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Longitudinal Kinetics Of Donor-derived Cell-free DNA In Pediatric Kidney Transplantation: Absolute Copy Number Per ml Vs. Percentage

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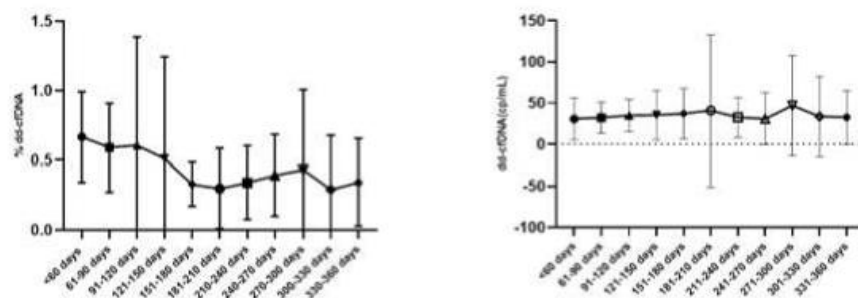
**Objectives :** Donor-derived cell-free DNA (dd-cfDNA) consists of DNA fragments released from injured donor allograft cells into circulation. In adults, post-transplant, levels decrease to about 0.92% ( $\pm$  0.43%) within 30 days or 0.46% ( $\pm$  0.21%) within 10 days. Previous research noted a prolonged stabilization period for dd-cfDNA in pediatric transplants, lasting at least 4 months due to donor-recipient size differences. As absolute counts of dd-cfDNA, measured as genomic copies per milliliter of plasma (cp/ml), remain unaffected by background cell-free DNA. We hypothesized that there will be no statistically significant differences observed in absolute counts, suggesting a consistent and stable trend

**Methods :** From a biobank of 71 children, plasma samples were collected monthly post-kidney transplant (2013 onward) we quantified dd-cfDNA using next-gen sequencing for % fraction and absolute counts. Subgroup analysis included 226 samples from 54 stable renal transplant recipients without major events, studying dd-cfDNA kinetics. We quantified dd-cfDNA in plasma by next generation sequencing using a targeted, multiplex PCR-based method for the analysis of single nucleotide polymorphisms (AlloSure, CareDx, Brisbane, CA). A subgroup of 226 samples from 54 stable renal transplant recipients with no major infectious events, rejection events or delayed graft function were identified to study the dd-cfDNA kinetics over time.

**Results :** The overall cohort had a median plasma % dd-cfDNA of 0.58 (25-75 percentile range 0.43-0.96) at 60 days post renal transplant, decreasing to 0.27% (0.11-0.72) by the fourth month, remaining steady thereafter. In contrast, absolute donor-derived cell-free DNA counts remained consistent, maintaining a median of 25 copies/ml (25-75 percentile range 12-36) at 2 months and 32 copies at month 4.

**Conclusions :** Post-transplant, children exhibit prolonged % dd-cfDNA elevation due to increased graft-derived dd-cfDNA and reduced self-cfDNA from lower BMI. In contrast, absolute counts are superior in pediatric patients, lacking consistent fluctuations

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Comparison of post transplant kinetics in donor derived cell free DNA