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Detection some clinical parameters in patients infected with human herpesvirus 6A that cause infertility

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Abstract---Human samples of Human Herpesvirus 6A were collected during October, 13teen, 2021 to 15 of December 2021. Human Herpesvirus 6A was including (15 - 59 years). The RT-qPCR. Method was detected of all samples; the results showed fifty five (55%) positive cases while forty five (45%) negative cases. The Population groups studied samples subject groups were distribution into (4) groups including (15-25, 26-36 and 37-47 and 48-58) year, changed age too gender. The second groups (26-36years) were high cases of human infected (43.6%) in compare of aged groups then [37-47 (32.7%); 15-25(14.5%); 48-58 (9%) years]. The percentage of males (54.5%) is higher than females (45.5%).The samples were isolated from the hospital including (Al-Sadr/ infertility center).The first study in Iraq to diagnose of human Herpesvirus 6A with infertility.

Keywords---human, clinical parameters, herpesvirus, infertility, real time, qPCR.

Introduction

Human *Herpesvirus* 6 (HHV-6) was divided into 2 distinct species, HHV-6A and HHV-6B, that had an overall nucleotide sequence identity of 90% (Miura *et al.*, 2021). Innate immune response was the first line of host defense against incoming microbial infection. After virus infection, viral nucleic acid could be detected by various pattern recognition receptors (PRRs). Following recognition, the antiviral immune response would activated, which results in the production of type I interferons (IFNs) and other cytokines to achieve the inhibition and/or

elimination of the virus infection (Jiang *et al.*,2021). In a *non-pregnant* woman, when endometrial epithelial cells were infected by HHV-6A, the NK cytotoxic attack was severe, lead to the production of proinflammatory cytokines that inhibit implantation. Thus, viral infection of endometrial NK cells was a plausible contributor to the pathogenesis of primary infertility. Similar to other herpes viruses (Halawi, 2015).

The capsid two fold symmetry has sixteen surfaces (icosadeltahedral) and its diameter from a hundred up to one hundred and twenty of partly depends on the thickness of the surfaces owns one hundred sixty-two capsomeres. Tumor necrosis factor alpha (TNF- α) was a cytokine – a small protein used by the immune system for cell signaling, if macrophages detect an infection, they release TNF to alert other immune system cells as part of an inflammatory response(Renu Heir and David Stellwagen,2020; Fadyia,2021). Human *Herpesvirus* 6 (HHV6) was considered to activate the autoimmune response that marks the pathogenesis of MS. Moreover, various studies suggest that HHV6 influences the concentration of TNF- α , a pro-inflammatory cytokine, which plays an important role in the development and progression of the disease (Joeri Rolwes and Ulrich Easel, 2020). Cytokine and natural killer (NK) cell levels were significantly different between women who were HHV-6A positive compared to controls and infertile women who were HHV-6A negative. While the Th2 cytokine IL-10 was higher in the HHV-6A positive group, the Th1 cytokine IFN-gamma was lower than in controls or HHV-6A negative women, caused an increase in the Th1/TH2 ratio, a condition common in female infertility. The authors note that HHV-6 was known to increased IL-10 expression by monocytes and reduced IFN-gamma by T lymphocytes (Leibovitch E and Jacobson S,2014). CD46 was a complement-inactivating protein in the innate immune system and had more recently also been implicated in the adaptive immune system as a costimulatory protein important for the generation of anti-inflammatory interleukin 10 (IL-10)-secreting T cells (Schack *et al.*, 2021).

Material and Methods

Collect affected specimens of Human *Parvovirus* B19

Samples were collected of Human *Herpesvirus* 6A through a start interval 13 October 2021 up to 15 December 2021. Fifty five positive cases including 30 (54.5 %) males and 25 (45.5%) females with infected human patients of age ranged fifteen up to fifty eight years of specimens.

Real Time qPCR Technique

This method was used to diagnose Human *Herpesvirus* 6A, via (this primer was designed based on the NCBI of human *Herpesvirus* U95 gene, GoTaq®qPCR Master mix kit (Cat. Number: 023484574400, abm, canada). Viral DNA was extracted by using Viral Nucleic Acid Extraction Kit (gSYNC™ DNA extraction kit)(Geneaid, Lot No.FA30411-GS,USA). This technique was performed in Alamin center for advanced research and biotechnology by using (Analytik Jena/Qtower3G) advice.

Table 1
Detection of tumor necrosis factor and gene U95 of human *Herpesvirus 6A*
depended to NCBI

Primer\Name	Sequence	Bases	PCR product size
HHV 6A			
U95-F	5-CTGCAAAGTGGTACGCTCAA -3	20	181
U95-R	5-GCATACGTGCACCAATCATC -3	20	
TNF -F	5-CATTCTCCTTCTCCCAACA-3	20	191
TNF -R	5-TTTCACCTCCATCCATCCTC-3	20	

Results

Genetic analytic method for diagnosis of Human *Herpesvirus 6A* through RT- qPCR

Fifty five cases appear positive from 100 samples of collected serum of different Areas were diagnosis by real-time qPCR, while 45 cases were negative as show in figure (1) .thirty cases of males infected consider the highest of twenty four females as in figure (2) . The age group (26-36 years) compared to other totals in terms of age in fig. (3).

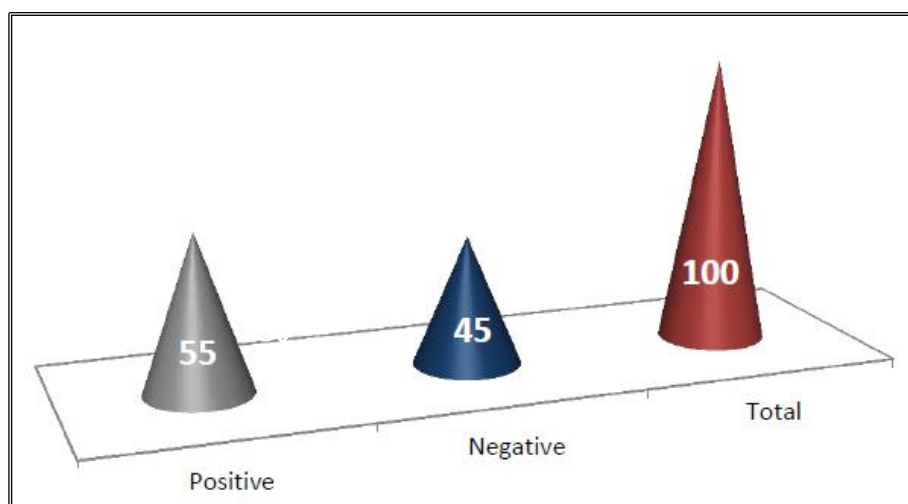


Figure 1. Shows the numbers collected for all cases

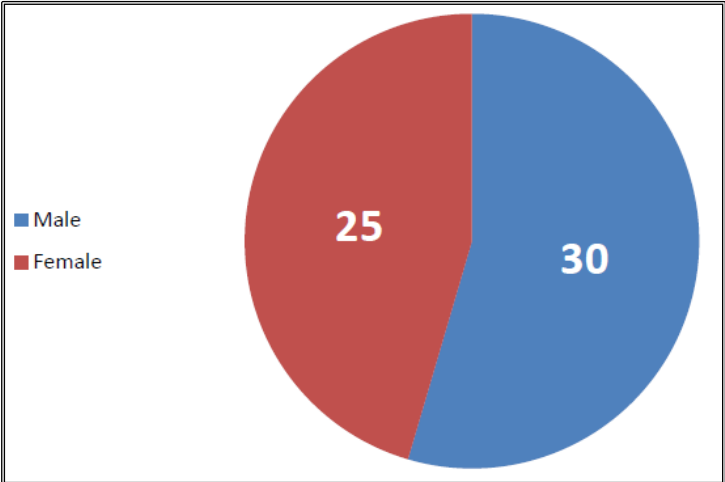


Figure 2. Positive numbers cases Human *Herpesvirus* 6A for both genders

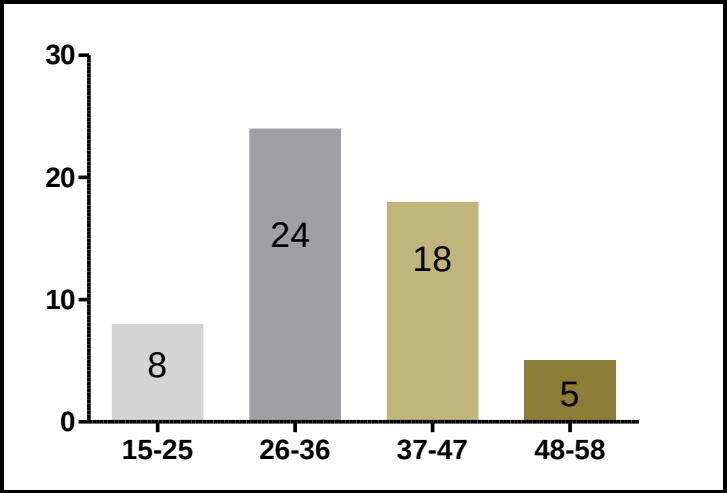


Figure 3. The distribution of patients according to age groups

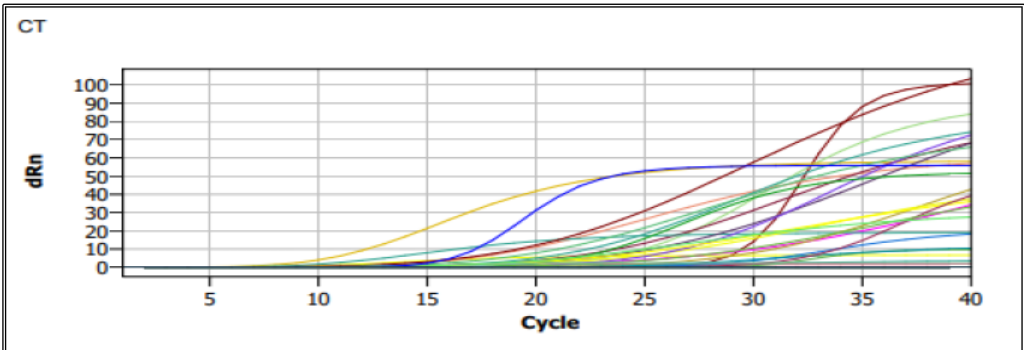


Figure 4. Detection of proinflammatory (TNF) of human infected *Herpesvirus* 6A by RT-qPCR

Table 2
Detection of Human *Herpesvirus* 6A infection, pro-inflammatory (TNF- α) by RT-qPCR

CT	HHV 6A	TNF- α
8-14	13	18
15-21	18	32
22-28	12	5
29-35	8	0
Total	55	55

Discussion

Diagnosis of *Human Herpesvirus* 6A with infertility the study is considered in Najaf Governorate and at the level of Iraq as well by RT-qPCR technicality which resembled with the (Agut *et al.*, 2015). In our study show that pro-inflammatory such as TNF was increased while, and this study is agreement with study Reynaud *et al.* (2014) and karmoff *et al.* (2020) and is agreement with study (Rizzo and Di Luca, 2018).

Conclusion

This is the first study in Iraq to diagnose of human *Herpesvirus* 6A with infertility.

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