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Determine The Immunological Parameters Of The Torque Teno Virus Among Blood Donors In Iraq / Mosul City

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Abstract

Background *Blood transfusions are one of the most common ways viruses are transmitted .Torque Teno Virus (TTV) is) is a member of the Anelloviridae family globally prevalent virus in humans, yet comprehensive knowledge about its prevalence, predominant transmission routes, and pathogenesis remains limited. TTV has an extremely high prevalence and is regarded as a part of the human virome, the replication of which is controlled by a functioning immune system. The viral load of TTV in the plasma of individuals is thought to reflect the degree of immunosuppression. Measuring and quantifying this viral load is especially promising in organ transplantation, as many studies have shown a strong correlation between high TTV loads and an increased risk of infection on one side, and low TTV loads and an increased risk of rejection on the other side. This study aims to detect this virus in blood donors of various age groups using the polymerase chain reaction (PCR) technique* ***Methods*** *One hundred and fifty blood samples were collected from male donors of various ages, between November 2024 and April 2025, at the General Blood Bank of Al-Jumhuri Hospital in Mosul, Iraq. All genes were characterized using polymerase chain reaction (PCR).* ***Results:*** *Positive results were 9.3% of all samples. The prevalence of TTV was as high as 21.4% in people between 25-33 years old, marking the highest percentage of all ages in this study.* ***In conclusion,*** *we can conclude that TTV is prevalent among healthy blood donors, and that polymerase chain reaction (PCR) is an effective and most accurate method for detecting this virus.*

Keywords: *Torque Teno Virus (TTV), PCR*

INTRODUCTION

Torque Teno Virus (TTV) is a small, non-enveloped, single-stranded circular DNA virus belonging to the Anelloviridae family (Brani et al.,2025). First discovered in 1997 in a patient with post-transfusion hepatitis of unknown etiology, TTV has since been recognized as a ubiquitous component of the human virome, with a global prevalence exceeding 90% in some populations (Nishizawa et al.,1999). TTV belongs to the alphatorquevirus genus, which is part of the Anelloviridae family of viruses (Spezia et al., 2023). Other Anello virus genera that infect humans include the betatorquevirus, Torque Teno Mini virus (TTMV), and the gammatorquevirus, Torque Teno Midi virus (TTDV). To date, 76 species associated with the three noted genera have been identified (Webb et al.,2020). Classification into genera is largely based on species-specificity and genome size. TTV belongs to the alphatorquetenovirus genus, which includes 39 genotypes (Hsiao et al., 2016; De Vlaminck et al., 2013). As clinical studies are underway, investigating if TTV viral load measurement is superior for gauging antirejection therapy compared to medication levels, some aspects nevertheless must be considered (Gore et al., 2023). In contrast with medication levels, TTV loads must be interpreted bearing in mind that viruses have properties including transmission, tropism, genotypes, and mutations (Van Rijn et al., 2023). TTV displays an extraordinary genetic diversity, with multiple genotypes and subtypes identified, complicating efforts to understand its pathogenesis and epidemiology (Nishiyama et al.,2013). Advances in molecular techniques, particularly next-generation sequencing (NGS), have facilitated more detailed investigations into TTV genomic variability and its interaction with the host immune system. Emerging evidence indicates that TTV load may reflect immune competence, suggesting its utility as a surrogate biomarker for immune monitoring (Maggi et al., 2018). Despite its widespread presence, the clinical significance of TTV remains largely unclear, as it has not been definitively associated with any specific disease (Bendinelli et al., 2001) However, recent studies suggest its potential role as a marker of immune function, particularly in immunocompromised individuals such as organ transplant recipients and patients with HIV (Spandole et al., 2015).

Ethical

This case-control study was conducted by the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with the patient's verbal and analytical approval before the sample was

taken. The study protocols, the subject information, and the consent were reviewed and approved by a local ethics committee according to document number 13759 (on 9/12/2025) to get this approval.

Material and methods

The study enrolled one hundred and fifty blood donors who were healthy people who were under regular blood transfusion at General Blood Bank – Aljumhuri Hospital in Mosul/ Iraq.

Five milliliters of blood were collected from each patient in a gel tube, serum was taken by centrifugation at 3000 rpm for 5 min, and DNA extraction was applied to it according to the procedure of the Add Prep Viral Nucleic Acid Extraction kit, REF10034, manufactured in Korea.

Amplifying DNA extraction by the PCR (The technology of polymerase chain reaction). The viral gene that was used in amplifying is sets T80 1 and T935 (Takahashi et al., 1998). , it is T80: 5'- _ GCTACGTCACTAACCACGTG - 3 ', T935: 5 ' - CTB6 CGGTGTGTAAACTCACC - 3 'sequence, and the amplicon size was 199 bp.

12.5 µl GoTaq® G2 Green Master Mix was added, 5 µl of extracted DNA, 1 µl of forward primer (F), 1 µl of reverse primer (R), and 5.5 µl of nuclease-free water. The optimum conditions were used for the PCR run for primers; initial denaturation temperature was 94°C for 5 min, and cycle number was 1, The denaturation step was performed at 94°C for 20 sec, and cycle number was 40, followed by annealing at 57°C for 25 sec, and cycle number was 40, the Adding occurred at 72°C for 30 sec, and cycle number was 40, with a final addition at 72°C for 5 minutes, and cycle number was 1. (Takahashi et. al. 1998).

After PCR amplification, 6 µl of the PCR products (amplicons) were either subjected to electrophoresis immediately on a 2% agarose gel using a UV transilluminator apparatus to see bands (Mankotia et al., 2017 ; Lapa et al.,2021).

RESULTS

From 150 samples, we obtained 12 positives, and according to Table 1, the distribution of TTV in blood donors was 0.6% in (18-25) years 2% in (26-33) years, and 1.3% in (34-41) years.

The results showed that the highest percentage recorded was 7 positive samples (2%) in (26-33 years).

Age/years	Number	Positive	Percentage
(18-25)	28	1	0.6%
(26-33)	73	3	2%
(34-41)	49	2	1.3%
TOTAL	150	6	4%

Table 1: Prevalence of human Torque Teno Virus (TTV) according to different age/year groups in healthy blood donors.

DISCUSSION

Torque Teno virus is a DNA virus and therefore its genome has wide scope to either integrate directly into the human genome or to promote certain mutations in the cellular genome that lead to oncogenesis (Bostan et al., 2013). Extensive studies are needed before this microorganism can be assumed to be a safer organism that does not harm the human body (Mankotia and Irshad, 2017). Several articles have been published on the prevalence and risk factors of TTV infection in ESRD patients. Most are studies on the epidemiology of TTV in maintenance hemodialysis (HD) patients (Lapa et al., 2021)

In this study, the prevalence of Torque Teno Virus (TTV) among blood donors was found to be 7%, which is significantly lower than the rates reported in various global and regional studies. For instance, research conducted in Baghdad, Iraq, reported a prevalence of 93.9% among healthy blood donors, with no significant association between TTV infection and demographic factors such as age and sex (Salman et al., 2023). Similarly, a study in Yazd Province, Iran, indicated a high frequency of TTV among blood donors, aligning with global findings (Naderipour and Behnezhad et al., 2024). The notably lower prevalence observed in our study could be attributed to several factors (Detection Methods, Geographical and Demographic Differences, Sample Size and Selection Criteria, and more). TTV is known to be a ubiquitous virus, with studies reporting prevalence rates approaching 100% in certain populations. Despite its widespread presence, TTV has not been conclusively linked to any specific disease. However, its viral load has been proposed as a potential marker for immune system status (Rezahosseini et al.,2019).Elevated TTV DNA levels have been observed in immunocompromised individuals, such as

organ transplant recipients and HIV patients, suggesting that TTV replication may be controlled by the host's immune competence (Maggi et al., 2024).

Given the low prevalence detected in our study, it is essential to consider the implications for blood safety and transfusion practices. While TTV is not currently associated with transfusion-transmitted diseases (Sinha et al. ,2024), understanding its prevalence among blood donors can provide insights into the virome of the donor population and potential interactions with other pathogens (Sauvage et al., 2016).

Limitations

- Small sample size limited to a single city (Mosul), which may not be representative of the broader population.
- The immune status of patients was not evaluated, which could influence viral detection.

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Conflict of interest

Others declare no conflict of interest.

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