LETTER

New prevalence estimate of Torque Teno virus (TTV) infection in healthy population and patients with chronic viral hepatitis in Jiujiang, China

Dear Editor,

Torque Teno virus (TTV) is a nonenveloped human DNA virus that was isolated from the serum of a patient with transfusion-transmitted hepatitis with unknown etiology in 1997 (Nishizawa et al., 1997). TTV is the first human virus with a single-stranded circular DNA genome to be identified, and is recently classified as the Alphatorquevirus genus of the Anelloviridae family by the International Committee on Taxonomy of Viruses (ICTV) (King et al., 2011). TTV shows very high genetic variability for a DNA virus (Hussain et al., 2012; Chen et al., 2013). Thus far, five main genetic groups (groups 1–5) including at least 39 genotypes have been identified based on phylogenetic analysis (Peng et al., 2002; Okamoto et al., 2004; Hussain et al., 2012; Mi et al., 2014).

Two distinct PCR methods have primarily been used for investigating the prevalence of TTV infection. The earlier N22-PCR, with primers derived from the N22 region within ORF1, can detect only a portion of TTV variants mainly representing genetic group 1 TTVs (genotypes 1–6) (Okamoto et al., 1999; Peng et al., 2002; Okamoto et al., 2004; Hussain et al., 2012), and this method is mostly used for investigating TTV prevalence in the Chinese population (Zhao et al., 2002). In contrast, the untranslated region PCR (UTR-PCR) can detect essentially all known TTV strains reported (Takahashi et al., 1998; Peng et al., 2002; Okamoto et al., 2004).

In the current study, UTR-PCR and N22-PCR were utilized for estimating the prevalence of TTV infection. As shown in Table 1, TTV viremia was detected by UTR-PCR in 96 (98.0%) of 98 healthy adults, 80 (100%) in 80 patients with chronic viral hepatitis B (PCVHB), and in 78 (97.5%) of 80 patients with chronic viral hepatitis C (PCVHC), while it was detected in 37 (37.8%) of 98 healthy adults, 28 (35.0%) of 80 PCVHB, and 34 (42.5%) of 80 PCVHC by N22-PCR. There was no significant difference in the prevalence of TTV viremia in healthy adults and patients with liver disease as detected by UTR-PCR and N22-PCR ($p > 0.05$). Furthermore, there was no significant difference in the positive rate of TTV DNA observed among healthy adults, PCVHB, and PCVHC ($p > 0.05$).

As shown below in Table 1, TTV viremia was detected by UTR-PCR in 47 (54.7%) of 86 healthy infants, while it was detected in 15 (17.4%) of 86 healthy infants by N22-PCR, both significantly lower than that obtained...
from the healthy adults and chronic hepatitis patients ($p < 0.01$). Furthermore, among 19 infants from whom blood samples were obtained less than 1 month after birth, no TTV DNA was detected by UTR-PCR or N22-PCR. However, positive TTV DNA obtained by UTR-PCR was detected in 9 (33.3%) of 27 infants at the age of 1–6 months, and 38 (95.0%) of 40 infants at the age of 7–12 months. Similarly, TTV DNA was detected by N22-PCR at a positive rate of 2 (7.4%) in the 1–6 months group and 13 (32.5%) in the 7–12 months group. Interestingly, the incidence of TTV infection in the infants at the age of 7–12 months was comparable to those among healthy adults and chronic hepatitis patients ($p > 0.05$).

In the absence of a serological system, detection of TTV DNA by PCR thus far has been the only confirmed method for TTV diagnosis. In China, TTV infection was found in 39.2%–48% of chronic hepatitis patients compared to 16.7%–52.0% of blood donors by N22-PCR or PCR utilizing primers in coding regions (Ren et al., 1999; Chen et al., 2001; Peng et al., 2002; Wang et al., 2003). Relatively few epidemiological surveys utilizing UTR-PCR for detecting TTV have been reported, especially in healthy adults and infants. In the present study, UTR- and N22-PCR were performed to test and compare the positive rate of TTV DNA in serum samples obtained from healthy infants and adults, PCVHB, and PCVHC.

Our results suggest that TTV is extremely common in the general Chinese population, including infants, providing further evidence that TTV is highly prevalent in the general population worldwide (Mancuso et al., 2013). Furthermore, the overall prevalence of TTV infection based on UTR-PCR in healthy infants, healthy adults, and patients with liver disease was almost 2–3 times higher than that obtained by N22-PCR ($p < 0.01$, Table 1), which highlights both the considerable influence of the PCR primers on the detection of TTV DNA and the benefits of using UTR-PCR to establish the true overall prevalence of TTV infection. On the other hand, our results also indicate the lack of a clear association of TTV infection with chronic viral hepatitis, which strongly suggests that TTV has little potential for causing hepatitis. However, the virulence and pathogenesis of the different genotypes or strains of TTV remain unclear and require further investigation.

In three different age groups of infants, all samples collected from infants before 1 month of age were negative for TTV DNA as detected by both UTR- and N22-PCR, while an increasing positive rate in the older infant age groups was observed. TTV infection in infants at 7–12 months of age was comparable to that of healthy adults and patients with liver disease living in Jiujiang city. This result was also observed in other studies in different countries (Davidson et al., 1999; Ohto et al., 2002; McLaughlin-Drubin and Munger, 2008). The age-related increase in TTV infection implied the existence of a very efficient means of transmission, the more powerful fecal oral route transmission other than the parenteral transmission. Thus, the real incidence of TTV infection, as well as its transmission mode and pathogenesis need to be further taken into account.

**FOOTNOTES**

This work was supported by the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry. We are very grateful to Prof. Okamoto for providing the PCR primers used in this study. The authors declared that they have no competing interest. The informed consents were given from the individuals or their custodians involved in this study.
New prevalence estimate of Torque Teno virus (TTV) infection detected by UTR-PCR

Jin Peng1, Yueyue Fang1, Xuesen Zhao1, Yihong Peng1,2

1. Department of Microbiology, School of Basic Medical Science, Peking University, Beijing 100191, China
2. Jiujiang Women’s & Children’s Hospital, Jiujiang 332000, China

Correspondence:
Phone: +86-10-82802963, Fax: +86-10-82802963, Email: ypeng78@bjmu.edu.cn
ORCID: 0000-0002-3603-8014

Published online: 25 March 2015

REFERENCES
