



A RETROSPECTIVE STUDY OF MIXED DENGUE (CO-INFECTIONS) IN THE TERTIARY HOSPITAL OF MUMBAI CITY

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ABSTRACT

Introduction: Dengue is a mosquito borne viral infection found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas (1). Mixed infections of dengue with other communicable diseases like malaria, leptospirosis, typhoid etc. are not uncommon in tropical and sub-tropical countries. This study was planned to find the trends of mixed dengue infections during 2013-2019 and describe the profile mixed dengue cases at a tertiary hospital in a metropolitan city. **Methods:** It was a retrospective, hospital based study of all the dengue mixed infection cases admitted in a tertiary care center in Mumbai. Hospital records of IDSP cell (2013-2019) were mobilised by official procedure. Rates and percentages were calculated wherever appropriate. **Results:** Total 268 cases of dengue that reported during year 2013-2019 were found to have other co-infections like Malaria (N=199) Leptospirosis (N=69) & Typhoid (N=12). Out of these dengue patients, 200 were Male and 68 were Female. Mean age was 28 years and median age was 25.2 years. **Conclusion:** Mixed dengue (co-infections) exists in the city however, the magnitude is not a public health problem. The trend suggested no epidemic of such cases during last 07 years. The mortality due to mixed dengue was significant although. Malaria and leptospirosis were most common associated dengue mixed infections.

KEYWORDS : Dengue, Co infection, Malaria, Leptospirosis, Chikungunya

INTRODUCTION:

The simultaneous infection in a host with more than one pathogen or parasite is referred as the Coinfection. Notably, common endemic infections such as leptospirosis, dengue, chikungunya, and malaria, harbour favourable environments to flourish in similar climates, which is aggregated with stagnated water and aggravated with the poor personal and environmental hygiene of the inhabitants. These factors aid the spread of pathogens and parasites to humans and potential vectors, eventually leading to outbreaks of public health relevance. Malaria, dengue and chikungunya need mosquitoes as vectors, in contrast with leptospirosis, which directly invades human, although the environmental bacterial load is maintained through other mammals, such as rodents. The more complicating issue is that infections by different pathogens exhibiting similar symptoms but require different treatment management.¹

Viral infections predispose a patient for super added infections and it is important to know the spectrum to suspect them.² Malaria, dengue and chikungunya are the some common mosquito infections that are very important and cause high morbidity and mortality for many patients around the world. Dengue infection along with other Concurrent infections like Malaria, chikungunya are commonly reported in India and worldwide as well. Co-infection with pathogens that cause acute febrile illness creates a diagnostic challenge as a result of overlapping clinical manifestations.³ Lots of studies have reported high rate of dengue with CHIK especially in states like Delhi, Varanasi and West Bengal. But some other infections like leptospirosis, hepatitis, scrub typhus are also an important conditions that is seldom reported. The symptoms of dengue may mimic other diseases such as leptospirosis, influenza A, Salmonella Typhi, Japanese encephalitis, chikungunya and malaria. Quite a few research have mentioned about the rate of such mixed infections and the rates are alarming. Concurrent infection with two microbiological agents can result in an illness having overlapping symptoms creating a diagnostic dilemma for the treating physician. Since 2005, chikungunya was also causing massive outbreaks in India and other parts of Asia. Both viruses are transmitted by aedes genus and both viruses can re-emerge in many regions due to climatic changes. The clinical presentation of both arthropod borne diseases are similar.⁴

There is paucity of data regarding dengue and typhoid co- infection both in the developed and developing countries. This study attempts to find the current co- infection rates in Mumbai.

METHODS:

The line list of all dengue patients entered at IDSP cell of the hospital was mobilised by official procedures. The records during 2013 to 2019 were taken on a separate excel sheet. This record then was checked for the positivity for other co infections. Few demographic details like age

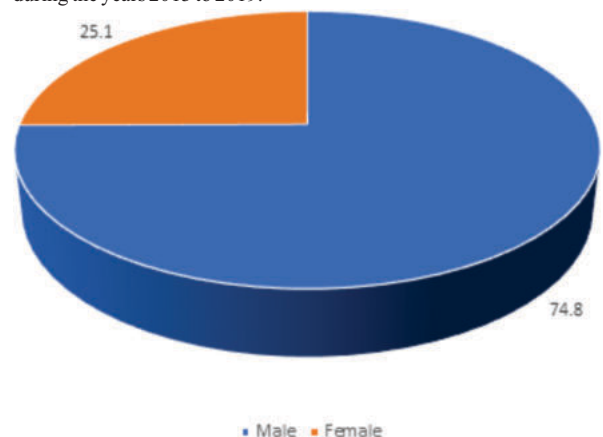
and sex were noted The rates of coinfection and percentages of mortality were calculated accordingly.

RESULTS:

Table: No. 1: Year Wise Probable Dengue And Mixed Dengue (co-infections) Cases In Tertiary Hospital (2013-2019)

Year	No. of probable dengue cases	No. of cases with mixed dengue (co-infections) among probable cases
2013	1126	96
2014	1598	79
2015	1606	7
2016	2076	16
2017	1952	19
2018	1864	5
2019	1930	6
TOTAL	12152	228

The number of mixed cases were taken from the list of probable cases because these were treated for dengue and other infections as well unlike confirmed dengue cases which were treated only for dengue. Total 12152 dengue cases (Rapid plus Elisa positive) with annual average of 1736 cases were reported in tertiary care hospital during 2013 to 2019. Average cases of mixed dengue were 32.5 with 34.6 as SD. There was no outbreak of probable dengue seen during 2013-2019. Total 228 dengue cases had presented with co infections and positivity for mixed dengue was 1.87 %. Cases ranged between 5 to 96 during the years 2013 to 2019.

**Figure no. 1:** Gender wise distribution of mixed dengue (co-infections) (N=228)

Proportion of male among mixed dengue was as high as 74.8 %. Male predominance in co infection cases was similarly reported by J. Suppiah in Malaysia as well.¹⁵

Mean age of patients with mixed dengue was 28 years with median as 25.2 years.

The range of patients age varied between 1.5 to 68 years.

The average duration of hospital stay of patients was 4 days with range of 1-16 days.

Table No. 2 : Mixed Dengue (co-infections) Cases And Deaths (2013-2019)

Year	Mixed dengue (co-infections)	Deaths among Mixed Infections (co-infections)	% of deaths
2013	96	4	4.16
2014	79	0	0
2015	7	0	0
2016	16	1	6.25
2017	19	3	15.7
2018	5	0	0
2019	6	1	16.6
TOTAL	228	9	

Total 228 dengue cases reported additional infections. Mean Deaths per year were 1.2. The data indicates no outbreak of mixed dengue (co-infections) during the period.



Figure no 2: Trend of positivity for mixed dengue (co-infections) cases. (2013-2019)

The rate of mixed dengue (co-infections) was observed highest in the year 2013 and lowest in the year 2018. The past studies at MH state and Mumbai city had shown the rate of mixed infections (co-infections) as high as 44.8 % and 10.2% in 2013 and 2014 respectively. A malaria and CHIK infection were found as coinfection of dengue in those studies.^{5,6} The rate range between 0.26 to 0.77 appears very low (< 1%) during the years 2015 to 2019. The rates were in 9%, 29.9% at Delhi, 10%, 15% at Varanasi and 23% at West Bengal.⁷⁻¹¹ T. Edwards also at Guatemala reported it as high as 32%.¹²



Figure no. 3: Trend of mortality rate among mixed dengue (co-infections) cases (2013-2019)

The mortality rate ranged between 4.16 to 16.6 among mixed dengue cases. The year 2014, 15 & 18 reported nil mortality among mixed dengue cases. The CFR was highest in the year 2019 followed by 2017. However, total cases in same year were negligible which in turn gave the high value for CFR. Overall mortality among mixed dengue was 3.94 %. Death rate in dengue with coinfections like hepatitis reported in other parts of India is as high as 25%.² There were studies that

indicated the organ involvement of one or more organs in dengue and its association with high mortality.^{13,14}

The association of mixed infection with high mortality is justifiable because addition of an infection deprives persons immunity and makes the treatment more complex.

Table No 3.: Pattern Of Dengue Coinfections (N=228)

Dengue with one coinfection	Dengue with two coinfections	Total
219	9	228

In present study, majority of the dengue showed addition of only one infection as compared to two additional infections. (96%; 4%) Three simultaneous infections including dengue were reported as an interesting case by few experts. An interesting case of dengue with malaria and CHIK from India was reported by C. Raut, N. Gupta and A. Tazeen in 2014 and 2016 respectively.¹⁶⁻¹⁸ Another triple case of dengue, malaria and typhoid was reported by P. Teja from Andhra Pradesh in 2012.¹⁹ Triple infection of dengue, malaria and leptospirosis was not found in the literature.

Table No. 4: Types Of Infections Found In Dengue Cases In Tertiary Care Hospital.(N=228)

Sr No	Infections	Number	% of probable dengue
1	Malaria	160	1.31
2	Leptospirosis	53	0.43
3	Typhoid	11	0.09
4	AGE	1	0.008
5	Hepatitis	3	0.02

Malaria was the most common co-infection of dengue followed by Leptospirosis. In 2012, Hati et al., reported that 1.54% of the cases diagnosed as dengue in Kolkata had concurrent Malaria.²⁰ The rate of present study appears low as compared to other studies. During similar period, the rate of dengue with malaria had been reported by researchers in different states of India. It was 7.4%, 10.2%, 3%, 3.14% and 2.84% at India, Mumbai, Odisha, Ahmedabad and Nigeria respectively.^{5,6,21-23} The city of Mumbai is hyperendemic for malaria and it is possible that the cases are primarily detected as malaria and not dengue and are being missed as coinfection. In contrast, A. Hasim et al at Rawalpindi, who studied the patients with AFI found zero co-existence of dengue with malaria in 2012.²⁴

Leptospirosis was another common coinfection found in the present study but much lower rate as compared to that found by A. Sachu (3.4%) Suppiah (4.1%).^{25,15}

The studies reporting hepatitis are scarce. Hepatitis in the present study was less common as compared to other infections like malaria, leptospirosis. It is far low as compared than that reported by P. Panda who found 25% rate for hepatitis among dengue patients.²

Dengue with typhoid was also very low in contrast with the findings of study by Y. Sharma who reported it 7.8% at Delhi.²⁶

Table: No. 5: Cases And Deaths Of Dengue Co-infections In The Tertiary Care Hospital In Mumbai.

Sr No	Infections	Cases	Deaths	Fatality rate
1	Dengue + Malaria	151	2	1.32
2	Dengue + Leptospirosis	47	5	10.6
3	Dengue + Typhoid	8	1	12.5
4	Dengue + AGE	1	0	0
5	Dengue +Hepatitis	3	0	0
6	Dengue + Malaria+ Leptospirosis	6	0	0
7	Dengue + Malaria+ Typhoid	3	1	33.3
	Total	219	9	

The death rate appears high in dengue cases with malaria as co infection. The dengue cases presented with additional two infections like leptospirosis and typhoid. The fatality was high with such triple infections. Fatality was highest when dengue is in combination with malaria and typhoid (33.3%) followed by dengue plus typhoid dual infection (12.5%). All three infections (dengue, malaria & leptospirosis) are monsoon related diseases. The Mumbai city is prone for floods during monsoon which is the important determinant for leptospirosis. Mosquito breeding is extreme during monsoon which

may increase the risk of dengue and malaria as well. No other study in India and across the country reported this type of combination.

Triple infection of dengue, malaria and typhoid is reported here with 33.3% mortality. The similar triple infection is reported as a case by P. Teja in the Andhra Pradesh in 2013.¹⁹

The mortality was elevated (10.6%) among the dengue -leptospirosis co infections (LDCI) as compared to 0.50 % in Malaysia where M. Hishamshah attributed deaths in leptospirosis patients to LDCI (2011 to 2015).²⁷ Few other scientists also have highlighted the leptospirosis as a cause of mortality in dengue patients case studies.²⁸⁻³⁰ On the contrary, other clinicians based on their case study, opined that spontaneous full recovery in these circumstances is still possible with supportive treatment in such dengue-lepto coinfection.^{31,32}

The concurrent triple infections of dengue, malaria and chikungunya has been reported in India by N.Gupta (4%) and A. Tazeem (2 out of 48 dengue positives) at Delhi.^{17,18} It was surprising that not a single dengue was reported with chikungunya as a co infection. Probably, there was lesser focus on screening for CHIK infection as compared to other infections like leptospirosis and malaria at the hospital.

CONCLUSION & RECOMMENDATION:

Mixed dengue (co-infections) exists in the city however; the magnitude is not a public health problem. Malaria and leptospirosis are most common associated dengue mixed infections. The analysis on trends indicated no epidemic of such cases during last 07 years. The mortality due to mixed dengue was significant although. This model of testing each dengue patients with other vector borne diseases may be replicated so as to control the prevalence and mortality due to coinfections.

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