Background

Chikungunya fever is an arthropod-borne disease caused by the Chikungunya virus (CHIKV), which was unknown until 1950s when it was described in an outbreak in southern Tanzania. It has re-emerged in the form of epidemics: first in the eastern hemisphere and, after 2007, it has become a public health problem in the western world, causing disability, with related deteriorations in quality of life and fatal complications (1-3). Aim: To determine the markers of immune response in patients with acute, chronic and fatal infections by CHIKV in Colombia, during the epidemic in 2015.

Methods

Cross-sectional study, carried out in serological samples of patients with laboratory-confirmed diagnosed for acute CHIKV (AC), chronic CHIKV (CC) and fatal CHIKV cases (FC). The samples were supplied by the virology laboratory of the National Health Institute, and include samples from a country-wide pool of patients, which were analyzed with a commercial kit 13 cytokines.

Results

A total of 164 samples were analyzed, 50 from patients with AC, 25 from FC due to CHIKV and 89 from patients with CC. The average age was 48.2 years ± 24.4 SD. 59.8% (98/164) were female, of which 28.5% (28/98) had AC, 8.1% (8/98) FC and 63.2% (62/98) CC. Of the total men (66/164), 33.3% (22/66) had AC, 25.7% (17/66) FC and 40.9% (27/66) had CC. AC was more prevalent in the extreme ages of life (<10 years and >70 years), and in young adults and intermediate-age adults (20-60 years) (p < 0.05). The median time to analyze each sample was 4.5 (IQR) days for AC and 7 days (IQR) 75 for CC.

Ten plasma cytokines (INF-γ, IL-10, IL-13, IL-17A, IL-2, IL-4, IL-5, IL-6, TGF-α, TNF-α) were significantly elevated in deceased patients compared to patients with acute infection (p < 0.005).

In patients with FC, IL-6 and IL-10 had the highest median values among the proinflammatory cytokines and the anti-inflammatory cytokines, respectively. When we compared patients with FC and CC, eleven cytokines (INF-γ, IL-10, IL-13, IL-17A, IL-2, IL-4, IL-5, IL-6, LT-α/TNF-β, TGF-α, TNF-α) showed statistically significant differences (p < 0.05). The levels of IFN-γ and INF-γ were 8 and 2 times higher in patients with AC than in the group with CC.

Figure 1. Comparison of cytokines in acute Vs Fatal cases

Figure 2. Comparison of cytokines in acute Vs chronic Chikungunya

Conclusion

This is the first study in Colombia about cytokine levels in the AC, FC and CC patients. AC had an increase in IFN-γ, IL-6, IL-10, IL-12, IL-17A and TNF-α cytokines, which if persistently elevated for more than 3 months may cause decreased levels of IFN-γ and IL-6, may progress to CC. If, in addition to acute phase cytokines, IL-2, IL-4, IL-13, LT-α/TNF-β, TGF-α increases, the disease may be severe or fatal. Cytokines, especially IL-6, are becoming a tool for monitoring, evolution and prognosis of CHIKV disease.