REVIEW ARTICLE

Dengue Outbreak, a growing endemic – an overview of dengue cases in Karachi.

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ABSTRACT… Objective: To study the epidemiological trends and risk factors during the dengue outbreak among population of East Karachi, Pakistan. **Study Design:** Retrospective Analysis and Review. **Setting:** Dengue Control and Prevention Center, East Karachi. **Period:** September 2020 to November 2020. **Methods:** We retrospectively analyzed the data of 1012 patients from East Karachi who were tested positive for dengue virus during the study period. Patients demographics, travel history, vector source, and outcomes were recorded. Statistical analysis was done using IBM-SPSS, version 26.0. **Results:** Most of the patients were male (60.6%), with the majority (21.0%) belonging to the 30- to 39-year-old age group. Majority (81.2%) were from Gulshan Town. Overall, UC14 and Faisal Can't have the highest number of cases (18.3%) followed by UC 5, Gulshan-1 (8.5%), and UC 10, Pehalwan Goth (8.3%). A total of 80% of the patients were alive, and 20% expired. The majority (40%) were found to have a vector-prone area in vicinity, primarily a botanical nursery. An abrupt surge in cases can be seen for the month of October. The number of dengue cases showed rapid increase in Karachi East, Pakistan. **Conclusion:** There is a need to educate the population about the preventive measures against the spread of viruses. The concerned authorities should devise an adequate and effective plan to flatten the infectivity curve. If necessary changes are not made, future outbreaks could be more serious, disastrous, and uncontrollable.

Key words: Dengue, Karachi, Outbreak, Vector, Virus.

INTRODUCTION

Our world has been hit hard by pandemics and endemics over time but there are certain diseases that are still prevalent and quite dangerous. One of such contagious diseases is dengue, which is a viral infection spread by mosquitoes and poses a global challenge to the health of many people around the world. It is caused by the dengue virus, also known as DENV, which has roughly 4 major serotypes that are more prominent and common.[1] A rough estimate suggests that a good 50% of the world population lives in areas prone to dengue endemic. The latest figures on this topic depict that a whopping 390 million dengue infections occur around the world every year, out of which half a million progress into severe dengue cases.

Dengue hemorrhagic fever is another adverse outcome of the disease that results in an approximate loss of 25000 precious lives globally each year.[2] One of the very first incidences of dengue in Pakistan was reported back in 1960 in the Baluchistan province, when at that time Pakistan's population was estimated at only 45.9 million. Over the next twenty years (between 1960 and 1980), only 12 cases were reported.[3] From there to 2010, the worldwide implications of this disease have been disastrous, as a roughly 30-fold increase in the number of cases was seen globally. Multiple factors incentivized the rapid increase in cases, such as inadequate mosquito control, irregular urbanization, multiplied population growth rate, frequent travel, and a lack of basic health amenities.

The mortality rate of the said disease now ranges from 5% to 20%, which is in itself a great alarming factor. People in Pakistan seem to be unaware of the danger that lurks. The lack of basic health facilities and bombardment of densely populated areas, especially in metropolitan cities

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like Karachi, aid in the spread of this infectious disease. The virus can present either in mild forms with symptoms ranging from none to moderate, or it could present in fatal form, such as those with symptoms of hemorrhagic fever, i.e., spontaneous bleeding, high-grade fever, multiple organ failure in patients with co-infections, and other accompanied symptoms.[4]

The total number of cases reported in Sindh for the year 2019 was 13800, out of which approximately 12844 were from Karachi. Comparing these statistics with those from a decade ago, we envision the fact that the disease is in fact endemic in a specific season, perhaps.[5] About 30% of patients with a dengue hemorrhagic fever (DHF) present with oral mucosa involvement, which has been more common in DHF than dengue fever. These manifestations include, but are not limited to, vesicles on the tongue and soft palate, crusting, and erythema of the lips. Involvement of floor of mouth and left lateral surface of tongue was also noted.[6] Karachi, a city with a population of more than 16 million, lacks basic health facilities, which turns out to be more disastrous when it comes to managing diseases like dengue.[7]

Etiopathogenesis
Dengue virus, being a single-stranded RNA virus, has roughly 4 serotypes, i.e., DEN 1-4, and the transmitting vector is a mosquito named Aedes aegypti. The viral genome can be made up of 10 genes with a length of approximately 10 KB, further divided into three structurally encoded proteins and seven non-structural proteins. Whenever someone is affected by any one of the serotypes, it is thought that the infection grants lifelong immunity to the infected person against variants of that particular serotype.[8]

A lot of theories have been put forward while discussing the probable reasons for dengue infection, including macrophages as the replication site for the virus and skin infections as the direct medium. The virus interacts with the host and induces both mechanisms, i.e., chemical and immunologic, and is proposed as one of the aetiologies.[9] However, some studies suggest that the release of chemical mediators when the virus interacts with the host leads to a lack of evidence for direct viral involvement and that rash on the skin is completely unrelated to the direct involvement and viral load.[10]

Children in Southeast Asia were found to be dying of a new severe disease in the early 1960s named dengue vascular permeability syndrome, which was characterized by a late phase of dengue illness denoting thrombocytopenia, increased liver transaminase, and other marked changes. These changes were then associated with a second heterotypic DNV infection or babies born to mothers who are immune to dengue.

Noticeable changes in thrombo-regulatory mechanisms and endothelial microvascular permeability are evident causes of the decrease in plasma and protein. Plasma leakage is mediated by endothelial cell activation, which is in turn activated by T-cells, monocytes, the complement system, and other molecules. Thrombocytopenia may be related to human hematopoietic cells being infected and progenitor cell growth being compromised, which leads to platelet depletion, damage, or dysfunction contributing to significant hemorrhage.[11]

Although extensive research has been done in this manner, this aspect of dengue fever still needs work to be fully understood. The role of monocytes is a detailed one and has been studied from different angles, which, though controlling the viremia, also aids in the destruction of tissue during infection.[12]

Classification of Dengue
Two classifications by the World Health Organization (WHO) for dengue fever are currently used, i.e., 1997 and 2009. The one that came out in 2009 basically utilizes clinical manifestations to describe and differentiate the disease.

According to the 1997 Classification
1. Symptomatic dengue infection can be divided into undifferentiated fever, dengue fever (DF), and dengue hemorrhagic fever (DHF).
2. There is a particular set of symptoms, markers, and differentiating characteristics that all need

to be met in order to classify dengue infection as either DF or DHF.

Figure 1: WHO classification of Dengue

According to the 2009 classification, the WHO classified dengue as either just dengue or severe dengue. The classification criteria remain almost the same for dengue fever, while in order to classify dengue, as severe dengue there should be:

1. Plasma leakage, resulting in severe respiratory distress or shock
2. Organ failure, i.e., elevated liver enzymes, a failing heart, a distorted level of consciousness
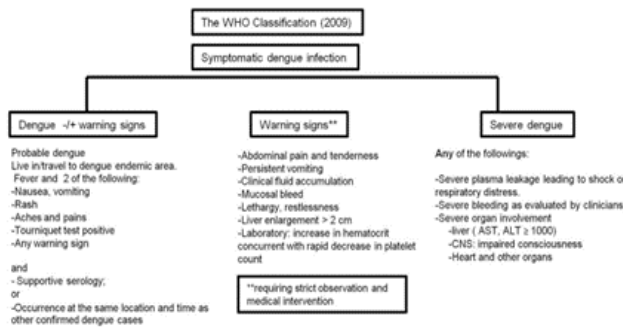3. Severe bleeding

Figure-1. WHO classification of dengue[13]

Dengue can be diagnosed in patients presenting with fever and with at least any of the mentioned two clinical symptoms or warning signs mentioned. Diagnosis cannot be completed without laboratory evidence.[13]

Clinical Manifestations
Fever (undifferentiated)
This feature is evident primarily in the initial infection phases but can also be seen during the early stages of secondary infection. The reason that the disease remains undiagnosed at this stage is the difficult diagnosis and absence of particular differentiating factors required to separate dengue from malaria, chikungunya, and other viral infections.[14]

Dengue Fever (DF)
Dengue fever can be characterized by a high-grade fever lasting for more than 3 days without any other obvious signs or symptoms. Bone-breaking pain, myalgia, metallic taste, nausea, vomiting, loss of appetite, diarrhea, severe headache, rash, and chills are all signs and symptoms of dengue fever. The symptoms can start anytime from 3 to 15 days after being bitten by a mosquito. The period of these symptoms can range from 2 to 7 days, after which these signs begin to reduce gradually. However, rash can present on different body parts and may extend from one area to another, only to subside completely after one or two weeks.

Dengue Haemorrhagic Fever (DHF)
Dengue hemorrhagic fever, or severe dengue, is characterized by severe implications for dengue, and when the progression of symptoms takes a serious turn, it could lead to severe bleeding, sudden shock, and even death. A positive tourniquet test, circulatory failure, hepatomegaly, and critical thrombocytopenia less than 100,000 cells/mm^3 are also evident in this case.[15] Intrinsic coagulopathy and plasma leakage from peritoneal or pleural cavities, gingival bleeding, gastrointestinal hemorrhage also occur during the course of dengue hemorrhagic fever (DHF). This severe type of infection is often a result of effect of secondary exposure to a virus, where the host is infected by a different serotype, and the interaction between the immune response generated by the host and the virus turns it into a complex outcome. Primary infection might have created cross-reactive antibodies, which then bind to the virus but are unable to neutralize the threat. This explanation, also known as antibody-dependent enhancement (ADE) theory, is evidence-based and is not the ultimate and definite explanation of the mechanism as it is not completely understood.

The release of different types of cytokines can also act as an indicator of the severity of the disease as macrophage inflammatory protein 1β denotes a less severe outcome. Interferon γ, which stimulates plasma leakage, is thought to be associated with a severe outcome.[16]

Outbreak in Karachi
Pakistan reported one of the very first dengue epidemics as early as 1994. Countries like India and Sri Lanka were infected by different serotypes, predominantly DEN-3. In the last 20

years, epidemics have become quite frequent and larger in Asian countries, which are already tackling other diseases. When it comes to Pakistan, there is a specific circulatory period for dengue endemic, which usually peaks around post-monsoon. Recurrent floods are also known to play a part in supporting such endemics in Pakistan. Back in October 2010, the Sindh dengue cell reported 1809 cases in Sindh, Pakistan. Since then, the yearly addition of cases has been a growing concern for health authorities. As far as the 2006 outbreak of dengue in Karachi was concerned, researchers concluded that DEN-2 and DEN-3 serotypes were responsible.[17]

Karachi, the biggest metropolitan and most diverse city of Pakistan, is located in the province of Sindh as a coastal city and is home to people from mixed ethnicities, races, and backgrounds. The city's healthcare system is inadequate to serve the needs of its population, estimated at roughly 20 million. The majority of private hospitals do provide adequate services but are too expensive for the majority of the residents.[18]

Fast forward to 2020, and the Sindh health department has reported a worrisome increase in dengue cases in Karachi. Only in September 2020, the city reported 480 cases, with the Karachi East District being the most affected. The total number of reported cases in 2020 was 1149, and there were still 3 months to go in that year. The central district reported roughly 112 cases, which include Gulberg and North Nazimabad. District Malir reported 25, District South reported 66, District West reported 19, and District Korangi reported 36 cases this year. All of the numbers include children, the elderly, and women.

Central Karachi reported 57,29, 21, 6,16, 16, 12, 17,62, 183, and 9 cases for the months of Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, and Nov respectively, bringing the 2020-year total for Central District to 428. South Karachi reported 34, 13, 3, 5, 3, 11, 6, 10, 42, 237, and 11 cases for the months of Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, and Nov respectively, bringing the 2020 year total for Karachi South to 385. West Karachi reported 30, 19, 7, 5, 8, 2, 3, 6, 15, 25, and 1 case

for the months of Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, and Nov respectively, bringing the 2020-year total for Karachi West to 121. Malir Karachi reported 8, 4,4, 1, 0, 5, 0, 4, 16, 47, and 1 cases for the months of Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, and Nov respectively, bringing the 2020 year total for Malir Karachi to 90. Korangi Karachi reported 30,15,10,2, 3, 7, 3, 4, 22, 56, and 0 cases for the months of Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct and Nov respectively, bringing the 2020-year total for Korangi Karachi to 152. Unspecified districts in Karachi reported a total of 128 cases till Nov 2020.[19]

The year-by-year increase in reported dengue infections is a dangerous trend and must be acknowledged as such by the observing and controlling authorities, respectively. Other than just symptomatic individuals, there were a large number of people who had no symptoms and had a confirmed laboratory diagnosis of dengue infection. The majority of these asymptomatic patients resided in Karachi, as suggested by a study done in 2017.[20]

Cases in Karachi East
A separate breakdown of cases for the district that has been hit the hardest is mentioned here. Karachi East district, which includes two administrative towns, i.e., Jamshed town and Gulshan town, reported about 220 cases this year alone. The breakdown of cases reported in Karachi East is as follows: 62 cases in Jan, 27 cases in Feb, 16 cases in Mar, 6 cases in Apr, 14 cases in May, 25 cases in Jun, 18 cases in Jul, 25 cases in Aug, 143 cases in Sep, 465 cases in Oct, and 17 in Nov 2020. An abrupt surge in cases can be seen for the months of September and October.

Management of Infection
The management of dengue infection is directly related to appropriate diagnosis and timely intervention. The course of the disease should be mapped out early so that the infection can be dealt with accordingly.

Sr. No.	Division/District	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sep	Oct	Nov	Total
1	East Karachi	62	27	16	6	14	25	18	25	143	465	17	818
2	Central Karachi	57	29	21	6	16	16	12	17	62	183	9	428
3	South Karachi	34	13	13	5	3	11	6	10	42	237	11	385
4	West Karachi	30	19	7	5	8	2	3	6	15	25	1	121
5	Malir Karachi	8	4	4	1	0	5	0	4	16	47	1	90
6	Korangi Karachi	30	15	10	2	3	7	3	4	22	56	0	152
	Cases of Karachi-Unspecified Districts	12	7	4	1	0	0	0	1	0	99	4	128

Table-I. Month wise confirmed dengue cases in 2020 in Sindh Province of Pakistan

Plasma leakage and bleeding are two hallmarks of severe dengue, and right detection and direction can help save lives. Poor outcomes and the progression of the disease to severe manifestations are two things that can be avoided with the correct management of dengue fever. Dengue should be considered a part of differential diagnosis in countries where outbreaks are frequent. A tourniquet test and a complete blood count are usually advised to make an initial diagnosis of dengue. Assays of the NS1 antigen are used to detect the disease early in illness but lose sensitivity over time.[21]

Daily CBC is obtained and recorded for continuous evaluation and monitoring of thrombocytopenia and leukopenia. A hematocrit great than 20% denotes plasma leakage, and a platelet count below 100,000 cells/mm^3 denotes it too. Patients should be closely monitored and called for follow-up if they are not admitted. Patients should be advised to take more fluids and follow a soft diet. Acetaminophen can be advised to tackle fever and offer some relief from illness. For severe infections, subsequent hospital care is required.[22]

CONCLUSION

Dengue and dengue hemorrhagic fever (DHF) both need to be addressed as a matter of health emergency in countries like Pakistan. The year-by-year increase in number of dengue cases points towards an unseen danger towards which the health authorities and government are both ignorant and insensitive. Planned health policies and healthy safety goals should be set and observed. For a city like Karachi, the dearth of basic amenities is like a nail in the coffin whenever an outbreak happens. Good health facilities should be provided and made accessible to each and every citizen. The underprivileged and marginalized segments of society find it hard to live a basic life, and when faced with such outbreaks, the situation becomes disastrous. Proper urban planning should be done so that haphazard construction does not aid in vector transmission. Every year, changes should be made and the necessary setup be done before the outbreak season arrives, which in the case of Pakistan is post-monsoon. If necessary changes are not made, future outbreaks could be more serious, disastrous, and uncontrollable.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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