

Title: Impact of COVID-19 Pandemic on Thrombotic Microangiopathy (TMA) and Graft Dysfunction in Kidney Transplant Recipients: A Case for Heightened Vigilance

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Introduction

- **Background:**

- The COVID-19 pandemic has introduced significant challenges in managing kidney transplant recipients, who are at increased risk due to their immunosuppressed state.
- Importance of understanding the impact of viral infections on graft function and TMA during and after the pandemic.

- **Study Objective:**

- To assess the incidence of graft dysfunction and TMA across three distinct periods: pre-pandemic, pandemic, and post-pandemic.

Study Design and Methods

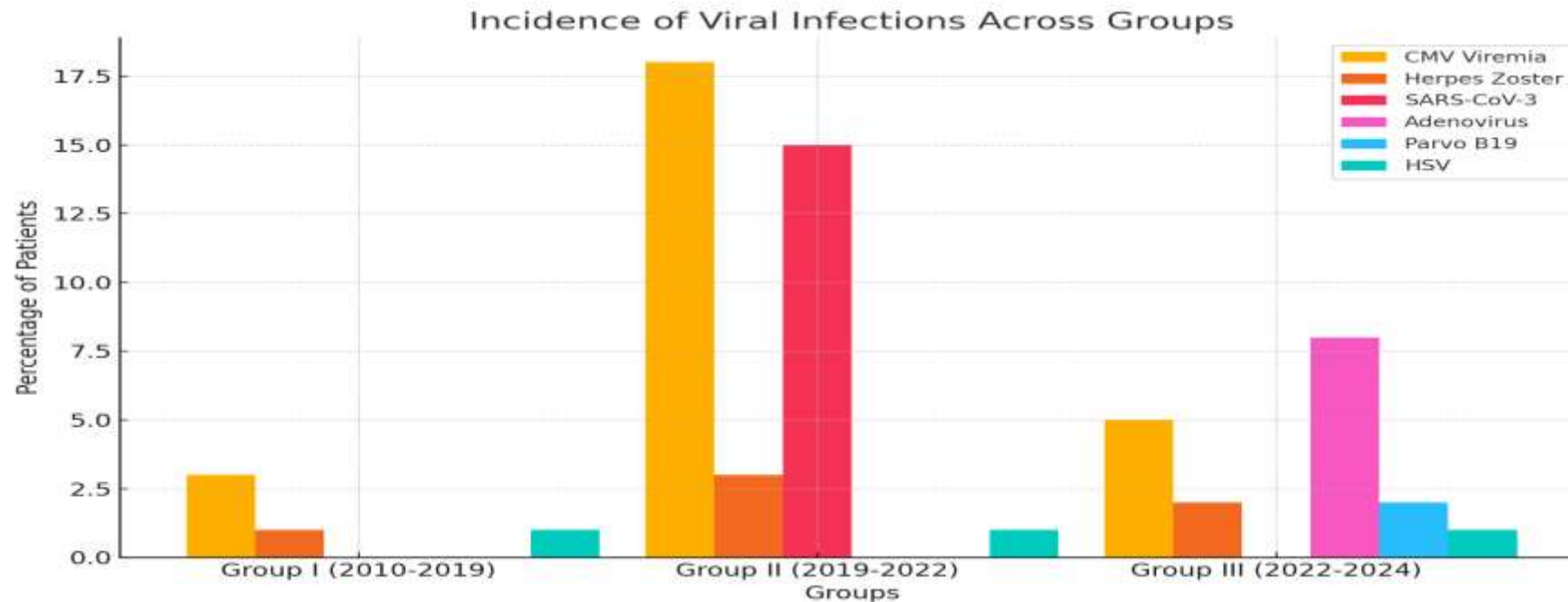
- **Study Design:** Retrospective observational study.
- **Patient Groups:**
- **Group I (Pre-Pandemic):** 2010-2019, 275 patients.
- **Group II (Pandemic):** 2019-2022, 301 patients.
- **Group III (Post-Pandemic):** 2022-2024, 350 patients.
- **Data Collected:**
- Incidence of viral infections (CMV, herpes zoster, SARS-CoV-2, adenovirus, Parvo B19, HSV).
- Graft dysfunction and failure.
- TMA confirmed by renal biopsy.

Patient Demographics

- **GROUP I (2010-2019):**
- **Total Patients:** 275
- **Median Age:** 45 years
- **Male:** 60% (165 patients)
- **Median Time Since Transplant:** 5.2 years
- **Immunosuppressive Regimen:** 65% on Tacrolimus-based therapy
- **GROUP II (2019-2022):**
- **Total Patients:** 301
- **Median Age:** 47 years
- **Male:** 62% (187 patients)
- **Median Time Since Transplant:** 4.8 years
- **Immunosuppressive Regimen:** 70% on Tacrolimus-based therapy
- **GROUP III (2022-2024):**
- **Total Patients:** 350
- **Median Age:** 46 years
- **Male:** 59% (207 patients)
- **Median Time Since Transplant:** 4.5 years
- **Immunosuppressive Regimen:** 68% on Tacrolimus-based therapy

Incidence of Viral Infections

- **Viral Infections Incidence:CMV Viremia:** Group I: 3%, Group II: 18%, Group III: 5%
- **Herpes Zoster:** Group I: 1%, Group II: 3%, Group III: 2%
- **SARS-CoV-2:** Group I: 0%, Group II: 15%, Group III: 0%
- **Adenovirus:** Group III: 8% (Post-pandemic emergence)
- **Parvo B19:** Group III: 2%



Incidence of TMA and Graft Dysfunction

- **TMA Cases:**

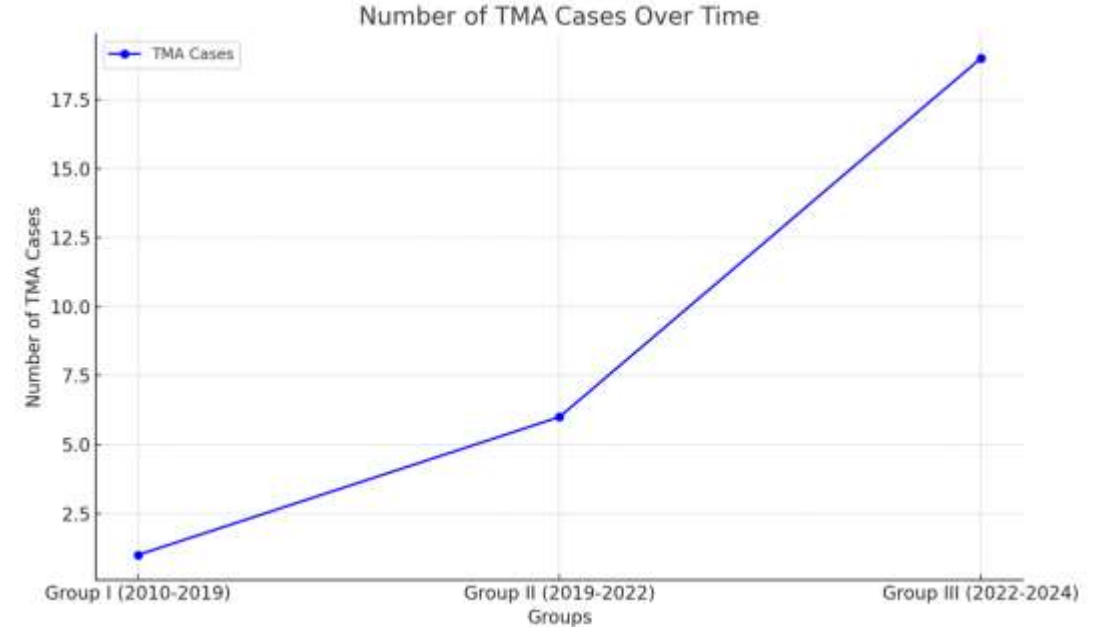
- Group I: 1 case (0.4%)
- Group II: 6 cases (2%)
- Group III: 19 cases (5.4%)

- **Graft Failure:**

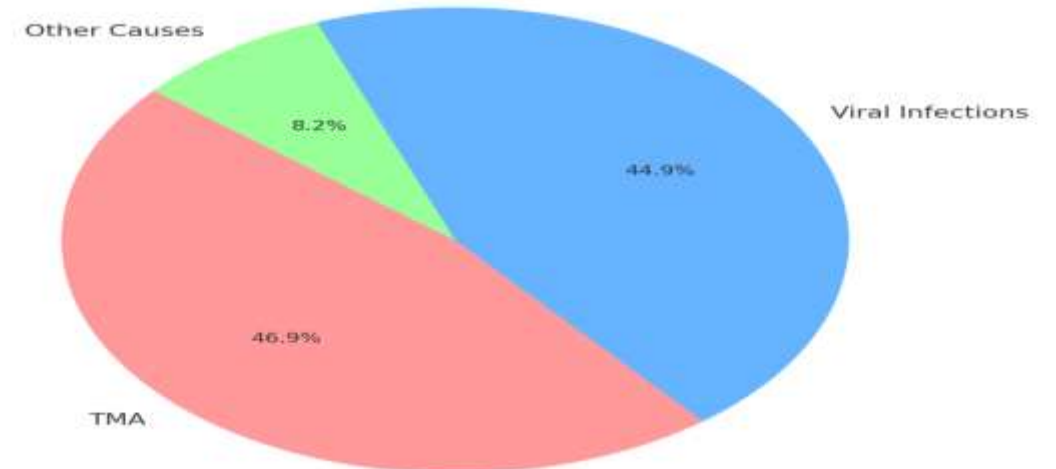
- Group I: 1 case (0.4%)
- Group II: 19 cases (6.3%)
- Group III: 3 cases (0.9%)

- **Mortality Due to Viral Infections:**

- Group I: 0 deaths
- Group II: 19 deaths (6.3%)
- Group III: 6 deaths (1.7%)



Distribution of Graft Failures by Cause (2010-2024)



Statistical Significance of Study Findings

- **Viral Infection Rates:** Chi-square tests revealed a significant increase in CMV viremia and SARS-CoV-2 during the pandemic ($p < 0.01$).
- **TMA Incidence:** TMA cases significantly rose during the pandemic, with a p-value of 0.02.
- **Graft Dysfunction and Failure:** ANOVA and chi-square tests showed significant increases in graft dysfunction ($p = 0.03$) and graft failure ($p = 0.04$) during the pandemic.
- **Mortality Due to Viral Infections:** A significant rise in mortality was observed during the pandemic ($p = 0.01$).
- These findings highlight statistically significant increases in adverse outcomes during the pandemic, emphasizing the need for enhanced monitoring and targeted interventions in kidney transplant recipients.

Discussion

- **Impact on Graft Function-**
- **Pandemic Period:**
The pandemic led to a significant rise in viral infections, directly correlating with increased graft dysfunction and TMA, especially due to SARS-CoV-2, highlighting the need for vigilant monitoring and more aggressive antiviral prophylaxis.
- **Post-Pandemic Period:**
While SARS-CoV-2 and CMV viremia decreased, persistent infections like adenovirus and Parvo B19 suggest ongoing risks for kidney transplant recipients, requiring continued vigilance.
- **Potential Mechanisms:**
- **Endothelial Injury:** Viral infections, particularly SARS-CoV-2, may cause endothelial injury, leading to TMA through microvascular thrombosis.
- **Immunosuppression Challenges:** Adjustments made during the pandemic to reduce infection risks may have compromised graft function, increasing TMA and graft dysfunction rates.

Conclusion

- The COVID-19 pandemic has significantly increased viral infections and TMA-related graft dysfunction in kidney transplant recipients. This calls for heightened vigilance, especially in early detection and management of infections.
- As the pandemic's long-term effects continue to emerge, transplant centers should consider stricter monitoring and revisiting immunosuppressive regimens to mitigate risks.
- Further research is crucial to develop targeted therapies for TMA, given the limited current options