EDITORIAL

DENGUE IN PAKISTAN: Journey from a Disease free to a Hyper Endemic Nation

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Dengue fever (DF), Dengue Hemorrhagic fever (DHF) and Dengue Shock syndrome have been causing significant and incremental morbidity and mortality in various parts of the world. It was characterized a viral infection in 1906. The earliest known documentation of symptoms resembling dengue fever was recorded during the Chin Dynasty (AD 265-420) in the Chinese Encyclopedia of Symptoms. The illness was associated with flying insects near water and labeled as "The water poison".[1]

Dengue virus is an enveloped positive single strand 11 kilo bases long RNA virus belonging to the Flaviviridae family.[2] Four serotypes, Den 1, 2, 3 and 4 are responsible for Dengue viral infection in different regions of the globe and their relative prevalence varies temporally. Clinicopathological events in Dengue viral infection are poorly understood due to its unique features as all the four serotypes behaved differently in various regions as well as chronological order in which the infection is introduced into a community. Primary infection by any one type leads to mild to moderate disease and confer short-term (approximately 6 months) immunity against all the four types and lifelong immunity to the specific infecting type. However, subsequent 'secondary' infection by any other type may cause mild to severe disease which may prove fatal. Several manifestations of dengue viral infection are due to immunologically mediated tissue damage causing thrombocytopenia, leucopenia, increase capillary permeability, multi-organ dysfunction etc. Infection during early pregnancy usually does not cause any damage to fetus but in later term it infects the infant.[3-5]

Virus transmission usually involves the ingestion of viremic blood by aedes mosquitoes followed by an extrinsic incubation period of 8-10 days for viral replication before virus appears in the saliva and transmission on re-feeding to a susceptible human can occur. As the blood meal stimulates oviposition by the female mosquito, which undergoes one or more reproductive cycles during the extrinsic incubation period, the virus may enter the egg and be passed to the next generation of mosquitoes.[6]

Before 1970 only nine countries had experienced DHF epidemics which escalated more than four-fold by 1995.[7] It is estimated that about 120 countries currently have endemic DENV transmission, 2.5 billion i.e. two fifths of the world's population is at risk of infection,[8] and there are between 70-500 million infections of which 2.1 million are clinically severe, 500,000 cases of DHF require hospitalization and 21,000 reported deaths annually.

Dengue Virus Infection In Pakistan:

Dengue is endemic in Pakistan with its usual peak incidence in the post monsoon period.[9] In children under 16 years of age it was reported for the first time in Pakistan as an undifferentiated fever in year 1985.[10] During 1995 in Hubb,Baluchistan 75 cases and 57 deaths were reported.[11] In 2003, Dengue occurred in Haripur in which 1000 subjects were infected and 7 deaths registered. DEN 2 was dominant serotype. The same year in Khushab, Nowshera 2500 cases reported and 11 died. DEN 2 was found in 7 individuals out of 17 cases serotyped. In 2004 only 25 cases were reported from Islamabad and Karachi. In 2005, Karachi witnessed death of 13 patients out of 500 cases. In 2006, dengue was reported from Karachi, Sukkar, Nawabshah, Rawalpindi and Islamabad with about 5400 cases and 55 deaths.[12-13] Co-circulation of the two serotypes DEN 2 and DEN 3 were noted in 2006 outbreak.[14-15] In 2007, Karachi, Hyderabad, Mirpurkhas, Lahore, Haripur, Rawalpindi and Islamabad were affected resulting in 24 deaths out of 2700 reported cases. In 2008, Lahore got 1800 positive cases with three dengue serotypes (DEN 2, 3 & 4) and high frequency of DHF. Genotype of DEN 2 was subtype IV and subtype III of DEN 3.[16-17] In 2009, overall 570 cases were reported and serotype 2 and 3 were prevalent.[18] In 2010, 5000 positive cases were documented. Study conducted in Lahore, Sheikhpura and Gujranwala on 320 patients DEN 2 was the most prevalent followed by DEN virus type 1.[19]

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while in federal capital Islamabad 35 cases with one death. In Khyber Pakhtunkhwah 25 cases and 3 deaths and in Azad Jammu Kashmir 5 cases were reported.[21]

In 2011, Pakistan had the worst strike of dengue in which more than 20,000 cases and 300 deaths were reported officially which according to experts reflect under reporting. Lahore was the epicenter with maximum number of cases followed by Faisalabad, Rawalpindi and Sargodha.[20] In Karachi, Sindh 196 cases were reported.

Clinical presentation, laboratory diagnosis and management of dengue in Pakistan has been quite complex due to concurrent or super infection with malaria, typhoid and hepatitis.[22-23] Highly variable mortality during various outbreaks may also be attributed to co-morbid conditions, lack of proper management guidelines and training of health care professionals.

Table 1: Dengue Infection, reported cases and deaths

Year	# of cases	# Deaths	# cases serotype/ genotype done	Prevalent Serotype /Genotype
1985	Unknown	1	N/A	N/A
1994	145	1	N/A	DEN 1 and 2
1995	75	57	N/A	DEN 1,2 and 3
2003	3500	18	14/28	DEN 2
2004	25	0	N/A	N/A
2005	500	13	150 approx	DEN 2 and 3
2006	5400	55	1800 approx	DEN 2 and 3
2007	2700	24	N/A	DEN 2 and 3
2008	1800	N/A	N/A	DEN 1, 2 and 3
2009	570	N/A	N/A	DEN 2 and 3
2010	5000	N/A	320 approx	DEN 2 and 1
2011	20,000 (estimated)	>300	N/A	DEN 2 and 3

Fig 1: Changing Dengue Scenarion of Pakistan

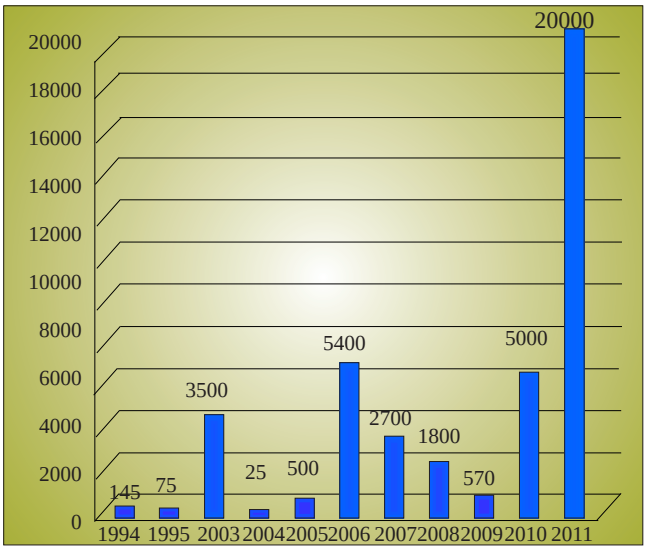
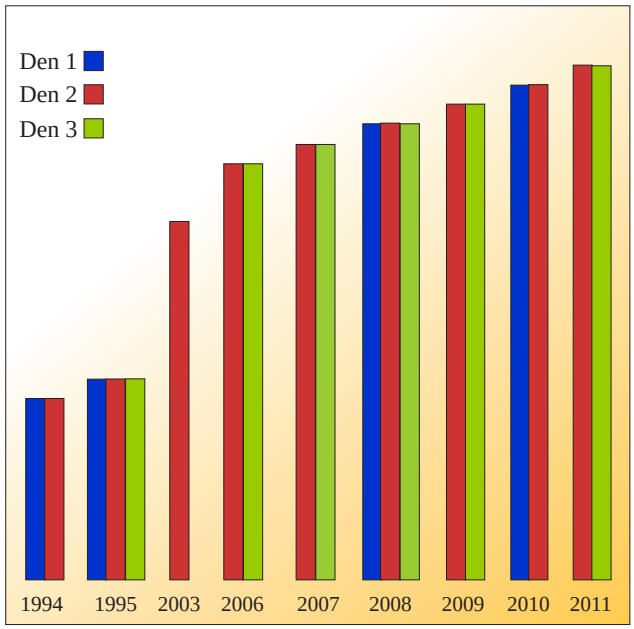


Fig 2: Dengue serotypes in various episodes



Prevention and Control:

Importance of conventional measures to reduce mosquito bites such as wearing full-sleeve clothes and long dresses to cover the limbs, use of repellents, coils and electric vapor mats, impregnated bed nets, trap lights, magnetic repellents and curtains can not be overemphasized.

Vector reduction is the most important measure in control of dengue but strategies differ from the ones which are employed for malaria control. Aedes is a domestic mosquito and attempts at spraying pesticides on streets and around the residential areas have forced the mosquitoes to move inside the homes aggravating the situation rather than improving it. Use of Long-lasting insecticide-treated materials (LL-ITMs) which can remain efficacious for >5 years, as bed nets and window curtains has potential for control of dengue in homes, offices and schools where people may be exposed to Ae. aegypti for 5 years at low cost.[24-25]

Other innovative technologies and approaches are being tested based on behavior of aedes mosquito and involve use of computers, Geographic Information System (GIS) and satellite imagery, cartographic, demographic, socioeconomic, and environmental data to implement Disease Early Warning and Response System.[26-27] Eisen and Beaty[28] proposed Dengue Decision Support System (DDSS) for gathering information to gain new insights for making evidence based decisions to manage and evaluate Integrated vector control strategies.

Use of clinical syndromic surveillance (clinical diagnosis of dengue) rather than laboratory confirmed dengue to trigger vector control response activities can shorten the response time for emergency vector control by several weeks; this approach can be used to rapidly implement vector control and remove local foci of dengue virus transmission within and around the homes of suspected dengue patients in less than 28 hours of clinical diagnosis.[29] If implemented with proper planning and at very early stage of outbreak there is a great potential for containing dengue.

There is a great need to conduct research in various aspects of dengue virus and mosquito vector. Genotype and serotype analysis, larval indices calculation and risk management, temporal and spatial pattern, statistics, reasons behind major breakthroughs, etc require thorough investigations.[30] An increased understanding of genetic factors that contribute to disease development and complications would also help define more clearly populations at risk.[31]

If Pakistan has to control dengue viral infection a multipronged strategy based on lessons learned from other countries, use of latest technologies involving all the stake holders for integrated vector control and dengue case management needs to be addressed as a national policy with adequate commitment of resources.

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