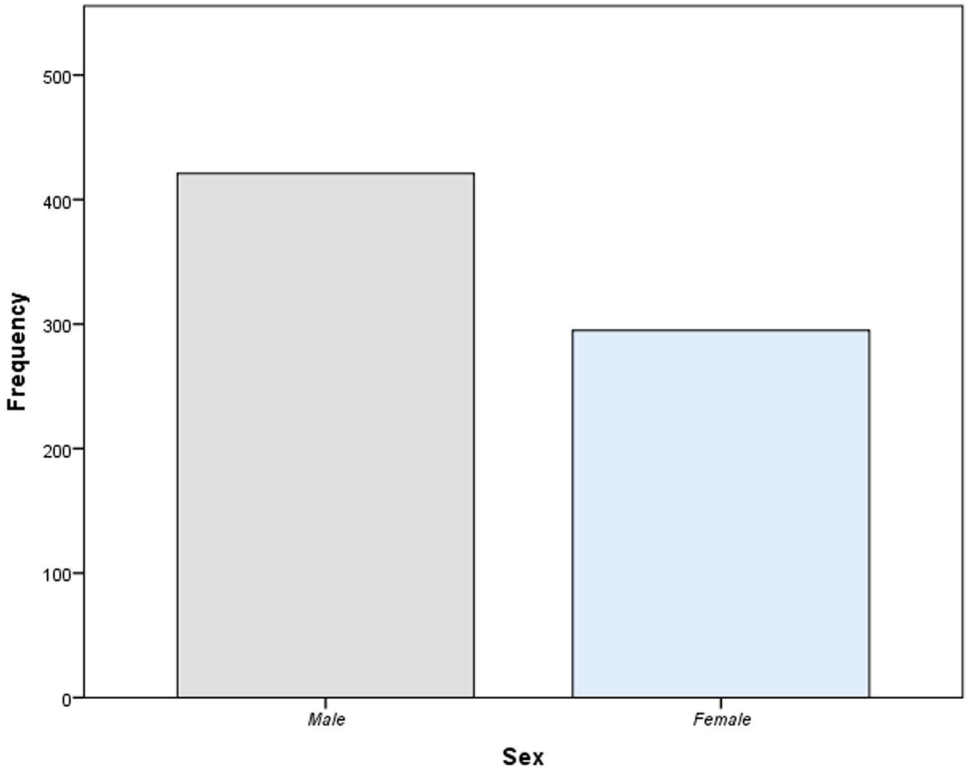

Fig. 2. Gender-wise distribution of DENV.

Table 1
Distribution of confirmed DENV cases Gender and Age wise.

Variables	Total (n = 716)	Percentage %	Average (Mode)	p-value
Male	421	58.8	Male	0.000
Female	295	41.2		
Age Group				
0–15	99	13.8	Age Group	0.000
16–30	301	42.0	[16–30]	
31–45	184	25.7		
> 46	132	18.4		
Travel History				
Yes	12	1.7	No	0.000
No	704	98.3		

febrile diseases. DENV fever is quite common among those who travel to tropical and subtropical areas. The likelihood of a traveler contracting a viral illness is, in most cases, determined by the risk factors that they are exposed to and the prevalence of the virus in the area. There is currently no prevention available for dengue fever. On the other hand, nosocomial transmission might occur in areas where dengue fever is endemic. This may be of utmost significance for medical staffs who treat people suffering from dengue hemorrhagic fever [35].

Because the causes of the vast majority of diseases are frequently found in this province, residents of KP are at an increased risk for a wide variety of fatal diseases. Wars, the most recent of which was waged against terrorism, have wreaked havoc across the nation and torn it to shreds. As a direct consequence of this, there have been several epidemics of illnesses that cause death in individuals. The spread of many diseases has been halted, and the negative impacts of those diseases have been mitigated, yet combating a fatal illness requires careful preparation. A successful prevention plans are able to stop the virus's transmission by getting rid of risk factors or significantly cutting down them. Even though there has been consistent progress to improve the quality of the province's healthcare system, there are still a great deal of issues requiring resolution.

The Pakistani Ministry of Health has instituted several interventions, including vector surveillance and control efforts. All the provinces have set up free diagnostic and clinical management services for the cases [36].

Effective medical care systems can stop the spread of infections and save lives, reducing fatality rates from 20% to < 1%. Infected environments trigger viral outbreaks. On July 19, 2017, over 95,000 people were affected by DENV during the pandemic. According to the WHO, as of October 24, 2017, there were 88,002 suspected cases, 19,002 confirmed cases, and 56 deaths (CFR 0.3%) in Peshawar, the capital of KP's province.

In this study, there were 716 confirmed cases of DENV fever, with 421 men (58.8%) and 295 women (41.2%). The age group 16–30 years suffered the most (301 (42.0%)), followed by 31–45 years (184 (25.7%)), over 46 years (132 (18.4%)), and 0–15 years (99 (13.8%)). Consistent with the previous studies, individuals aged 16–30 were the most prevalent DENV fever from 2013 to 2015, followed by those aged 31–45 [37,38]. The male infection rate was higher than females, consistent with previous findings from KP and neighboring countries (India and Bangladesh) studies [37, 39, 40]. This epidemic spreads from Swat to nearby districts such as Malakand, Kohat, Mansehra, lower and upper Dir, and Peshawar, and then to other districts such as Mardan, Nowshera, and Swabi. According to the Dawn News, 11,685 infected cases were registered in Peshawar on November 7, 2017, with seven deaths recorded on August 22, 2017. Until August 25, 2017, the total number of DENV patients in Mardan was 12. In Nowshera, 18 cases have been reported since August 22, 2017.

Fever caused by the DENV virus is most common in low-income urban areas. However, it can also be found in the suburbs, rural areas, and even more wealthy districts of tropical and subtropical regions. Comorbidities, blood products that have been contaminated

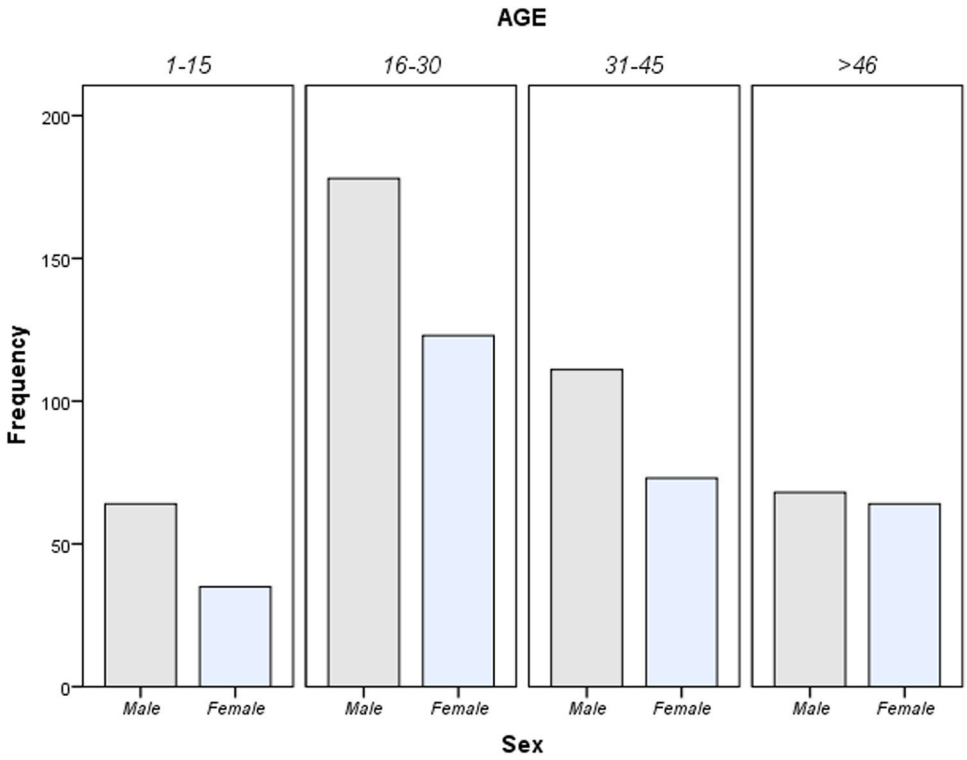

Fig. 3. Age-wise distribution of DENV-infected patients.

Table 2
Clinical features for DENV fever among respondents in Haripur district, Pakistan.

Variables	Gender	Clinical features		P-value
		Yes (%)	No (%)	
Fever	Male	421 (58.8)	0	0.000
	Female	295 (41.2)	0	
Body ache	Male	421 (58.8)	0	0.169
	Female	293 (40.9)	2 (0.3)	
Bleeding	Male	0	421 (58.8)	0.000
	Female	0	295 (41.2)	
Skin rashes	Male	0	421 (58.8)	0.000
	Female	0	295 (41.2)	

with infection, and the presence of several risk factors are all relatively frequent in Pakistan. Several elements might contribute to an area's susceptibility, including the intensity of the rainfall, the temperature, the relative humidity, the amount of urbanization, and the efficiency of the vector control services.

As one of the suggestions for combating the illness, the local population should be aware of the variables that put them at risk for DENV infection and the possibly deadly consequences that can arise from the infection. Seminars and workshops on awareness should be organized to educate the general population. Primarily, healthcare professionals must be recruited to launch a broad campaign that informs people how to stay safe from dengue fever and avoid contracting it in the first place. This is because those who work in healthcare have specific credentials for doing these tasks.

There are some limitations to the study. It was carried out in the endemic district of Haripur in Khyber Pakhtunkhwa province. Therefore, the results cannot be generalized to the entire country. Also, because the study is cross-sectional in nature, we can't assume that the link between risk factors and DENV prevalence is caused by one or the other. Another study should be conducted over a longer period of time to assess seasonal variation and other risk factors for DENV prevalence in this district.

Conclusion

DENV fever has become increasingly common in Pakistan over the last decade. There were 716 confirmed cases of dengue fever in our study, with 421 males (58.8%) and 295 females (41.2%). The age group 16–30 years 301 (42.0%) suffered the most, followed by 31–45 years 184 (25.7%), over 46 years 132 (18.4%), and 0–15 years 99 (13.8%). An effective monitoring and evaluation strategy is required to prevent and combat the spread of DENV. This involves tracking mosquito populations in high-risk areas as part of vector surveillance and the identification and genetic characterization of infected human cases as part of disease surveillance. Monitoring the impact of people's behaviors is also vital if one is interested in determining whether or not the community is adopting and supporting preventative measures against the spread of DENV.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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