

However, 10% higher values of the QTc in cases are well beyond what could be ascribed to measurement error. In fact, to illustrate this point, there are clinically established 2.5% higher values of the QTc in women compared with men (upper limits of normal, 450 ms in women vs 440 ms in men).⁵ We agree that potential mechanisms by which serum calcium levels may affect SCA risk are poorly understood, but our findings should serve as an impetus for efforts to improve the understanding of this phenomenon. In this context, it is important to recognize that differences in serum calcium values in the “clinically normal” range could still have implications for pathophysiology. Today, the general consensus in the field for mechanisms of the SCA complex trait is that there are likely to exist multiple overlapping substrates, risk factors, and triggers. How can we exclude the possibility that moderately lower serum calcium could be a risk modifier? In fact, one of the reported associations between low magnesium levels and SCA that Husain et al refer to was also in the “clinically normal” range.⁴ Moreover, none of these previous studies were able to adjust for serum calcium values. We could not adjust for magnesium levels but did account for other potential confounders including potassium levels, hypothyroidism, diabetes, creatinine clearance, use of diuretics, and left ventricular ejection fraction, and the association between serum calcium level and SCA remained robust.

We remain excited about the potential mechanistic and risk stratification implications of reporting this new association but certainly do not advocate for acting on these findings in terms of health promotion or SCA prevention without considerable further investigation.

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1. Lee HC. Serum calcium: a sudden cardiac arrest risk factor [editorial]. *Mayo Clin Proc.* 2017;92(10):1466-1468.
2. Chiuvè SE, Komgold EC, Januzzi JL Jr, Gantzer ML, Albert CM. Plasma and dietary magnesium and risk of sudden cardiac death in women. *Am J Clin Nutr.* 2011;93(2):253-260.
3. Kieboom BC, Niemeijer MN, Leening MJ, et al. Serum magnesium and the risk of death from coronary heart disease and sudden cardiac death. *J Am Heart Assoc.* 2016;5:e002707.
4. Peacock JM, Ohira T, Post W, Sotoodehnia N, Rosamond W, Folsom AR. Serum magnesium and risk of sudden cardiac death in the Atherosclerosis Risk in Communities (ARIC) study. *Am Heart J.* 2010;160:464-470.
5. Rautaharju PM, Mason JW, Akiyama T. New age- and sex-specific criteria for QT prolongation based on rate correction formulas that minimize bias at the upper normal limits. *Int J Cardiol.* 2014;174(3):535-540.

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Cardiac Compromise in Zika Virus Infection



To the Editor: We have read with interest the case report of Schwartzmann et al¹ reporting a single case of Zika virus (ZIKV) meningoencephalitis, but also with ZIKV propagation to other organs, including the heart. As in other arboviral diseases (dengue and chikungunya),²⁻⁴ cardiovascular disorders such as arrhythmias, among others, are being observed in previously healthy cases. But there is a lack of publications assessing it. We take this opportunity to discuss 2 cases of pregnant women from an endemic area (Sucre, Colombia), with confirmed

ZIKV infection who presented with cardiovascular and electrocardiographical (ECG) alterations (myocarditis).

Case 1. Age 30 years, 34.2 gestational weeks, presenting with rash and pruritus. Zika-RT-PCR positive, negative for dengue and chikungunya. Her ECG showed a sinus tachycardia with a prolonged QTc (associated with Torsade de Pointes) (using Bazett formula) (Figure A). Cardiac enzymes were negative. At the echocardiogram, 200 cc of pericardial fluid was found. She had not presented with cardiovascular disease earlier. After 2 weeks, ECGs and echocardiograms were normal.

Case 2. Age 25 years, 10.1 gestational weeks, presenting with rash and pruritus. Zika-RT-PCR positive, negative for dengue and chikungunya. Her ECG showed a left anterior hemiblock (Figure B). At the echocardiogram, 300 cc of pericardial fluid was found. Cardiac enzymes were negative. She had not presented with cardiovascular disease earlier. After 2 weeks, ECGs and echocardiograms were normal.

The ECG alterations were seen in patients, previously healthy and young patients, as well as also reported recently in congenital cases.⁵ Although a large epidemic of ZIKV has affected the Americas, there is a lack of literature about cardiovascular manifestations in adult patients with ZIKV infection, including those who are pregnant. This would lead to prospective systematic ECG assessments in patients with ZIKV infection.⁴ As has been recently proposed with chikungunya, in patients with suspicion of ZIKV infection, cardiovascular assessment and ECG should be routinely performed, especially in pregnant women.

Although this case report has limitations, it would be the first in the Caribbean region of Colombia and in the country, adding evidence that ECG alterations in patients with confirmed ZIKV infection would

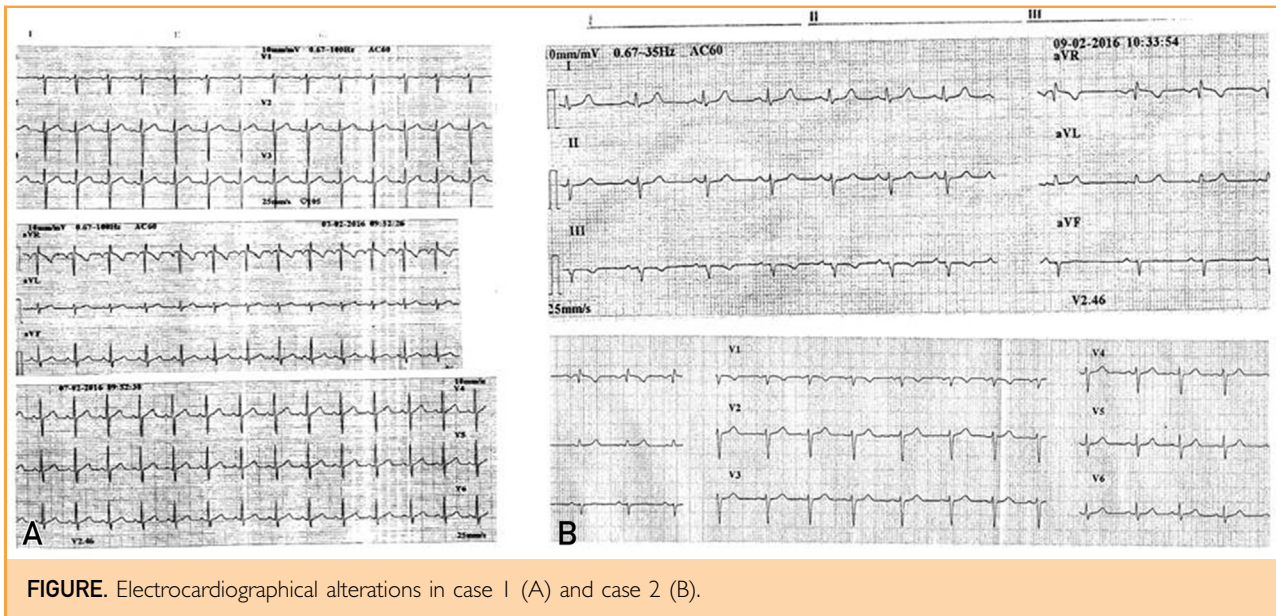


FIGURE. Electrocardiographical alterations in case 1 (A) and case 2 (B).

occur. We agree with Schwartzmann et al¹ regarding the relevance of ZIKV infection as a global public health emergency still with limited available information about ZIKV infection with neurologic and cardiovascular involvement in immunocompromised patients, including those who are pregnant. Prospective studies are necessary to establish the relative frequency of cardiovascular and ECG alterations in patients with ZIKV infection.

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- Schwartzmann PV, Ramalho LN, Neder L, et al. Zika virus meningoencephalitis in an immunocompromised patient. *Mayo Clin Proc.* 2017; 92(3):460-466.
- Villamil-Gómez WE, Ramirez-Vallejo E, Cardona-Ospina JA, Silvera LA, Rodríguez-Morales AJ. Electrocardiographic alterations in patients with chikungunya fever from Sucre, Colombia: a 42-case series. *Travel Med Infect Dis.* 2016;14(5):510-512.
- Hidalgo-Zambrano DM, Jimenez-Canizales CE, Alzate-Piedrahita JA, Medina-Gaitán DA, Rodríguez-

Morales AJ. Electrocardiographic changes in patients with Chikungunya fever. *Rev Panam Infectol.* 2016; 18(1):13-15.

- Alvarez MF, Bolívar-Mejía A, Rodríguez-Morales AJ, Ramirez-Vallejo E. Cardiovascular involvement and manifestations of systemic Chikungunya virus infection: a systematic review. *F1000Research.* 2017;6:390.
- Cavalcanti DD, Alves LV, Furtado GJ, et al. Echocardiographic findings in infants with presumed congenital Zika syndrome: retrospective case series study. *PLoS One.* 2017;12(4):e0175065.

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In Reply—Cardiac Compromise in Zika Virus Infection



To the Editor: We read with interest the letter from Villamil-Gómez et al,¹ which reinforces the possibility of frequent subclinical cardiovascular involvement in Zika virus (ZIKV) infection, especially in immunocompromised patients.

The 2 cases reported by Villamil-Gómez et al are suggestive that ZIKV can frequently affect the heart, as shown by electrocardiographic changes and pericardial effusion by echocardiogram, but without clinical manifestations of the cardiac involvement. It is relevant to consider that

with the lack of documentation of ZIKV presence in heart tissues, the described changes could also be part of a systemic inflammation response and not be due to a direct virus aggression. Nevertheless, this kind of report raises the possibility that ZIKV infection could be more frequently associated with subclinical cardiac involvement than previously suspected, demanding prospective studies to investigate this hypothesis.

In our previously reported clinical case,² the patient had undergone cardiac transplantation and was on immunosuppressive therapy previously to the ZIKV infection. During the course of the infection, because of the suspicion of ZIKV meningoencephalitis, we were forced to withdraw the immunosuppressive therapy and the patient unfortunately died as a consequence of acute cardiac rejection and circulatory shock. Therefore, in our previous case, there was no clear evidence of ZIKV infection directly affecting the heart.

In conclusion, there is preliminary evidence suggesting that ZIKV infection may affect other organs besides neurologic involvement and its impact could be even more