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CLINICAL SIGNIFICANCE OF CORRELATIONAL RELATIONSHIPS BETWEEN LABORATORY PARAMETERS IN POST-KIDNEY TRANSPLANT PATIENTS

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1. Background and Rationale

Kidney transplantation has become the most effective treatment modality for end-stage chronic renal failure, demonstrating superior outcomes in patient survival and quality of life compared to hemodialysis and peritoneal dialysis. Globally, the number of kidney transplants continues to grow year on year — more than 25,000 procedures were performed in the United States alone in 2022, and in 2018 a total of 95,479 transplants were recorded worldwide across North America, Europe, the Asia-Pacific region, Southeast Asia, the Eastern Mediterranean, and Africa.

Post-transplant patients constitute a distinct clinical population requiring long-term monitoring. Key challenges include strict adherence to immunosuppressive therapy, management of comorbidities, and ongoing surveillance of mineral and metabolic homeostasis. Studies show that between 28% and 67% of recipients do not fully adhere to their immunosuppressive regimen, resulting in a sevenfold increase in the risk of graft rejection. Lifestyle factors — physical inactivity, smoking, and alcohol misuse — further compound these risks.

In Uzbekistan, kidney transplantation is being successfully implemented at several national centres, including the Samarkand Regional Medical Centre (one of the first regional facilities to adopt the procedure) and the National Medical Centre in Tashkent. More than 300 kidney transplants were performed in the

country in 2023. Understanding the post-transplant dynamics of laboratory parameters is therefore of direct national clinical relevance.

Keywords: kidney transplantation, quality of life, HRQoL, immunosuppression, renal failure

2. Research Objective

To evaluate the changes in laboratory parameters at different time points following kidney transplantation and to determine the correlational relationships between key markers of mineral, biochemical, and hormonal metabolism.

3. Materials and Methods

The study enrolled 60 patients who underwent kidney transplantation at the National Medical Centre of Tashkent. The mean age was 44.6 ± 3.5 years; the majority were male. Patients were stratified into three groups according to post-transplant follow-up duration:

- Group 1 — up to 6 months post-transplant (n = 20)
- Group 2 — 1–2 years post-transplant (n = 20)
- Group 3 — more than 2 years post-transplant (n = 20)

The following parameters were assessed in all patients:

- Complete blood count (leukocytes, haemoglobin, neutrophil and lymphocyte percentages)
- Biochemical markers (urea, creatinine, albumin, transferrin)
- Mineral metabolism (serum phosphorus, serum calcium)
- Hormonal and growth markers (vitamin D, fibroblast growth factor-23 [FGF-23], parathyroid hormone [PTH])

Pearson correlation analysis was applied to determine the strength and direction of associations between mineral metabolism parameters. Statistical significance was set at $p < 0.05$ and $p < 0.01$.

4. Key Findings

4.1 Haematological and Biochemical Parameters

In the early post-transplant period (6 months), laboratory values remained relatively stable. Leukocyte counts showed a mild upward trend from $6.4 \pm 1.8 \times 10^9$/L (Group 1) to $7.3 \pm 2.2 \times 10^9$/L (Group 3), without reaching statistical significance ($p > 0.05$). Haemoglobin levels peaked at 124.1 ± 8.1 g/L in Group 2 before declining to 116.5 ± 9.3 g/L in Group 3. A gradual reduction in lymphocyte percentage (from 22.1% to 17.5%) across the groups is attributable to the ongoing effect of immunosuppressive therapy.

Urea levels increased significantly from 7.1 ± 0.4 to 8.3 ± 0.3 µmol/L between Groups 1 and 3 ($p < 0.001$), and creatinine rose from 104.8 ± 5.1 to 122.7 ± 5.6 µmol/L ($p < 0.05$), consistent with a gradual, relative decline in graft function over time. Serum albumin showed a modest downward trend (37.1 → 34.8 g/L) across the three groups.

4.2 Mineral Metabolism and FGF-23

Phosphorus levels increased from 1.25 ± 0.1 to 1.52 ± 0.1 mmol/L across groups, and calcium from 2.05 ± 0.1 to 2.24 ± 0.1 mmol/L, though neither change reached significance ($p > 0.05$). Vitamin D levels remained broadly stable (21.1 → 21.8 ng/mL), reflecting relative metabolic stability of vitamin D following transplantation.

FGF-23 levels showed a notable dynamic: 68.9 ± 6.3 ng/mL at 6 months, declining to 46.7 ± 3.9 ng/mL at 1 year, and rising again to 76.2 ± 8.2 ng/mL at 2

years post-transplant. This non-linear trajectory reflects the evolving role of FGF-23 in phosphate regulation in the post-transplant context.

4.3 Correlation Analysis at 6 Months Post-Transplant

Key Pearson correlation coefficients at 6 months included:

- Phosphorus ↔ FGF-23: strong positive correlation ($r = 0.926$; $p < 0.001$)
- Phosphorus ↔ Calcium: moderate negative correlation ($r = -0.523$; $p < 0.01$)
- Phosphorus ↔ Vitamin D: moderate negative correlation ($r = -0.456$; $p < 0.05$)
- Calcium ↔ Vitamin D: strong positive correlation ($r = 0.802$; $p < 0.001$)
- Calcium ↔ FGF-23: moderate negative correlation ($r = -0.562$; $p < 0.01$)
- Vitamin D ↔ FGF-23: moderate negative correlation ($r = -0.658$; $p < 0.05$)

These findings confirm that FGF-23 is already a dominant regulator of phosphate homeostasis in the early post-transplant period.

4.4 Correlation Analysis at 2 Years Post-Transplant

By 2 years post-transplant, all correlations strengthened considerably (all $p < 0.01$):

- Phosphorus ↔ FGF-23: strong positive ($r = 0.926$)
- Phosphorus ↔ Calcium: strong negative ($r = -0.823$)
- Phosphorus ↔ Vitamin D: strong negative ($r = -0.814$)
- Calcium ↔ Vitamin D: strong positive ($r = 0.857$)
- Calcium ↔ FGF-23: strong negative ($r = -0.767$)
- Vitamin D ↔ FGF-23: strong negative ($r = -0.853$)

The progressive intensification of these correlations indicates that the interconnected regulatory mechanisms of mineral metabolism not only persist but become more pronounced over time following kidney transplantation.

5. Conclusions

Laboratory parameters in kidney transplant recipients are relatively stable in the early post-transplant period (up to 6 months), reflecting satisfactory graft function. However, biochemical changes emerge progressively: rising urea and creatinine values indicate a gradual decline in graft function over time, while mineral metabolism parameters — though remaining within broadly acceptable ranges — develop increasingly strong interrelationships.

The consistently strong positive correlation between phosphorus and FGF-23 across all time points confirms the central regulatory role of FGF-23 in post-transplant phosphate homeostasis. The negative correlations of FGF-23 with both vitamin D and calcium suggest that elevated FGF-23 may suppress vitamin D metabolism and reduce the availability of its active forms — an important mechanism that clinicians should monitor.

The progressive strengthening of mineral metabolism correlations between 6 months and 2 years post-transplant provides scientific evidence that dynamic monitoring of these markers is clinically essential. These findings underscore the need for comprehensive, longitudinal surveillance and early correction of phosphorus-calcium imbalances in post-kidney-transplant patients.

6. Clinical Implications

• Regular monitoring of FGF-23, phosphorus, calcium, and vitamin D is recommended as a standard of care throughout the post-transplant follow-up period.

• The non-linear trajectory of FGF-23 warrants targeted investigation at 1 and 2 year intervals.

• Rising urea and creatinine in the long-term post-transplant period should prompt early evaluation of graft function.

• Correction of vitamin D deficiency may be particularly important, given its strong coupling with calcium absorption and its inverse relationship with FGF-23.

• Immunosuppressive therapy compliance should be continuously reinforced, given the documented risk of non-adherence leading to graft rejection.

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