

#### **Review Article**

# Burden and distribution of dengue infection in Pakistan (2000-19): a review

Carga e distribuição geral de infecção por dengue no Paquistão entre 2000 e 2019: uma revisão

A. Khattak<sup>a</sup> (0), S. Khan<sup>a\*</sup> (0), I. Ali<sup>b.c</sup> (0), A. Gul<sup>a</sup> (0), M. N. Khabir<sup>a</sup> (0), B. Javed<sup>a</sup> (0), Ayesha<sup>a</sup> (0), M. Adnan<sup>a</sup> (0), S. N. Khan<sup>d</sup> (10) and S. Attaullah<sup>e</sup> (10)

<sup>a</sup>University of Peshawar, Department of Zoology, Khyber Pakhtunkhwa, Pakistan

<sup>b</sup>Gulf University for Science and Technology, Center for Applied Mathematics and Bioinformatics, Mubarak Al-Abdullah, Kuwait <sup>c</sup>COMSATS University, Department of Biosciences, Islamabad, Pakistan

<sup>d</sup>Kohat University of Science and Technology, Department of Zoology, Kohat, Pakistan

eIslamia College Peshawar, Department of Zoology, Peshawar, Pakistan

#### Abstract

The goal of this study is to review the overall prevalence, burden, and distribution of the dengue disease in Pakistan from 2000 to 2019. Literature was searched using different search engines like Google scholar, PubMed, etc. providing the keywords "Dengue disease/infection, Dengue virus, DENV, DF/DHF/DSS Pakistan". All the published research papers/reports on the dengue virus over the period 2000 to 2019 were studied and selected data were summarized using MS Excel for windows such as total cases, age wise, gender, DENV serotype distribution, total DHF, and DSS patients. The literature providing insufficient data was excluded. The total number of cases reported during 2000-19 were 201,269. The maximum number of cases during the mentioned literature survey period was reported in Khyber Pakhtunkhwa (KP) (23.3%) followed by Punjab (3.8%) and Sindh (1.9%). The majority of dengue-infected cases were reported as Dengue fever (74.4%) followed by DHF (24.1%) and DSS (1.5%). Overall the deaths during the mentioned literature survey were 1082, of which the maximum mortalities were reported from KP (N=248) followed by Punjab (N=220).

DENV remains a major public health problem in Pakistan and seems to remain endemic for a long time. The total prevalence of dengue infection is increased accordingly with time from 2000 to 2019. Moreover, all the four serotypes exist in Pakistan with increased mortalities.

Keywords: dengue disease/infection, dengue virus, DENV, DF/DHF/DSS Pakistan.

#### Resumo

 $\bigcirc$ 

A literatura foi examinada através de diferentes mecanismos de pesquisa, como *Google Acadêmico*, *PubMed*, etc., fornecendo as palavras-chave "Dengue disease/infection, Dengue virus, DENV, DF/DHF/ DSS Pakistan". Todos os trabalhos/relatórios de pesquisa publicados sobre o vírus da dengue no período de 2000 a 2019 foram analisados e os dados selecionados foram coletados e resumidos usando o MS Excel para janelas como total de casos, idade, sexo, distribuição de sorotipos, total de DHF e pacientes com DSS. A literatura que forneceu dados insuficientes foi excluída. O número total de casos notificados de 2000 a 2019 foi de 201.269. O número máximo de casos durante o período de levantamento da literatura mencionado foi relatado em KP (23,3%), seguido por Punjab (3,8%) e Sindh (1,9%). A maioria dos casos de infecção por dengue foi relatada como Dengue (74,4%), seguida por FHD (24,1%) e DSS (1,5%). No geral, as mortes durante a pesquisa de literatura mencionada foram 1.082, das quais as morbidades máximas foram relatadas em KP (248), seguidas por Punjab, com um total de 220 mortes. O DENV continua sendo um grande problema de saúde pública no Paquistão e é considerado endêmico agora e provavelmente permanecerá por muito tempo. A prevalência total de infecção por dengue foi aumentada conforme a pesquisa de literatura publicada entre 2000 e 2019. A mortalidade por DENV também aumentou. Todos os 4 sorotipos, bem como em várias formas, existem no Paquistão.

Palavras-chave: dengue/infecção, vírus da dengue, DENV, DF/DHF/DSS, Paquistão.

\*e-mail: sanaullahkhan@uop.edu.pk Received: September 19, 2022 – Accepted: February 22, 2023

This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### 1. Introduction

Dengue is an infectious disease caused by the dengue virus (DENV) of the family *Flaviviridae* through *Aedes* mosquitoes. DENV is a sense RNA virus of 11kb having three structural proteins (capsid, a precursor of the membrane, and an envelope protein), and seven non-structural proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5). The virus is classified into four different serotypes known as DENV-I, DENV-II, DENV-III, DENV-IV (Iqtadar et al., 2017a; Rafique et al., 2015; Ali et al., 2016; Koo et al., 2013).

Dengue infection can be febrile known as Dengue Fever (DF) that may lead to Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS) in case of secondary infection of different dengue serotypes (Khan et al., 2007). The symptoms of DF are mild while that of DHF are severe and can be fatal (Yousaf et al., 2018; Hasan et al., 2013). DF is prevalent in many countries of Asia, Africa, and America. The DF occurs about 50-100 million cases per year while that of DHF is reported about 0.2-0.5 million cases annullay worldwide with a total death rate of 2.5% (Ali et al., 2016; Yousaf et al., 2018). According to WHO, about 2.5 billion people are at risk of dengue (Khan et al., 2010).

In Pakistan, all four different serotypes have been reported in different outbreaks (Haroon et al., 2019). DENV-I, DENV-II, and DENV-III, DENV-IV were found that co-circulated in outbreaks in 1998 and 2006 respectively while in the 2011 the leading serotype reported was DENV-II (Rehman et al., 2017). Of the four serotypes, in Pakistan the predominant types were DENV-I and DENV-II (Khan et al., 2007). The serotypes distribution in Pakistan in not even and in dengue outbreak, DENV-II was reported in 1994, subsequently in 2005 and 2006 DENV-II and III were found that leads to about 52 deaths (Raza et al., 2014). A large number of dengue cases were reported during 2005-06 with a majority of cases from Karachi where about 37 out of 40 deaths were reported Sindh province only (Khan et al., 2007). An overwhelming dengue outbreak was reported in 2011 from Lahore where >23000 individuals were admitted

to various hospitals and about 365 deaths were reported (Ali et al., 2016). A study reported >50 thousand dengue cases in Lahore (2011) and about 8546 cases with 33 deaths (2013) in Swat (Haroon et al., 2019). The situation could be worsening as there is no vaccine available that cover all dengue serotypes and no antiviral treatment yet (Fatima et al., 2011; Iqtadar et al., 2017b).

Dengue epidemics are reported at different times from various parts of Pakistan with a large number of morbidities and mortalities but lack of comprehensive data analysis the epidemiology of dengue in the country is unclear. This review analyzed a 20-year (2000-19) data and highlights the prevalence of dengue, serotype distribution, and frequency of DF, DHF and DSS.

# 2. Methods

#### 2.1. Search strategy and inclusion/exclusion criteria

The data was searched through different search engines (Google scholar, PubMed etc) providing the keywords "Dengue virus, Dengue infection/Serotypes, DHF/DSS Pakistan. All the published research articles/reports on the dengue virus/infection from 2000 to 2019 were downloaded and selected for this study. The data were extracted and summarized using Microsoft Excel for Windows for different variables like total positive cases, patients' age, gender, serotype distribution, DHF and DSS patients, death cases.

The general review of dengue, single case studies and literature with insufficient information were excluded. Moreover, articles regarding KAP (knowledge, attitude, practices) studies, treatment, diagnosis, control and prevention, seasonal effects and dengue vectors were also excluded. Articles with same data but different aspects were considered once. The detail of articles included in this study are summarized in Figure 1.



Figure 1. Result of literature survey.

# 2.2. Geography

Pakistan is situated in temperate zone with a total area of about 79.61 million hectares (Ahmed et al., 2007). The country has importance in South Asia and creates links among different regions of the world. Pakistan's border lies with two highly populated states China in the northeast and India in the east. Afghanistan and Iran lie in the west and southwest consequently. The Arabian Sea paved the way for the gulf region and the Middle East located in the south of Pakistan (Chaudhry et al., 2009; Daud et al., 2017; Qureshi et al., 2003). The climate of the country is varied due to topography. Furthermore, due to climate change and rainfall, the chances of dengue infection increases as the availability of suitable breeding sites for the vector such as *Aedes aegypti* and *Aedes albopictus* are widely available (Atique et al., 2016) (Figure 2).

# 3. Results

# 3.1. Overall prevalence

A total of 201269 suspected cases were reported from Pakistan in the selected research articles (77) included in this study and 62780 were found positive for dengue infection. The overall prevalence was 31.2%. The data were grouped into two decades i.e. decade I (2000-2010) with 28 articles and decade II (2011-2019) with 49 articles. One of the articles i.e. Koo et al. (2013) contained data of 2006 to 2011, the data of 2011 was added in decade II. The total cases reported were 10.5% and 89.5% in during decade I and decade II respectively. It is found that the number of dengue cases were increased in decade II as compared to decade I i.e. from 21151 to 180118. The incidence rate of dengue infection was constantly high in decade II. Of the total dengue cases 31.2% were confirmed by serological or PCR methods except a few that was declared positive through WHO criteria for dengue fever (Table 1). Two (2) of the research articles with an unknown year of study were added to the decade in which the articles were published (Rafique et al., 2017; Parkash et al., 2010).

Male were more infected [38915 (62%)] as compared to female [17541 (27.9%)] (References are given in Province wise distribution). In some articles the gender distribution was not given therefore the number of male and female are not equal to the total confirmed value. The cases reported during decade II were higher as compared to decade I (Table 1).

# 3.2. Province-wise distribution

The dengue cases were analyzed provinces wise and the maximum number of cases were reported from Khyber Pakhtunkhwa (KP) (23.3%) followed by Punjab (3.8%) and



Figure 2. Map of Pakistan showing various geographical locations.

Sindh (1.9%) (Table 2). The minimum number of cases (N=38) were reported from KP (Usman et al., 2011) while the maximum number of cases (N=3342) were reported from Sindh during decade I (Khan et al., 2007, 2008; Hasan et al., 2013, Ahmed et al., 2008; Riaz et al., 2009; Shamim, 2010; Wasay et al., 2008a, b; Khalil et al., 2014; Baqi et al., 2010; Ali et al., 2011; Jahan et al., 2011). Of all the cases from KP, high number of cases (N=22740) were reported from district Swat during 2013 which are 48.6% of the total dengue cases reported from the province (Ali et al., 2016; Khan and Khan, 2015; Chaudhry et al., 2017; Lutfullah et al., 2017; Suleman et al., 2016; Khan et al., 2017a; Khan, 2018; Khan et al., 2018; Khan and Bari, 2018). Similarly, 58.5% (4475/7649) of the total cases reported from Punjab were from the capital city Lahore only during 2011 (Iqtadar et al., 2017b; Khan et al., 2013a, b; Ahmed et al., 2013; Rashid et al., 2012; Mahmood et al., 2013; Saqib et al., 2014a, b; Asghar and Farooq, 2011; Idrees et al., 2012; Raza et al., 2017; Naeem et al., 2018; Assir et al., 2014a, b; Sheikh et al., 2012; Chaudhry et al., 2018).

Of the total dengue cases, 15124 were confirmed for dengue infection from multiple cities of the country including Islamabad, Rawalpindi, Lahore, Faisalabad, Peshawar, Karachi (Rafique et al., 2015, 2017; Ali et al., 2016; Koo et al., 2013; Khan et al., 2010; Atif et al., 2016; Munir et al., 2014; Suleman et al., 2017a; Shahid et al., 2019; Zamir et al., 2012; Zafar et al., 2010, 2013; Bhatti et al.,

Table 1. Prevalence of dengue positive cases during 2000-19.

2015), Azad Jammu and Kashmir (Tariq et al., 2006) and Swat (Ali et al., 2016).

#### 3.3. Prevalence of DF, DHF, and DSS

The data regarding the DHF/DSS were available in 39 articles (Ahmed et al., 2008, 2013; Asghar and Farooq, 2011; Assir et al., 2014a, b; Baqi et al., 2010; Humayoun et al., 2010; Hasan et al., 2013; Iqtadar et al., 2017a; Ishtiaq et al., 2018; Khalil et al., 2014; Khan et al., 2007, 2008, 2010, 2013a, b, c, 2017a, 2018; Khurram et al., 2014; Koo et al., 2013; Mahboob et al., 2012; Mahmood et al., 2009, 2012, 2013; Munir et al., 2014; Parkash et al., 2010; Perveen et al., 2016; Quadri et al., 2015; Rafique et al., 2015; Rashid et al., 2012; Raza et al., 2014, 2018; Rehman et al., 2017; Riaz et al., 2009; Saqib et al., 2014a, b; Shamim, 2010; Usman et al., 2011; Wasay et al., 2008a, b). The majority of dengue-infected cases were reported with Dengue fever (74.4%) while DHF was reported in 24.1% cases (N=5022) and DSS in 1.5% (N=309) cases. The DHF cases were increased from 1162 in decade I to 3776 in decade II while the DSS cases were decreased from 700 in decade I to 225 in decade II (Table 3, Figure 3). The prevalence of DF was high as compared to DHF/DSS.

# 3.4. Serotype distribution

In Pakistan, all four serotypes of DENV are reported. Data from 2000-2005 are not known while the prevalent

Year of study	Number of accor (N)	Confirmed cases N(%)	Gender		
	Number of Cases (N)	Commined cases N (%) =	Male N (%) Female N (%)		
2000- 2010	21151	9096 (43.0)	4897 (53.8)	2813 (30.9)	
2011-2019	180118	53684 (29.8)	34018 (63.4)	14728 (27.4)	
Total	201269	62780 (31.2)	38915 (62.0)	17541 (27.9)	

Table 2. Province wise distribution of total confirmed dengue cases (2000-19).

		Province / territory											
Year of study (N)	Punjab		Sindh		КР	KP Az		Azad Kashmir		Twin city		Miscellaneous	
	N (%)	+ve	N (%)	+ve	N (%)	+ve	N (%)	+ve	N (%)	+ve	N (%)	+ve	
2000-10 (N=21151)	1208 (5.7)	906	3342 (15.8)	2962	38 (0.2)	38	52 (0.2)	38	600 (2.8)	346	15911 (75.2)	4806	
2011-19 (N=1,80118)	6,441 (3.6)	5,416	494 (0.3)	347	46,766 (26.0)	36,853	-	-	798 (0.4)	750	125619 (69.7)	10318	
Total (N=2,01,269)	7649 (3.8)	6322	3836(1.9)	3309	46804 (23.3)	36891	52 (0.02)	38	1398 (0.7)	1096	141530 (70.3)	15124	

Table 3. Prevalence of DF/DHF/DSS in various dengue epidemics.

Year of study (N)	DF N (%)	DHF N (%)	DSS N (%)
2000-2010 (4142)	2910 (70.3)	1162 (28.1)	70 (1.7)
2011-2019 (16017)	12016 (75.0)	3776 (23.6)	225 (1.4)
Unknown (699)	601 (86.0)	84 (12.0)	14 (2.0)
Total (20858)	15527 (74.4)	5022 (24.1)	309 (1.5)

genotype in 2006 was DENV-II and DENV-III (Khan et al., 2008). From 2007 to 2019 different serotypes were found in different epidemics from various regions of Pakistan (Table 4). In 2006-2011, all the serotypes were reported from Karachi and Lahore and DENV- II the most prevalent (Hasan et al., 2013; Mahmood et al., 2013; Koo et al., 2013). In Lahore the prevalent serotype was DENV II, III, and multiple serotypes were reported from 2007-09 (Fatima et al., 2011). While some reported all four serotypes from Lahore in 2008 (Javed et al., 2009; Humayoun et al., 2010). During 2011 all the four serotypes as well as mixed infections were reported from Punjab and KP (Ali et al., 2016) while some studies reported only II, III (Atif et al., 2016; Assir et al., 2014a; Idrees et al., 2012). The prevalent serotype in 2013 was DENV-II in the country (Shahid et al., 2019). In 2015 all the four serotypes were reported from Rawalpindi and Malakand (Ghani et al., 2017: Suleman et al., 2017b). The prevalent serotypes in Faisalabad in 2011 were DENV-II, DENV-III, and DENV-IV while during 2014-17, DENV-I, DENV-II, DENV-III were reported (Ahmed et al., 2017; Raza et al., 2018).



Figure 3. Prevalence of DF, DHF, and DSS during dengue outbreaks (2000-19).

Year of study	Serotype detected	References
2000-06	DENV-II, DENV-III	Khan et al. (2008)
2007-11	DENV-I, DENV-II, DENV-III, DENV-IV, multiple	Ali et al. (2016); Koo et al. (2013); Hasan et al. (2013); Fatima et al. (2011); Humayoun et al. (2010); Atif et al. (2016); Ahmed et al. (2017); Javed et al. (2009); Idrees et al. (2012); Assir et al. (2014a); Mahmood et al. (2012)
2012-19	DENV-I, DENV-II, DENV-III, DENV-IV, multiple	Ghani et al. (2017); Raza et al. (2018); Suleman et al. (2017a); Shahid et al. (2019)

KP N (%)

1(1.6)

247 (24.7)

248 (22.9)

Twin cities N (%)

5 (7.9)

9(0.9)

14(1.3)

Sindh N (%)

48 (76.2)

15(1.5)

18 (100.0)

81 (7.5)

Punjab N (%)

216 (21.6)

220 (20.3)

Year of study (N)

2011-19 (1001)

Unknown (18)

Total (1082)

B

Table 5. Overall mortalities during 2000-19.

#### 3.5. Overall mortalities

Over all death toll due to dengue complications were 1082 (Ahmed, 2009; Ahmed et al., 2008, 2013; Akhtar et al., 2014; Ali et al., 2011, 2013; Assir et al., 2014a, b; Baqi et al., 2010; Chaudhry et al., 2017; Iqtadar et al., 2017b; Khalil et al., 2014; Khan, 2018; Khan et al., 2007, 2013a, b, 2017a, b, 2018; Khurram et al., 2014; Mahboob et al., 2012; Munir et al., 2014; Nazeer et al., 2009; Parkash et al., 2010; Quadri et al., 2015; Rashid et al., 2012; Rehman et al., 2017; Riaz et al., 2009; Saqib et al., 2014; Shamim, 2010; Suleman et al., 2017a; Usman et al., 2011; Wasay et al., 2008a, b; Zamir et al., 2012).

The maximum number of mortalities were reported in KP (N=248) with the majority of deaths reported from District Swat in 2013 (Khan and Khan, 2015; Akhtar et al., 2014; Chaudhry et al., 2017; Khan et al., 2017a, b, 2018; Ali et al., 2013; Usman et al., 2011). A total of 220 deaths were reported (majority from Lahore) in 2011 dengue outbreak from Punjab province (Iqtadar et al., 2017b; Ahmed et al., 2013; Mahboob et al., 2012; Rashid et al., 2012; Assir et al., 2014a; Nazeer et al., 2009; Saqib et al., 2014b). The twin cities (Islamabad, and Rawalpindi) of the country also added in the total death toll of 14 (1.3%) individuals (Tables 3 and 4).

Overall deaths during decade I were 5.8% (63/1082) (Khan et al., 2007; Ahmed et al., 2008; Ahmed, 2009; Mahboob et al., 2012; Munir et al., 2014; Riaz et al., 2009; Shamim, 2010; Wasay et al., 2008a, b; Khalil et al., 2014; Usman et al., 2011; Baqi et al., 2010; Nazeer et al., 2009; Ali et al., 2011) while during decade II 92.5% (1001/1082) deaths were reported (Table 5, Figure 4) (Iqtadar et al., 2017b; Rehman et al., 2017; Ahmed et al., 2013; Khan and Khan, 2015; Rashid et al., 2012; Akhtar et al., 2013a; Khan et al., 2017a, b; Khan et al., 2018; Quadri et al., 2015; Suleman et al., 2017a; Ali et al., 2013; Saqib et al., 2014a; Khurram et al., 2014; Zamir et al., 2012; Assir et al., 2014a).

razilian Journal of Biology, 2024, vol. 84, e267982	
---	--

Table 4. Vario	us Serotypes i	identified o	luring 2000-19.
Augue II fullo	ab beroeypeb.	active a c	. a

5	I	1	0
-	L	-	-

Miscellaneous N (%)

5 (7.9)

514 (51.3)

519 (48.0)



Figure 4. Number of deaths in various outbreaks during 2000-19.

The deaths reported in Karachi during an unknown period were 18 (Parkash et al., 2010).

# 4. Discussion

Dengue is a life-threatening viral infectious disease and is a major health problem in tropical regions worldwide (Khan et al., 2010). Every year 50 to 100 million morbidities and about 24,000 mortalities are reported and according to World Health Organization dengue is endemic in south Asia (Jahan et al., 2011). The disease is present in >125 countries (Murray et al., 2013), and different DENV serotypes are circulating in neighboring countries of Pakistan like India (Gupta et al., 2006), Bangladesh (Aziz et al., 2002), and Iran (Aghaie et al., 2014). This review provides a wide overview of the growing epidemiology of dengue infection in Pakistan over the period 2000-2019. This analysis supports an overall rise in the yearly number of reported cases and deaths over the decade.

In Pakistan dengue infection was first reported from Karachi in 1994 and Punjab in 2003 (Hasan et al., 2013) and then, regular outbreaks are reported since 2005 (Ahmed et al., 2013). The DENV became endemic in Pakistan, found throughout the year mainly after the monsoon rainy season (Rehman et al., 2017; Khan et al., 2010). The main reason of emergence of the infection after monsoon rains are the availability of ultimate breeding sites of the mosquito vector, (Aedes aegypti and Aedes albopictus), and the environmental and climatic conditions, humidity, and the introduction of a new viral strain (Raza et al., 2014; Ahmed et al., 2013; Akhtar et al., 2014). The worst outbreak of dengue in KP (Swat) was reported in 2013 and then in the following years the infection rate decreased rapidly and might be due to awareness among people to deal with the mosquito vectors (Khan et al., 2018). In some areas the infection is spreading and may be it is due to increased population, urbanization, uncontrolled vector growth, traveling, unawareness, and failure of public health departments (Ahmed et al., 2013; Atif et al., 2016). Similar situations were faced by developed countries also like Germany (Murray et al., 2013).

The data obtained shows that in Pakistan males population are more infected as compared to females. Due to customs of the region females are restricted to houses and their dresses protect them from the mosquito bites as compared to males (Rehman et al., 2017; Raza et al., 2014; Saqib et al., 2014a, b; Khan et al., 2018; Rafique et al., 2017; Assir et al., 2014a). Similar factors are also observed in other countries with similar customs and conditions (Anker and Arima, 2011).

According to the study of Saqib et al. (2014a, b) male predominance was reported during the 2011 outbreak in Lahore but according to Ali et al. (2016) gender was affected equally during the 2011 outbreak in Punjab that was the most severe outbreak resulting in a large number of deaths. There was a significant difference between gender distribution during 2013 in dengue outbreak in district Swat KP. The difference of infection in gender in these two provinces may be due to the same reason as male are more exposed and spend more time outside homes and are not that much covered as females in KP where the situation is almost opposite in Punjab where most of the female are working women. Male predominance is also reported in other countries like India, Singapore, Malaysia etc but in America, both genders are found equally affected (Guha-Sapir and Schimmer, 2005).

The sever form of dengue infection i.e. DHF and DSS has increased in the study period (Ahmed et al., 2017). The increasing number of DHF could be related to the virulence of the virus and also with co-infection with other pathogens (Raza et al., 2014). DHF and DSS can also result due to a severe response of the immune system to the incoming pathogen. DHF is mostly the result of secondary infection but primary infection of DENV can also lead to DHF/DSS (Khurram et al., 2014).

Although all four serotypes are found in different dengue epidemics and the most predominant serotypes found were DENV-I and II (Fatima et al., 2011; Atif et al., 2016). A study (Khan et al., 2018) suggested that serotypes that circulate in KP were having ancestral linkage with those previously found in Karachi and Lahore. In District Swat KP during 2013 epidemic, DENV-III was found widely distributed and some researchers associate it with mosquito spp. (*Aedes albupictus*) there (Ali et al., 2016).

The death toll can be reduced if proper care of dengue patient is taken. However, mortality rate in DHF and DSS cases is high due as platelets count reduced and the patient needs transfusions and enhanced healthcare facilities which are not widely available in Pakistan (Hasan et al., 2013). The factor responsible for a large number of morbidity and mortality during the 2011 and 2013 outbreaks is being susceptibility to infection and lack of diagnostic facilities in an early stages of infection (Suleman et al., 2016). Due to the lack of vaccine availability and specific antiviral treatment besides the symptomatic treatment and taking preventive measures, deaths are increasing. Early detection and prevention can decrease the risk of developing further complications (Sulaiman et al., 2015).

There is a need of vaccine against DENV to prevent the infection (Sulaiman et al., 2015). In Pakistan, dengue is also moving towards non-endemic and rural areas and more care is needed in those regions as there are fewer facilities in rural areas. Mosquito vector control should be taken that alternatively will help in control of dengue infection (Fatima et al., 2011). The large number of outbreaks that result in huge morbidities and mortalities in Pakistan are due to uncovered fresh water sources that provides

dwelling for mosquitoes, poor hygienic conditions, lack of vaccines, increasing number of immigrants, and increased urbanization.

# 5. Conclusion

It is concluded that DENV is highly prevalent and the number of cases is increased decade-wise. All the serotypes are reported and DENV-II and DENV-III are widely distributed in Pakistan. The death toll is high and found to be increased according to the published literature survey 2000-2019.

#### References

- AGHAIE, A., AASKOV, J., CHINIKAR, S., NIEDRIG, M., BANAZADEH, S. and MOHAMMADPOUR, H.K., 2014. Frequency of dengue virus infection in blood donors in Sistan and Baluchestan province in Iran. *Transfusion and Apheresis Science*, vol. 50, no. 1, pp. 59-62. http://dx.doi.org/10.1016/j.transci.2013.07.034.
- AHMED, A., IFTIKHAR, H. and CHAUDHRY, G.M., 2007. Water resources and conservation strategy of Pakistan. *Pakistan Development Review*, vol. 46, no. 4II, pp. 997-1009. http:// dx.doi.org/10.30541/v46i4IIpp.997-1009.
- AHMED, I., REZA, F.A., IQBAL, M. and ASHRAF, M., 2017. Dengue virus serotypes and epidemiological features of dengue fever in Faisalabad, Pakistan. *Tropical Biomedicine*, vol. 34, no. 4, pp. 928-935. PMid:33592962.
- AHMED, S., ARIF, F., YAHYA, Y., REHMAN, A., ABBAS, K., ASHRAF, S. and AKRAM, D.S., 2008. Dengue fever outbreak in Karachi 2006--a study of profile and outcome of children under 15 years of age. *The Journal of the Pakistan Medical Association*, vol. 58, no. 1, pp. 4–8. PMid: 18297966.
- AHMED, S., MOHAMMAD, W.W., HAMID, F., AKHTER, A., AFZAL, R.K. and MAHMOOD, A., 2013. The 2011 dengue haemorrhagic fever outbreak in Lahore-an account of clinical parameters and pattern of haemorrhagic complications. *Journal of the College of Physicians and Surgeons*, vol. 23, no. 7, pp. 463-467. PMid:23823947.
- AHMED, S.I., 2009. Dengue fever in northern Pakistan: the hepatic implications. *Journal of Rawalpindi Medical College*, vol. 13, no. 2, pp. 56-59.
- AKHTAR, N., KHAN, J. and KHAN, R., 2014. Dengue outbreak in Khyber Pakhtoonkhwa, Pakistan 2013. European Academic Research, vol. 1, pp. 3842-3857.
- ALI, A., AHMAD, H., IDREES, M., ZAHIR, F. and ALI, I., 2016. Circulating serotypes of dengue virus and their incursion into non-endemic areas of Pakistan; a serious threat. *Virology Journal*, vol. 13, no. 1, pp. 144. http://dx.doi.org/10.1186/s12985-016-0603-6. PMid:27565893.
- ALI, A., REHMAN, H.U., NISAR, M., RAFIQUE, S., ALI, S., HUSSAIN, A., NAUSHEEN., IDREES, M., SABRI, S., ZADA, H. and HUSSAIN, S., 2013. Seroepidemiology of dengue fever in Khyber Pakhtunkhawa, Pakistan. *International Journal of Infectious Diseases*, vol. 17, no. 7, pp. e518-e523. http://dx.doi.org/10.1016/j. ijid.2013.01.007. PMid:23523057.
- ALI, F., BAIG-ANSARI, N., SALEEM, T. and SALAHUDDIN, N., 2011. Clinical profile and management of dengue fever at a tertiary care hospital in Pakistan. *Infectious Disease Journal of Pakistan.*, vol. 20, no. 3, pp. 1.

- ANKER, M. and ARIMA, Y., 2011. Male-female differences in the number of reported incident dengue fever cases in six Asian countries. Western Pacific Surveillance and Response Journal : WPSAR, vol. 2, no. 2, e1. http://dx.doi.org/10.5365/ wpsar.2011.2.1.002.
- ASGHAR, J. and FAROOQ, K., 2011. Radiological appearance and their significance in the management of dengue hemorrhagic fever. *Pakistan Journal of Medical & Health Sciences*, vol. 5, no. 4, pp. 685-692.
- ASSIR, M.Z.K., AHMAD, H.I., MASOOD, M.A., KAMRAN, U. and YUSUF, N.W., 2014a. Deaths due to dengue fever at a tertiary care hospital in Lahore, Pakistan. *Scandinavian Journal of Infectious Diseases*, vol. 46, no. 4, pp. 303-309. http://dx.doi.org/10.3109 /00365548.2013.877155. PMid:24491144.
- ASSIR, M.Z.K., MASOOD, M.A. and AHMAD, H.I., 2014b. Concurrent dengue and malaria infection in Lahore, Pakistan during the 2012 dengue outbreak. *International Journal of Infectious Diseases*, vol. 18, pp. 41-46. http://dx.doi.org/10.1016/j.ijid.2013.09.007. PMid:24183717.
- ATIF, M., RAHEEL, U., ALAM, F., ARSHAD, H.U. and BALOCH, F.U.H., 2016. Serotyping of dengue virus from deadly outbreaks of Pakistan. *Journal of Human Virology & Retrovirology*, vol. 3, no. 3, pp. 92-96.
- ATIQUE, S., ABDUL, S.S., HSU, C.Y. and CHUANG, T.W., 2016. Meteorological influences on dengue transmission in Pakistan. Asian Pacific Journal of Tropical Medicine, vol. 9, no. 10, pp. 954-961. http://dx.doi.org/10.1016/j.apjtm.2016.07.033. PMid:27794388.
- AZIZ, M.M., HASAN, K.N., HASANAT, M.A., SIDDIQUI, M.A., SALIMULLAH, M., CHOWDHURY, A.K., AHMED, M., ALAM, M.N. and HASSAN, M.S., 2002. Predominance of DEN-3 genotype during the recent dengue outbreak in Bangladesh. *The Southeast Asian Journal of Tropical Medicine and Public Health*, vol. 33, no. 1, pp. 42-48. PMid:12118459.
- BAQI, S., NASIM, A., ANIS, S., AZIZ, T. and RIZVI, S.A.H., 2010. Dengue Viral Infection in Renal Transplant Recipients in Karachi Pakistan. *Transplantation*, vol. 90, pp. 399. http://dx.doi. org/10.1097/00007890-201007272-00736.
- BHATTI, A.B., ALI, F. and SATTI, S.A., 2015. Cross-reactivity of rapid Salmonella Typhi IgM immunoassay in dengue fever without co-existing infection. *Cureus*, vol. 7, no. 12, e396. http://dx.doi. org/10.7759/cureus.396. PMid:26798572.
- CHAUDHRY, K.A., JAMIL, F., RAZZAQ, M. and JILANI, B.F., 2018. Survival analysis of dengue patients of Pakistan. *International Journal of Mosquito Research*, vol. 83, pp. 5-9.
- CHAUDHRY, M., AHMAD, S., RASHID, H.B. and DIN, I.U., 2017. Dengue epidemic in post conflict swat district, Khyber Pakhtunkhwa, Pakistan, 2013. *The American Journal of Tropical Medicine and Hygiene*, vol. 96, no. 4, pp. 899-902. PMid:28093537.
- CHAUDHRY, Q.U.Z., MAHMOOD, A., RASUL, G. and AFZAAL, M., 2009. Climate change indicators of Pakistan. Islamabad: Pakistan Meteorological Department, pp. 1-43. Technical Report, no. PMD-22/2009.
- DAUD, M.K., NAFEES, M., ALI, S., RIZWAN, M., BAJWA, R.A., SHAKOOR, M.B., ARSHAD, M.U., CHATHA, S.A.S., DEEBA, F., MURAD, W., MALOOK, I. and ZHU, S.J., 2017. Drinking water quality status and contamination in Pakistan. *BioMed Research International*, vol. 2017, pp. 7908183. http://dx.doi.org/10.1155/2017/7908183. PMid:28884130.
- FATIMA, Z., IDREES, M., BAJWA, M.A., TAHIR, Z., ULLAH, O., ZIA, M.Q., HUSSAIN, A., AKRAM, M., KHUBAIB, B., AFZAL, S., MUNIR, S., SALEEM, S., RAUFF, B., BADAR, S., NAUDHANI, M., BUTT, S., AFTAB, M., ALI, L. and ALI, M., 2011. Serotype and genotype

analysis of dengue virus by sequencing followed by phylogenetic analysis using samples from three mini outbreaks-2007-2009 in Pakistan. *BMC Microbiology*, vol. 11, no. 1, pp. 200. http:// dx.doi.org/10.1186/1471-2180-11-200. PMid:21906394.

- GHANI, E., MUSHTAG, S. and KHAN, S.A., 2017. Multiplex polymerase chain reaction-based serotype analysis of dengue virus during 2015 dengue outbreak in Pakistan. *Eastern Mediterranean Health Journal*, vol. 23, no. 9, pp. 594-597. http://dx.doi. org/10.26719/2017.23.9.594. PMid:29178115.
- GUHA-SAPIR, D. and SCHIMMER, B., 2005. Dengue fever: new paradigms for a changing epidemiology. *Emerging Themes in Epidemiology*, vol. 2, no. 1, pp. 1. http://dx.doi.org/10.1186/1742-7622-2-1. PMid:15743532.
- GUPTA, E., DAR, L., KAPOOR, G. and BROOR, S., 2006. The changing epidemiology of dengue in Delhi, India. *Virology Journal*, vol. 3, no. 1, pp. 92. http://dx.doi.org/10.1186/1743-422X-3-92. PMid:17083743.
- HAROON, M., JAN, H., FAISAL, S., ALI, N., KAMRAN, M. and ULLAH, F., 2019. Dengue outbreak in Peshawar: clinical features and laboratory markers of dengue virus infection. *Journal of Infection and Public Health*, vol. 12, no. 2, pp. 258-262. http://dx.doi. org/10.1016/j.jiph.2018.10.138. PMid:30466902.
- HASAN, S.R., RIAZ, M. and JAFRI, F.A., 2013. Characteristics and outcome of dengue infection; clinical perspective from a secondary care hospital of Karachi. *Pakistan Journal of Medical Sciences*, vol. 29, no. 1, pp. 115-118. PMid:24353520.
- HUMAYOUN, M.A., WASEEM, T., JAWA, A.A., HASHMI, M.S. and AKRAM, J., 2010. Multiple dengue serotypes and high frequency of dengue haemorrhagic fever at two tertiary care hospitals in Lahore during the 2008 dengue virus outbreak in Punjab, Pakistan. *International Journal of Infectious Diseases*, vol. 14, suppl. 3, pp. e54–e59. http://dx.doi.org/10.1016/j.ijid.2009.10.008. PMid:20171916.
- IDREES, M., HUSSAIN, W., REHMAN, H.U., TAYYAB, G.N., AFZAL, S., FATIMA, Z., AKRAM, M., RAZA, S.M., ALI, L., HUSSAIN, A., AMIN, I., SHAHID, M., KHUBAIB, B., SALEEM, S., NASIR, B., TARIQ, A., WASIM, M. and WAQAR, M., 2012. Dengue virus serotype 2 (DEN-2): the causative agent of 2011-dengue epidemic in Pakistan. American Journal of Biomedical Sciences, vol. 4, no. 4, pp. 307-315. http://dx.doi.org/10.5099/aj120400307.
- IQTADAR, S., AKBAR, N., HUMA, N. and RANDHAWA, F.A., 2017a. Profile of hepatic involvement in dengue infections in adult Pakistani population. *Pakistan Journal of Medical Sciences*, vol. 33, no. 4, pp. 963-967. http://dx.doi.org/10.12669/pjms.334.13026. PMid:29067074.
- IQTADAR, S., AKBAR, N., MEHMOOD, M. and ABAIDULLAH, S., 2017b. Clinical audit of dengue related deaths in 2011- Mayo Hospital Lahore Pakistan. *Pakistan Journal of Medical Sciences*, vol. 33, no. 5, pp. 1070-1073. http://dx.doi.org/10.12669/pjms.335.13051. PMid:29142540.
- ISHTIAQ, R., IMRAN, A., RAZA, H., ANWAR, Q., ISHTIAQ, D., JAMIL, A., ALI, Q.M. and KHAN, R., 2018. Acute Hepatitis in Infections Caused by Dengue Virus in Southern Punjab, Pakistan. *Cureus*, vol. 10, no. 12, pp. e3788. http://dx.doi.org/10.7759/cureus.3788. PMid:30868002.
- JAHAN, F., NANJI, K., QIDWAI, W., ROSHAN, R. and WASEEM, H., 2011. Clinical and biochemical characteristics of suspected dengue fever in an ambulatory care family medical clinic, Aga Khan University, Karachi, Pakistan. *Dengue Bulletin*, vol. 35, pp. 59-64.
- JAVED, F.T., JAVED, T.A., YUSUF, N.W., MANNAN, A., AKRAM, J., SHEIKH, U.N. and SHAHZAD, M., 2009. Prevalence of all four dengue virus serotypes confirmed by using real time RT-PCR among population of Lahore Pakistan. *International Journal of*

Livestock Research, vol. 3, no. 1, pp. 1-3. http://dx.doi.org/10.5455/ ijavms.20101124115052.

- KHALIL, M.A.M., TAN, J., KHALIL, M.A.U., AWAN, S. and RANGASAMI, M., 2014. Predictors of hospital stay and mortality in dengue virus infection-experience from Aga Khan University Hospital Pakistan. *BMC Research Notes*, vol. 7, no. 1, pp. 473. http://dx.doi. org/10.1186/1756-0500-7-473. PMid:25064632.
- KHAN, E., HASAN, R., MEHRAJ, V., NASIR, A., SIDDIQUI, J. and HEWSON, R., 2008. Co-circulations of two genotypes of dengue virus in 2006 out-break of dengue hemorrhagic fever in Karachi, Pakistan. *Journal of Clinical Virology*, vol. 43, no. 2, pp. 176-179. http://dx.doi.org/10.1016/j.jcv.2008.06.003. PMid: 18639489.
- KHAN, E., KISAT, M., KHAN, N., NASIR, A., AYUB, S. and HASAN, R., 2010. Demographic and clinical features of dengue fever in Pakistan from 2003-2007: a retrospective cross-sectional study. *PLoS One*, vol. 5, no. 9, e12505. http://dx.doi.org/10.1371/ journal.pone.0012505. PMid:20856935.
- KHAN, E., SIDDIQUI, J., SHAKOOR, S., MEHRAJ, V., JAMIL, B. and HASAN, R., 2007. Dengue outbreak in Karachi, Pakistan, 2006: experience at a tertiary care center. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, vol. 10, no. 11, pp. 1114-1119. http://dx.doi.org/10.1016/j.trstmh.2007.06.016. PMid:17706259.
- KHAN, H. and BARI, F., 2018. Dengue Fever. Role of non-structural protein-1 (NS-1) positivity in dengue cases: an experience from a Qazi Hussain Ahmed Medical Complex Nowshera. *The Professional Medical Journal*, vol. 25, no. 6, pp. 876. http://dx.doi. org/10.29309/TPMJ/2018.25.06.274.
- KHAN, J., 2018. Outbreak investigation of dengue fever in District Malir, Karachi, Sindh, Pakistan, 2015. *I Proceedings*, vol. 4, no. 1, pp. 10632.
- KHAN, J. and KHAN, A., 2015. Incidence of dengue in 2013: dengue outbreak in District Swat, Khyber Pakhtunkhwa, Pakistan. *International Journal of Fauna and Biological Studies*, vol. 2, no. 1, pp. 1–7.
- KHAN, J., GHAFFAR, A. and KHAN, S.A., 2018. The changing epidemiological pattern of Dengue in Swat, Khyber Pakhtunkhwa. *PLoS One*, vol. 13, no. 4, pp. e0195706. http:// dx.doi.org/10.1371/journal.pone.0195706. PMid:29689060.
- KHAN, M., KHAN, K., MAHMOOD, A. and AHMED, A., 2013a. Experience with dengue in tertiary Care Centre. *Medical Channel*, vol. 19, no. 3, pp. 51-55.
- KHAN, M.A., ELLIS, E.M., TISSERA, H.A., ALVI, M.Y., RAHMAN, F.F., MASUD, F., CHOW, A., HOWE, S., DHANASEKARAN, V., ELLIS, B.R. and GUBLER, D.J., 2013b. Emergence and diversification of dengue 2 cosmopolitan genotype in Pakistan, 2011. *PLoS One*, vol. 8, no. 3, e56391. http://dx.doi.org/10.1371/journal. pone.0056391. PMid:23520453.
- KHAN, M.I.H., ANWAR, E., AGHA, A., HASSANIEN, N.S.M., ULLAH, E., SYED, I.A. and RAJA, A., 2013c. Factors predicting severe dengue in patients with dengue fever. *Mediterranean Journal* of Hematology and Infectious Diseases, vol. 5, no. 1, e2013014. PMid:23505602.
- KHAN, W., AMIN KHAN, B., KHAN, Z., AKBAR, M. and ALI KHAN, I., 2017a. Dengue fever. The clinical pattern and mortality in epidemic and post epidemic years in Swat. *The Professional Medical Journal*, vol. 24, no. 10, pp. 1466-1470.
- KHAN, W.M., KHAN, A., SHAH, F., ZAMAN, F. and AYUB, M., 2017b. An epidemiological study of patients admitted with viral hemorrhagic fever (VHF): a single center experience. *Rawal Medical Journal*, vol. 42, no. 4, pp. 479–483.
- KHURRAM, M., QAYYUM, W., UL HASSAN, S.J., MUMTAZ, S., BUSHRA, H.T. and UMAR, M., 2014. Dengue hemorrhagic fever: comparison

of patients with primary and secondary infections. *Journal of Infection and Public Health*, vol. 7, no. 6, pp. 489-495. http://dx.doi.org/10.1016/j.jiph.2014.05.005.

- KOO, C., NASIR, A., HAPUARACHCHI, H.C., LEE, K.S., HASAN, Z., NG, L.C. and KHAN, E., 2013. Evolution and heterogeneity of multiple serotypes of Dengue virus in Pakistan, 2006–2011. Virology Journal, vol. 10, no. 1, pp. 275. http://dx.doi.org/10.1186/1743-422X-10-275. PMid:24007412.
- LUTFULLAH, G., AHMAD, J., KHAN, A., IHSAN, H. and AHMAD, J., 2017. Evaluation of Non-Structural Protein-1 (NS1) positive patients of 2013 dengue outbreak in Khyber Pakhtunkhwa, Pakistan. *Pakistan Journal of Medical Sciences*, vol. 33, no. 1, pp. 172-176. http://dx.doi.org/10.12669/pjms.331.11237. PMid:28367194.
- MAHBOOB, A., IQBAL, Z., JAVED, R., TAJ, A., MUNIR, A., SALEEMI, M.A. and YAQUB, F., 2012. Dermatological manifestations of dengue fever. *Journal of Ayub Medical College, Abbottabad*, vol. 24, no. 1, pp. 52-54. PMid:23855095.
- MAHMOOD, K., JAMEEL, T., ASLAM, H.F. and TAHIR, M., 2009. Incidence of dengue haemorrhagic fever in local population of Lahore, Pakistan. *Biomedica*, vol. 25, no. 3, pp. 93-96.
- MAHMOOD, N., RANA, M.Y., QURESHI, Z., MUJTABA, G. and SHAUKAT, U., 2012. Prevalence and molecular characterization of dengue viruses serotypes in 2010 epidemic. *The American Journal of the Medical Sciences*, vol. 343, no. 1, pp. 61-64. http://dx.doi. org/10.1097/MAJ.0b013e3182217001. PMid:21760476.
- MAHMOOD, S., HAFEEZ, S., NABEEL, H., ZAHRA, U. and NAZEER, H., 2013. Does comorbidity increase the risk of dengue hemorrhagic fever and dengue shock syndrome? *ISRN Tropical Medicine*, vol. 2013, pp. 1-5. http://dx.doi.org/10.1155/2013/139273.
- MUNIR, M.A., ALAM, S.E., KHAN, Z.U., SAEED, Q., ARIF, A., IQBAL, R., SAQIB, M.A. and QURESHI, H., 2014. Dengue fever in patients admitted in tertiary care hospitals in Pakistan. *Journal of the Pakistan Medical Association*, vol. 64, no. 5, pp. 553-559. PMid:25272543.
- MURRAY, N.E.A., QUAM, M.B. and WILDER-SMITH, A., 2013. Epidemiology of dengue: past, present and future prospects. *Clinical Epidemiology*, vol. 5, pp. 299-309. PMid:23990732.
- NAEEM, M., SHAHEEN, A., BATOOL, S., RUBAB, S., SABA, T., RIAZ, T. and MAHMOOD, M.A., 2018. Dengue fever: a clinical experience. *The Professional Medical Journal*, vol. 21, no. 2, pp. 243-246. http://dx.doi.org/10.29309/TPMJ/2014.21.02.1972.
- NAZEER, A., KAMAL, A., QAISERA, S. and WAHEED, K., 2009. Dengue fever outbreak in Lahore, Pakistan: a clinical management experience. *Pakistan Journal of Medical & Health Sciences*, vol. 3, pp. 204.
- PARKASH, O., ALMAS, A., JAFRI, S.W., HAMID, S., AKHTAR, J. and ALISHAH, H., 2010. Severity of acute hepatitis and its outcome in patients with dengue fever in a tertiary care hospital Karachi, Pakistan (South Asia). *BMC Gastroenterology*, vol. 10, no. 1, pp. 43. http://dx.doi.org/10.1186/1471-230X-10-43. PMid:20459677.
- PERVEEN, S., FIRDOUS, H., KHALID, M.A., AHMED, N. and BAQAI, H.Z., 2016. Relationship between serum lactate dehydrogenase levels and dengue severity. *Journal of Rawalpindi Medical College*, vol. 21, no. 1, pp. 9-12.
- QUADRI, S.M.A., KHAN, M. and YASMIN, N., 2015. Epidemiological surveillance of dengue infections: a community based study in rural, Karachi (2010-2012). Annals of Abbasi Shaheed Hospital and Karachi Medical & Dental College, vol. 20, no. 1, pp. 4-9.
- QURESHI, A.S., SHAH, T. and AKHTAR, M., 2003. The groundwater economy of Pakistan. Lahore: International Water Management Institute. Working Paper, no. 64.
- RAFIQUE, I., SAQIB, M.A.N., MUNIR, M.A., QURESHI, H., TASEER, I.U., IQBAL, R., AHMED, W., AKHTAR, T. and RIZWANULLAH., 2017.

Asymptomatic dengue infection in adults of major cities of Pakistan. *Asian Pacific Journal of Tropical Medicine*, vol. 10, no. 10, pp. 1002-1006. http://dx.doi.org/10.1016/j.apjtm.2017.09.013. PMid:29111183.

- RAFIQUE, I., SAQIB, M.A.N., MUNIR, M.A., SIDDIQUI, S., QURESHI, H., HABIBULLAH, S., BASHIR, S., REHMAN, S. and ASHRAF, S., 2015. Economic burden of dengue in four major cities of Pakistan during 2011. JPMA, vol. 65, no. 3, pp. 256. PMid:25933556.
- RASHID, A., KHAN, H.I. and UR-RASOOL, N., 2012. Dengue hemorrhagic fever/dengue shock syndrome. *The Professional Medical Journal*, vol. 19, no. 5, pp. 661-667. http://dx.doi. org/10.29309/TPMJ/2012.19.05.2330.
- RAZA, F.A., IQBAL, M., AHMAD, J. and HUSSAIN, S., 2017. Epidemiological features of dengue fever in a four-year hospital based study in Faisalabad, Pakistan. *Journal of Fatima Jinnah Medical University.*, vol. 11, no. 2, pp. 50-55.
- RAZA, F.A., ASHRAF, S., HASNAIN, S., AHMAD, J. and IQBAL, M., 2018. Dengue seroprevalence and its socioeconomic determinants in Faisalabad, Pakistan: a cross-sectional study. *Revista da Sociedade Brasileira de Medicina Tropical*, vol. 51, no. 4, pp. 503-507. http:// dx.doi.org/10.1590/0037-8682-0246-2017. PMid:30133634.
- RAZA, F.A., REHMAN, S., KHALID, R., AHMAD, J., ASHRAF, S., IQBAL, M. and HASNAIN, S., 2014. Demographic and clinicoepidemiological features of dengue fever in Faisalabad, Pakistan. *PLoS One*, vol. 9, no. 3, e89868. http://dx.doi.org/10.1371/journal. pone.0089868. PMid:24595236.
- REHMAN, M.M.U., ZAKARIA, M. and MUSTAFVI, S.A., 2017. Clinical and laboratory profile of dengue fever patients admitted in combined military hospital rawalpindi in year 2015. *Pakistan Armed Forces Medical Journal*, vol. 67, no. 4, pp. 496-501.
- RIAZ, M.M., MUMTAZ, K., KHAN, M.S., PATEL, J., TARIQ, M., HILAL, H., SIDDIQUI, S.A. and SHEZAD, F., 2009. Outbreak of dengue fever in Karachi 2006: a clinical perspective. *Journal of the Pakistan Medical Association*, vol. 59, no. 6, pp. 339-344. PMid: 19534364.
- SAQIB, M.A.N., RAFIQUE, I., BASHIR, S. and SALAM, A.A., 2014a. A retrospective analysis of dengue fever case management and frequency of co-morbidities associated with deaths. *BMC Research Notes*, vol. 7, no. 1, pp. 205. http://dx.doi. org/10.1186/1756-0500-7-205. PMid:24690140.
- SAQIB, M.A.N., RAFIQUE, I., SALAM, A.A. and BASHIR, S., 2014b. Persistence of dengue symptoms among discharged dengue cases of Lahore, Pakistan. *Pakistan Journal of Medical Research*, vol. 53, no. 4, pp. 93.
- SHAHID, M., AMIN, I., AFZAL, S., FATIMA, Z. and IDREES, M., 2019. Comparative analysis of immunological and genomic outcomes of dengue virus outbreak in Pakistan. *Pakistan Journal of Zoology*, vol. 51, no. 5, pp. 1971-1974. http://dx.doi.org/10.17582/journal. pjz/2019.51.5.sc4.
- SHAMIM, M., 2010. Frequency, pattern and management of acute abdomen in dengue fever in Karachi, Pakistan. Asian Journal of Surgery, vol. 33, no. 3, pp. 107-113. http://dx.doi.org/10.1016/ S1015-9584(10)60019-X. PMid:21163407.
- SHEIKH, K.R., SHEHZAD, A., MUFTI, S. and MIRZA, U.A., 2012. Skin involvement in patients of dengue fever during the 2011 epidemic in Lahore, Pakistan. *Journal of Pakistan Association of Dermatologists*, vol. 22, no. 4, pp. 325–330.
- SULAIMAN, S., HADI, S., KARIM, K., IQBAL, S., ALI, A.A. and RAFIQ, F., 2015. Dengue more prevalent than previously thought: an epidemiology approach. *i-Manager's Journal on Nursing*, vol. 4, no. 4, pp. 1-5. http://dx.doi.org/10.26634/jnur.4.4.3071.
- SULEMAN, M., FARYAL, R., AAMIR, U.B., ALAM, M.M., NISAR, N., SHARIF, S., SHAUKAT, S., KHURSHID, A., ANGEZ, M., UMAIR, M., MUJTABA, G., SUFIAN, M.M., ARSHAD, Y., REHMAN, L. and ZAIDI,

S.S.Z., 2016. Dengue outbreak in Swat and Mansehra, Pakistan 2013: an epidemiological and diagnostic perspective. *Asian Pacific Journal of Tropical Medicine*, vol. 9, no. 4, pp. 380-384. http://dx.doi.org/10.1016/j.apjtm.2016.03.010. PMid:27086157.

- SULEMAN, M., LEE, H.W., ZAIDI, S.S.Z., ALAM, M.M., NISAR, N., AAMIR, U.B., SHARIF, S., SHAUKAT, S., KHURSHID, A., ANGEZ, M., UMAIR, M., MUJTABA, G. and FARYAL, R., 2017a. Preliminary Seroepidemiological survey of dengue infections in Pakistan, 2009-2014. *Infectious Diseases of Poverty*, vol. 6, no. 1, pp. 48. http://dx.doi.org/10.1186/s40249-017-0258-6. PMid:28274279.
- SULEMAN, M., FARYAL, R., ALAM, M.M., KHURSHID, A., SHARIF, S., SHAUKAT, S., ANGEZ, M., UMAIR, M., SUFIAN, M.M., ARSHAD, Y., INAM, T. and ZAIDI, S.S.Z., 2017b. Outbreak of dengue virus type-3 in Malakand, Pakistan 2015; A laboratory perspective. *Acta Tropica*, vol. 169, pp. 202-206. http://dx.doi.org/10.1016/j. actatropica.2017.02.011. PMid:28219668.
- TARIQ, W.Z., KHURSHID, S., HUSSAIN, A.B. and GHANI, E., 2006. Outbreak of dengue fever in Mangla and Mirpur area. *Pakistan Journal of Pathology*, vol. 17, no. 3, pp. 122-124.
- USMAN, M., JAMAL, S., TABASSUM, S. and ZAFRAN, M., 2011. Outcome of dengue fever in adults. *Gomal Journal of Medical Sciences.*, vol. 9, no. 1, pp. 70-73.
- WASAY, M., CHANNA, R., JUMANI, M. and ZAFAR, A., 2008a. Changing patterns and outcome of Dengue infection; report from a

tertiary care hospital in Pakistan. *The Journal of the Pakistan Medical Association*, vol. 58, no. 9, pp. 488-489. PMid:18846796.

- WASAY, M., CHANNA, R., JUMANI, M., SHABBIR, G., AZEEMUDDIN, M. and ZAFAR, A., 2008b. Encephalitis and myelitis associated with dengue viral infection: clinical and neuroimaging features. *Clinical Neurology and Neurosurgery*, vol. 110, no. 6, pp. 635-640. http://dx.doi.org/10.1016/j.clineuro.2008.03.011. PMid:18467022.
- YOUSAF, M.Z., SIDDIQUE, A., ASHFAQ, U.A. and ALI, M., 2018. Scenario of dengue infection & its control in Pakistan: an up—date and way forward. Asian Pacific Journal of Tropical Medicine, vol. 11, no. 1, pp. 15. http://dx.doi.org/10.4103/1995-7645.223529.
- ZAFAR, H., BALOUCH, A.H., AKHTAR, N., TAUSEEF, K. and ASHRAF, H.M., 2013. Seroprevalence of dengue fever (IgG) in adults of Rawalpindi district. *Population*, vol. 4, no. 11, pp. 12.
- ZAFAR, H., DHODHY, M., HAYYAT, A., AKHTAR, N., RIZWAN, F., CHAUDHARY, B. and ZAREEF, S., 2010. Seroprevalence of dengue viral infection in healthy population residing in rural areas of District Rawalpindi. *International Journal of Pathology*, vol. 8, no. 1, pp. 13-15.
- ZAMIR, Q., MUHAMMAD, C.N., USMAN, J., IMRAN, A. and IMTIAZ, F., 2012. Dengue: a myth or reality. *American Journal of Clinical Pathology*, vol. 138, no. 2, suppl. 2, pp. A374. http://dx.doi. org/10.1093/ajcp/138.suppl2.212.