Letter to the Editor

Why is severe dengue rare in Nigeria: an ecologic-epidemiology and host genetic perspective?

[1]Idris Nasir Abdullahi, [2]Chisom Emmanuel Okechukwu, [3]Bamidele Soji Oderinde

[1]Department of Medical Laboratory Science, Faculty of Allied Health Sciences, College of Medical Sciences, Ahmadu Bello University, Zaria, Nigeria
[2]Department of Medical Microbiology, School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto, Nigeria
[3]Department of Medical Laboratory Science, University of Maiduguri, Maiduguri, Nigeria

Dear Editor,

Dengue is an old viral disease that has re-emerged in recent time. It is regarded as a tropical fever infection placing more than 2 billion of the world's population at high risk. [1] The lack of potent antiviral drugs and availability of dengue vaccine in less than 5 countries have placed about 500,000 individuals (mainly children) being hospitalized with severe dengue every year. This has caused tremendous socioeconomic losses for both households and nations. [1]

In 1960s, Dengue virus was first isolated in Africa at Ibadan. [2] Several reports have consistently shown that all dengue virus serotypes and its vectors (*Aedes spp*) are endemic in Nigeria. The demonstration of dengue neutralizing antibodies in monkeys, and galagos suggest the occurrence of a forest cycle of dengue in Nigeria. [3] Fagbami *et al* demonstrated that 17 flavivirus neutralizing antibody-positive sera contained infection-enhancing antibodies to dengue. [4] In that report heterologous infection-enhancing antibody titers were lower than the homologous ones. [4] In another study in Oyo state, involving mild febrile illness, 81% of the patients examined had antibody to dengue type-1.[5] In another study involving four ecological zones in Nigeria, the highest percentage (63%) of dengue neutralizing antibody was observed in the rain forest zone and plateau zone showed lowest (10%). [6]

In addition, a high prevalence of antibody to DEN-2 has been reported in Kainji Lake area of Nigeria. [7] In 2009, Baba and Talle detected DENV 1 & 4 in serum sample of febrile patients as well as from mosquitoes identified as *Aedes aegypti*. [8] In 2013, Idris *et al*, reported that out of 256 sera from febrile patients analyzed using microneutralization test, 26 (10.1%) had neutralizing antibodies to DENV-3 virus. [9] Thereafter, few ELISA-based studies were conducted all over Nigeria with IgG seropositivity ranging between 45 to 65%. [10]. In 2017, Nasir *et al* and Kolawole *et al* separately reported acute dengue cases among febrile patients at Abuja and Ilorin, respectively. [11, 12]

The transmission of dengue is climate sensitive for several reasons: mosquitoes require standing water to breed and a warm ambient temperature is critical to adult feeding behavior, the mortality rate of larval development and as well as speed of virus replication. [13] In countries where transmission does routinely occur, short-term changes in weather, particularly temperature, precipitation, and humidity, are often correlated with dengue incidence. [13] Some studies on relationship between climatic change and dengue showed possible increase in dengue virus transmission due to higher temperatures, humidity, and precipitation. [14] In a

Corresponding author:
Idris Nasir
Abdullahi Department of Medical Laboratory Science,
Faculty of Allied Health Sciences, College of Medical Sciences,
Ahmadu Bello University, Zaria, Nigeria
Email: eedris888@yahoo.com
Tel: +2348030522324, +2348027771068

related study, it was found that the monthly dengue virus activity was highest during the rainy season of the months of June, July, and August and lowest in the dry months of January and February respectively. [15]

Antibody-Dependent Enhancement mechanism (ADE) has dominated as the explanatory model for severe dengue disease in secondary infections. However, evidence for ADE in humans is indirect and controversial results against ADE exist. [16] Many parts of the world have become hyperendemic, implying that all four serotypes of DENV co-circulate in the same country, with the consequence that secondary infections are common scenarios. [17] Epidemiological data indicated that not all secondary infections cause DHF/DSS, and that there are even cases of tertiary and quaternary DENV infections. [18] In Cuba, 17.5% of the total DHF dengue cases were caused by third or fourth infections. [17]

The severity of DENV infection is modulated by multiple risk factors such as age, sex, viral serotype /genotype, host genetic background, and non-primary dengue virus infection by heterologous serotypes. Apart from the influence of viral genetic profile, the host's genetic background with varying polymorphisms has important consequences for severe dengue. [19] Evidence of the host's genetic importance has been derived from Cuban dengue epidemics where a reduced risk for DHF/DSS was observed in those with an African ancestry compared to those with European ancestry. The Cuban observations coincide with the low susceptibility to DHF reported in African and Black Caribbean populations. [19] It is interesting that despite the circulation of dengue virus in many African nations, there are only sporadic reports of DHF.

A significantly higher frequency of HLA class I alleles A*31 and B*15 have been found in Cuban individuals with symptomatic DENV infection compared to asymptomatic controls, who showed an elevated frequency of HLA II alleles DRB1*07 and DRB1*04. [19] This shows that polymorphisms in HLA class I gene place dengue infected individuals to higher risk of disease severity than those without polymorphisms. Genetic polymorphism that confers protection against development of severe dengue have also been recently described in mannose binding lectin-2 (MBL2) gene and HLA class II. Polymorphism in MBL2 gene has been shown to be associated with thrombocytopaenia and an increased risk for developing DHF. Findings have shown that 10% of Caucasian and mongoloids have wild type of this gene and non from the black race. This might also be another explanation for racial susceptibility to dengue severity. [20] Despite positive virologic pre-conditions in Hiati dengue outbreak, DHF cases were not recorded by experienced Port-au-Prince pediatricians. These observations, which are reminiscent of those in Africa, provide further evidence of a dengue resistance gene in black populations. [21] Effective vector control measures are the sole weapon against dengue. Hence, educational and adherence to preventive measures should focus on minimizing people susceptibility of acquiring dengue through barrier from vector breeding sites and bite on humans.

Conflict of interest

None declared

REFERENCES

1. World Health Organization (WHO). Dengue Control. 2017. www.who.int/demguecontrol/epidemiology/en cited on 4th October, 2017
2. Vasilakis N, Tesh RB, Weaver SC. Sylvatic dengue virus type 2 activity in humans, Nigeria, 1966. Emerg Infect Dis. 2008; 14: 502-504
3. Fagbami A. Epidemiological investigations on arbovirus infections at Igbo -.Ora, Nigeria. Trap Geogr Med. 1977; 29 (2): 187 – 191
4. Fagbami A, Halstead SB, Marchette NL. Heterologous flavivirus infection - enhancing antibodies in sera of Nigerians. Am.J. Trop. Med. Hyg. 1988; 38 (1): 205-207.
5. Fagbami AH. Zika virus infections in Nigeria: virological and seroepidemiological

investigations in Oyo State. J Hyg (Lond). 1979; 83(2): 213-9

6. Fagbami AH, Monath TP, Fabiyi A. Dengue virus infections in Nigeria: a survey for antibodies in monkeys and humans. Trans R Soc Trop Med hyg. 1977: 71 (1): 60-5
7. Adekolu –John EO, Fagbami AH. Arthropod-home virus antibodies in sera of residents of Kainji lake Basin, Nigeria,1980. TrailS.R.Soc.Trap.Med.Hyg. 1983;,77(2): 149-151.
8. Baba MM, Talle M. The effect of Climate on Dengue virus infections in Nigeria. New York Sci. J. 2011; 4:28-33.
9. Idris AN, Baba MM, Thairu Y, Bamidele O. Seroprevalence of dengue type-3 Virus among patients febrile illnesses attending a tertiary hospital in Maiduguri, Nigeria. Int J Med Med Sci. 2013; Vol. 5(12), pp. 560-563
10. Oladipo EK, Amanetu C, Gbadero TA, Oloke JA. Detectable anti-dengue virus IgM antibodies among healthy individuals in ogbomoso, Oyo State, Nigeria. Am J Infect Dis.2014; 10 (2): 64-67
11. Kolawole OM, Seriki AA, Irekeola AA, Bello KE, Adeyemi OO. Dengue virus and malaria concurrent infection among febrile subjects within Ilorin metropolis, Nigeria. J Med Virol; 2017; 89(8): 1347-1353
12. Nasir IA, Agbede OO, Dangana A, Haruna AS, Baba M. Dengue Virus non-structural protein-1 expression and associated risk factors among febrile patients attending University of Abuja Teaching Hospital, Nigeria. Virus Research, 2016; 230: 7-12
13. Centers for disease control and prevention. Dengue fever: www.cdc.gov/dengue. 2018. Accessed on 3rd July, 2019
14. Hales S, de Wet N, Maindonald J, Woodward A. Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. Lancet. 2002;360 (9336):830–834
15. Moore DL, Causey OR, Carey DE, Reddy S, Cooke AR, Akinkugbe FM, et al. Arthropod-borne viral infections of man in Nigeria, 1964-1970. Ann Trop Med Parasitol. 1975; 69 (1): 49-64.
16. Halstead SB. Dengue. Lancet 2007; 370: 164452.
17. Murray NEA, Quam MB, Wilder-Smith A. Epidemiology of dengue: past, present and future prospects. Clin Epid. 2013; (5): 299-309
18. Alvarez M, Rodriguez-Roche R, Bernardo L, Vazquez S, Morier L, Gonzalez D, et al. Dengue hemorrhagic fever caused by sequential dengue 13 virus infections over a long time interval: havana epidemic, 20012002. Am J Trop Med Hyg 2006; 75: 11137.
19. Guzman MG, Sierra B, Kouri G, Farrar J, Simmons C. Host and virus determinants of susceptibility and dengue disease severity. In: Hanley KA, Weaver SC, eds. Frontiers in dengue virus research. Norfolk, UK: Caister Academic Press; 2010, pp. 79102.
20. Nascimento EJ, Silva AM, Cordeiro MT, Brito CA, Gil LHVG, Braga-Neto U, et al. Alternative complement pathway deregulation is correlated with dengue severity. PLoS One 2009;4:e6782
21. Halstead SB, Streit TG, Lafontant JG, Putvatana R, Russell K, Sun W, et al. Haiti: absence of dengue hemorrhagic fever despite hyperendemic dengue virus transmission. *Am. J. Trop. Med. Hyg.,* 65(3), 2001, pp. 180–183