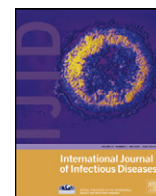


Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Letter to the Editor

Sickle-cell erythrocytes in the placentas of dengue-infected women

Dengue is the most rapidly advancing vector-borne disease, with an estimated 50 million infections occurring annually.¹ The occurrence of dengue in pregnancy has been described in the literature since 1948,² mostly in the form of case reports, with the two largest series reported from French Guiana, involving 38 cases³ and 53 cases.⁴ In the last two decades, the first reports of vertical transmission and maternal deaths related to infection with the dengue virus (DENV) have been confirmed.^{5–7}

The aim of this study was to investigate the pathological changes found in the placentas of women infected with DENV. Twenty-eight placentas and seven ovular remnants were analyzed by macroscopic examination after fixation in 10% formalin. Cleavage was performed, and seven samples were retrieved from the placenta and annexes. Samples were subsequently stained using hematoxylin–eosin (HE). The ovular membranes, umbilical cord, and placental tissue were observed by histological study.

The mean maternal age was 24 ± 7 years, the mean gestational age of the infants at birth was 38 ± 2 weeks, and the mean birth weight was 2953 ± 531 g. Seventy-eight percent of events (birth, stillbirth, and abortion) occurred in the period of maternal viremia. The main pathological changes were deciduitis in 14 (40%), coriodeciduitis in 12 (34%), intervillitis in 10 (28.5%), villitis in 10 (28.5%), and hypoxia in 26 (74%) (villous stromal edema, excessive formation of syncytial knots, corioangiosis). Five showed erythrocyte sickling in the placental intervillous space. None of these patients had a history of sickle-cell disease. All showed warning signs, usually predictors of severe illness and indicative of capillary leak syndrome, and were classified as dengue hemorrhagic fever.⁸ One progressed to dengue shock syndrome and died.

Using the Fisher's exact test at the $\alpha = 0.05$ significance level, the sample data provided valuable insights into a trend of association between the presence of sickle erythrocytes and the presence of warning signals in the mother (Fisher's exact test, bilateral p -value = 0.057, and unilateral p -value = 0.048).

Sickle cell anemia is associated with a fatal outcome in patients infected with DENV,⁹ but there is no reference about the sickle-cell trait, which in the presence of hypoxia may sickle the red blood cells that are deposited in the intervillous space. It may be a surrogate marker of severity in pregnant women with dengue, especially in a population like that of Brazil, which has approximately 2% HbS carriers, reaching 5% among negroids.¹⁰ Further studies should confirm this association.

Conflict of interest: No conflict of interest to declare.

References

1. Khan E, Kisat M, Khan N, Nasir A, Ayub S, Hasan R. Demographic and clinical features of dengue fever in Pakistan from 2003–2007: a retrospective cross-sectional study. *PLoS One* 2010;**5**:e12505.
2. Waddy R. Dengue in early pregnancy. *Lancet* 1948;**11**:950.
3. Carles G, Talarmin A, Peneau C, Bertsch M. [Dengue fever and pregnancy. A study of 38 cases in French Guiana]. *J Gynecol Obstet Biol Reprod (Paris)* 2000;**29**:758–62.
4. Basurko C, Carles G, Youssef M, Guindi WE. Maternal and fetal consequences of dengue fever during pregnancy. *Eur J Obstet Gynecol Reprod Biol* 2009;**147**:29–32.
5. Carroll ID, Toovey S, Van Gompel A. Dengue fever and pregnancy—a review and comment. *Travel Med Infect Dis* 2007;**5**:183–8.
6. Pouliot SH, Xiong X, Harville E, Paz-Soldan V, Tomashek KM, Breart G, et al. Maternal dengue and pregnancy outcomes: a systematic review. *Obstet Gynecol Surv* 2010;**65**:107–18.
7. Alvarenga C, Silami V, Brasil P, Boechat ME, Coelho J, Nogueira RM. Dengue during pregnancy: a study of thirteen cases. *Am J Infect Dis* 2009;**5**:295–300.
8. World Health Organization. Dengue guidelines for diagnosis, treatment, prevention and control. Geneva: WHO; 2009.
9. Limonta D, González D, Capó V, Torres G, Pérez AB, Rosario D, et al. Fatal severe dengue and cell death in sickle cell disease during the 2001–2002 Havana dengue epidemic. *Int J Infect Dis* 2009;**13**:e77–8.
10. Alvares Filho F, Naoum PC, Moreira HW, Cruz R, Manzano AJ, Domingos CR. [Age and racial geographic distribution of S hemoglobin in Brazil]. *Sangre (Barc)* 1995;**40**:97–102.

Christiane Fernandes Ribeiro^{a*}

Vânia Glória Silami^a

Patrícia Brasil^b

Rita Maria Ribeiro Nogueira^c

^aDepartament of Pathology, Universidade Federal Fluminense, 303, Marquês de Paraná Street, Centro, Niterói, Rio de Janeiro, 24033-900, Brazil

^bInstitute of Clinical Research Evandro Chagas/Fiocruz, Rio de Janeiro, Brazil

^cFlavivirus Laboratory, Oswaldo Cruz Institute/Fiocruz, Brazil

*Corresponding author. Tel.: +55 21 26218824;

fax: +55 21 26299128/26299124

E-mail address: chrisribeiro@vm.uff.br (C.F. Ribeiro).

Corresponding Editor: William Cameron, Ottawa, Canada

23 July 2011

8 September 2011