به نام آن که هستی از اوست

Detection of Active CMV and clinical risk factors in Renal Transplantation

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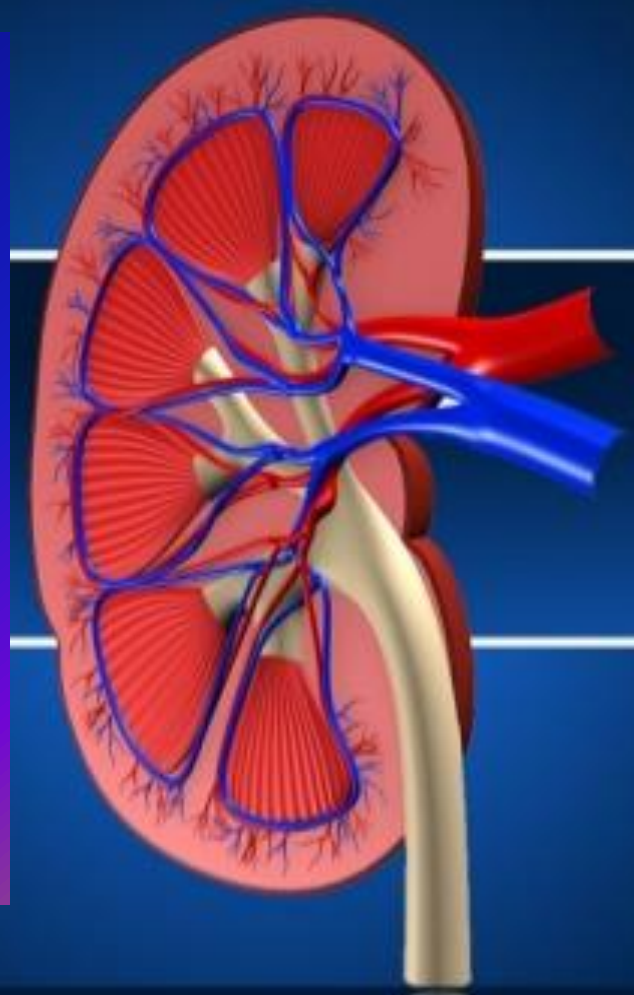
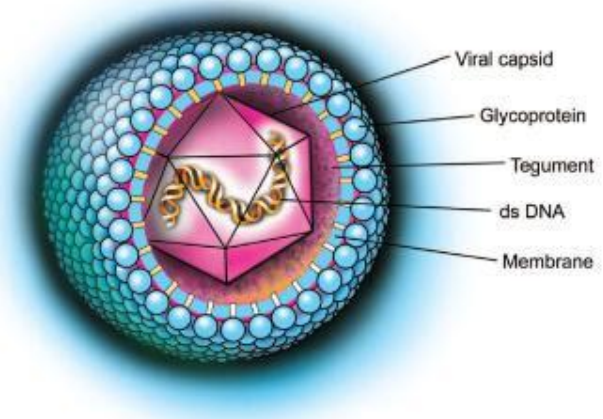


Introduction



HCMV Human Cytomegalovirus

- **CMV is a member of the *ß-herpesviridae* family of *herpes viruses***
- **CMV infection in immunocompromised patients causes serious complication in early post transplants :**

such as prolonged fever, leukopenia, hepatitis, colitis, retinitis, allograft injury, and increased susceptibility to opportunistic infections.

- **Therefore, it is necessary to find a reliable prognostic test and the cut of point because of high rate of CMV infection in allograft transplantation.**
- **The incidence of CMV disease among all kidney recipients is around 63% over the first 100 days following transplantation**

Diagnosis

- Serology
- Cell culture
- DEAFF
- CMV antigenemia – pp65
- NAT : CMV DNA PCR
  - Qualitative
  - Quantitative
- Histopathology + tissue immunoflorescence

AIMS:

- Therefore, in the present study, we evaluated both qualitative and quantitative CMV, DNA PCR for early detection of infection, Particularly, before onset of symptoms in kidney transplant patients and their donors.

The results are the part of an article:

Tahereh Hasanni, Houshang Rafatpanah, Reza Hekmat, *et al, D*etection of active CMV and EBV infections and clinical risk factors in kidney transplant patients, Renal Failure, 2016, DOI: 10.1080/0886022X.2016.1214147.

Materials and Methods

- prospective study of 150 hospitalized renal transplanted
- 129 renal transplants (55 female, 74 male) with the mean age of 36.99 years (range, 9 to 66) and 21 donors .
- Most donors and recipients (more than 98.5%) were CMV sero-positive.
- The demographic information such as sex, age, and residence location, medical history including, the cause of ESRD, the duration of dialysis, and their para-clinical findings such as CBC differentiation, ABO blood groups plus other viral infections (HBV, HCV, HIV and HTLV-I) and anti CMV and EBV IgG and IgM at the time of admission were collected.
- Moreover, the clinical and para-clinical records during hospitalization were collected.

- DNA were isolated from 200 µl plasma sample using High Pure Viral Nucleic Acid Kit (Roche Applied Science, Germany).
- Conventional PCR was performed using a PCR thermal cycler machine (Astec, Japan) with specific primers for CMV; sense:

5'- GGTGGAGATACTGCTGAGGTC and Antisense:

5'-CAAGGTGCT GCGTGATATGAAC-3’.

- Real-time PCR (RT-PCR) tests were carried out using Q-6000 Rotor-Gene (Qiagene, Germany) and in the next step, were analyzed by Rotor Gene 6000 software.
- Quantification was performed by a Taqman CMV RG kit (Qiagene, Germany).

Results

- **59% showed CMV-related clinical manifestations include: fever (30%), reject (13.3%), rise of blood creatinine level (31.8%), and cardiac symptoms (11.6%). 12.4% of patients had UTI, 9.3% nephrectomy, 3.1% abdominal pain, 14% hypertension, 3.1% fatigue and weakness, 3.1% hyperlipidemia, 5.4% nausea and diarrhea**

Qualitative PCR:

CMV DNA was detected in 63.5% of pyogenic episodes during early hospitalization and in 46.42% of readmitted patients using conventional PCR.

Quantitative PCR:

- **However, in the new renal transplants 15% of patients and in the readmitted transplants 42.85% of patients had copy numbers more than cut off point of the study (900 copies/ml) .**
- **The sensitivity of the qRT-PCR was 100% and the specificity was 87.8%.**

Table2.Summary of patients with CMV load

gender	age	CMV PCR	CMV load	serology	Related symptoms
female	20	positive	1100	CMV IgG+ ,CMV IgM-	Fever
male	58	positive	26000	CMV IgG+, CMV IgM-	Acute rejection & fever
female	50	positive	100	CMV IgG+, CMV IgM-	Fever& creatinine rise
female	49	positive	16500	CMV IgG+, CMV IgM-	Fever & creatinine rise& UTI
male	38	positive	980	CMV IgG+, CMV IgM-	Fever & acute rejection
male	45	positive	20000	CMV IgG+, CMV IgM-	Acute rejection & creatinine rise
female	51	Strong positive	2600	CMV IgG+, CMV IgM-	creatinine rise
female	59	Strong positive	20972	CMV IgG+, CMV IgM-	Fever& cardiac issue
female	33	positive	20000	CMV IgG+, CMV IgM-	Fever& creatinine rise
male	55	positive	21235	CMV IgG+', CMV IgM-	Creatinine rise& thrombosis

- The mean CMV viral load in symptomatic patients was 3,651, 800 copies/ml and in asymptomatic patients was 432, 590 copies/ml.
- *However, The cut off for Active CMV infection was 900 copies/ml.*

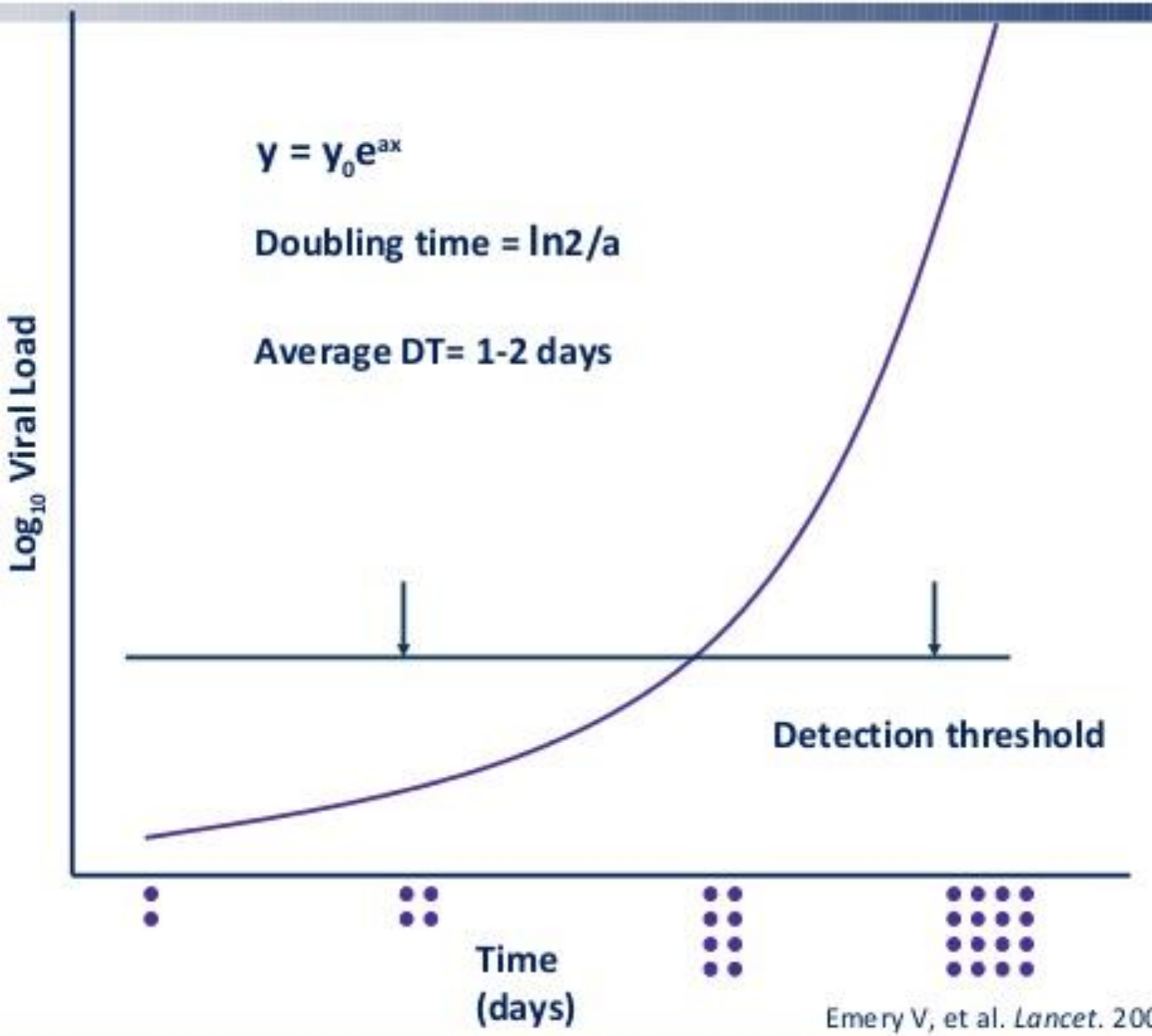
- CMV viral load in kidney recipients was significantly correlated with:

creatinine rise, hypertension, fatigue and weakness and hyperlipidemia

- We found that in patients who underwent nephrectomy, CMV viral load was significantly associated with hypertension, fatigue and weakness.

Discussion

Modeling the Dynamics of CMV Replication



Emery V, et al. *Lancet*. 2000;355(9220):2032-2036.

amplification test

Viral load / CMV DNA by PCR

- Main option for diagnosis, decision making in preemtive and monitoring response
- Advantages (RT-PCR) – rapid, highly sensitive
- Can detect the presence of viremia even before the onset of symptoms
- Issues :
  - Plasma or whole blood
  - Copies/ml or IU,
  - log based result to prevent overinterpretation
  - Lower cutoff ? 1000/2000/5000…. (trend over time)
  - Poor interinstitutional correlation

- **The incidence of CMV disease among all kidney recipients is around 63% over the first 100 days following transplantation**

- **In our study, the incidence of CMV infection in the new renal transplants 15% (22 days) and in the readmitted transplants 42.85% (over 100 days).**

- **Since effective anti-CMV treatment is available and the number of CMV copies correlated well with the severity of clinical symptoms, early detection of CMV DNA in the blood is of great importance in identifying those patients who are at risk of infection and disease.**

- **In the present study CMV viral load was significantly correlated with hypertension, fatigue and weakness, hyperlipidemia and rise in creatinine levels**

برای مطالعه بیشتر به فارسی: Further reading in Persian

حسن نیا طاهره :روش های تشخیصی CMV، در وارسته عبدالرضا و همکاران، روش های تشخیص عفونت ها و بیماری های ایمونولوژیک، انتشارات دانشگاه وارستگان 1394

Quantitative CMV DNA for Transplant patients must be carried out in 24h, M.

It's a responsibility we all take……

To do our BEST TO SERVE OUR CLIENTS TO OUR BEST