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Abstract (publication only)

Iron overload is a major risk factor for infectious complications in kidney transplant recipients

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Objectives: The impact of iron overload on the pathogenesis and outcome of infections has been documented in various patient populations but, to our knowledge, it has never been assessed in kidney transplant (KT) recipients. Methods: In this observational cohort study we prospectively analyzed 159 patients (102 males; mean age: 53.6 ± 14.9 years) who underwent KT at our institution from November 2008 to August 2010. Serum iron markers (iron level, ferritin level, total iron-binding capacity [TIBC], and transferrin saturation) were measured within the first month after transplantation before any infectious event had occurred. Primary outcome was the occurrence of any episode of infection in the first 6 months post-transplant. Secondary outcome included all-cause mortality at the end of follow-up. Multivariate adjusted odds ratios (ORs) were calculated using those covariates that were found to be significant at $P < 0.10$ by univariate analysis. We compared Kaplan-Meier survival curves with the log rank test. Results: During the first 6-month follow-up period, 95 (59.7%) recipients developed at least one episode of infection (bacterial in 44.7%, cytomegalovirus [CMV] in 23.9%, viral non-CMV in 8.2%, and fungal in 6.3%). Serum iron markers were assessed in samples taken at a median interval of 2 days after KT (interquartile range, 1-5 days) and a median interval of 24 days before any infectious event occurred (interquartile range, 12-64 days). Mean ferritin levels were significantly higher in those patients who developed any episode of infection (540.8 vs. 391.0 ng/mL; $P = 0.024$), as compared to the rest of the cohort. As an inverse marker of iron status, TIBC was lower in the group with any infection (213.1 vs. 229.0 µg/dL; $P = 0.048$). After adjustment for other factors (including age, pre-transplant comorbidities, number of red blood cells transfused intraoperatively, and induction therapy), a ferritin level >600 ng/mL (above percentile 75) emerged as an independent risk factor for any infection (OR = 4.61; 95% confidence interval = 1.89-11.23; $P = 0.001$). Overall mortality at the end of follow-up (median 544 days) was 5.0% (infection-related mortality of 2.5%). Patients with ferritin levels >600 ng/mL exhibited a nearly significant trend towards a worse survival ($P = 0.088$). Conclusion: Our results suggest that iron overload plays an important role on the risk of infectious complications after KT and may be considered as a potential marker of poor outcome.