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Original Article

Prevalence and Factors Associated with Iron Deficiency in Renal Transplant Recipients at the Gabriel Montpied University Hospital: A Retrospective Study

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Abstract

Introduction: Chronic kidney disease (CKD) is a major worldwide public health issue. Renal transplantation improves survival in end-stage CKD, but iron deficiency (ID) remains common, even in the absence of anemia, and may negatively impact kidney graft function and patient quality of life. Studies assessing the prevalence and associated factors of ID in kidney transplant recipients are rare.

Methods: We conducted a retrospective cohort study that included 104 adult renal transplant recipients followed at Gabriel Montpied University Hospital between January and December 2023. Iron deficiency and anemia were defined according to KDIGO guidelines, with iron deficiency as ferritin < 100 µg/L and/or transferrin saturation (TSAT) < 20%, and anemia thresholds corresponding to WHO criteria (hemoglobin < 13 g/dL in men and < 12 g/dL in women). We collected and analyzed clinical, biological, and therapeutic data. Multivariate logistic regression was performed to identify factors independently associated with iron deficiency.

Results: Thirty-six percent of patients had iron deficiency, independent of anemia, in a significant proportion. ID was positively associated with longer graft duration and basiliximab induction (OR 2.90, 95% CI 1.25–6.74, $P=0.013$), whereas thymoglobulin induction appeared protective (OR 0.37, 95% CI 0.16–0.85, $P=0.019$). Lower serum iron levels were also significantly associated with ID (OR 0.18, 95% CI 0.06–0.56, $P=0.003$).

Conclusion: Iron deficiency is common in kidney transplant recipients, even without anemia. Systematic screening and targeted management may improve graft outcomes and patient quality of life.Study Highlights: - Iron deficiency (ID) affected 36% of renal transplant patients. - ID occurred independently of anemia in a significant portion of patients. - Longer graft duration and use of basiliximab were positively associated with ID. - Thymoglobulin induction appeared to be protective against ID. - Routine iron status screening is recommended post-transplant.

Introduction

Chronic kidney disease (CKD) represents a major public health issue. It is projected to become the fifth leading cause of global mortality by 2040.[1] In its end-stage, renal replacement therapy is required, either through dialysis or transplantation. The latter is the preferred treatment for end-stage CKD, significantly enhancing both quality of life and survival rates.[2] However, despite advancements in surgical techniques and immunosuppressive therapies that have extended graft survival, other factors such as cardiovascular complications and anemia continue to negatively impact the health of transplant recipients.[2] According to the 2023 KDIGO (Kidney Disease Improving Global Outcomes) Clinical Practice Guideline for the Management of Chronic Kidney Disease, transplant recipients should be carefully monitored for complications

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such as anemia and iron deficiency.[3]

Iron deficiency (ID), the primary cause of anemia, is a common complication of CKD. It exacerbates uremic syndrome, reduces physical capacity and quality of life, increases cardiovascular risk, promotes hospitalizations, and diminishes the survival of dialysis patients.[4-6] Iron deficiency was defined according to KDIGO guidelines as ferritin < 100 µg/L and/or transferrin saturation (TSAT) < 20%, and anemia in adults was defined according to KDIGO criteria, corresponding to WHO thresholds of hemoglobin < 13 g/dL in men and < 12 g/dL in women.[3,7]

In renal transplant recipients, iron status is often overlooked.[8-10] Even with targeted management of anemia before and after transplantation, iron deficiency remains prevalent in the months following the transplant.[11] Independently of anemia, ID can affect muscle function, the central nervous system, cardiac function, and immune response.[12]

Several factors contribute to this deficiency: low iron stores at the time of transplantation, intraoperative blood loss, repeated postoperative blood draws, and the reinitiation of erythropoiesis due to improved renal function. Moore et al. observed iron deficiency in transplant recipients six months after transplantation. Around 60% of patients were iron-replete at the time of transplantation, suggesting that prevention of post-transplant anemia may be feasible.[13]

Post-transplant anemia has been associated with left ventricular hypertrophy and heart failure,[1314] as well as with reduced graft and patient survival.[15] Post-transplant iron deficiency itself is correlated with excess mortality, independent of anemia, highlighting the pathogenic role of iron deficiency.[16]

In this context, the aim of this study is to determine the prevalence of iron deficiency – with or without anemia – and identify its associated factors among renal transplant recipients followed at the Gabriel Montpied University Hospital. A more profound understanding of these determinants would help optimize anemia management and improve long-term graft outcomes.

Methods

Study Characteristics

This retrospective descriptive study was conducted at the Department of Nephrology, Gabriel Montpied University Hospital, Clermont-Ferrand, France, over the period from January to December 2023. The study included only patients with at least six months of post-transplant follow-up. Age ≥ 18 years, active follow-up in the nephrology department during the study period, complete medical records with pertinent parameters, and informed consent for participation were the requirements for inclusion. Pregnancy, acute intercurrent conditions (such as severe infection or graft rejection), and incomplete or interrupted medical follow-up were among the exclusion criteria.

Study Objectives and Outcome Measures

The primary outcome of this study was to determine the prevalence of iron deficiency in adult renal transplant recipients and to identify factors associated with it. Iron deficiency was defined as ferritin < 100 µg/L and TSAT < 20% according to KDIGO[24] recommendations. Secondary outcomes were clinical parameters (age, sex, body mass index, pre-transplant comorbidities, time since kidney transplantation, graft duration, induction and maintenance therapy), biological parameters (hemoglobin, serum creatinine, serum iron, ferritin, transferrin saturation, C-reactive protein, vitamins B9 and B12), and therapeutic parameters (erythropoietin therapy, oral or intravenous iron supplementation, antihypertensive and immunosuppressive therapy).

Data Collection and Statistical Analysis

Data were collected through a standardized form that included sociodemographic, clinical, biological, and therapeutic variables. Descriptive statistics summarized the population characteristics by iron deficiency status. Categorical variables were presented as counts and percentages, and continuous variables as medians and interquartile ranges. Categorical variables were compared by chi-square test or Fisher's exact test, and continuous variables by Mann–Whitney U test. Multivariate logistic regression was performed to identify independent factors associated with iron deficiency. Results were presented as odds ratios (OR) with 95% confidence intervals (CI), and P values < 0.05 were considered statistically significant.

Ethical Considerations

This study was performed in accordance with the principles of the Declaration of Helsinki. The study was approved by the institutional ethics committee of Gabriel Montpied University Hospital before its initiation (Ref: CE-CCHUGM-2023-104). All patient data were anonymized and handled confidentially in accordance with the General Data Protection Regulation (GDPR). All patients included in the study signed informed consent for the use of their medical data for research purposes. Ethical approval and consent procedures are built into the overall design of the study so that information is not duplicated.

Results

Demographic Characteristics

A total of 104 adult renal transplant recipients were enrolled. Mean age was 57.2 ± 14.2 years and 69% were male. Mean body mass index (BMI) was 26.2 ± 5.1 kg/m 2. No statistically significant differences were observed in age, sex, or BMI between patients with and without iron deficiency (Table 1).

Clinical Characteristics

The mean graft duration was significantly longer in the iron-deficient group (7.38 ± 5.81 years) than in the non-deficient group (4.58 ± 4.85 years; $P = 0.015$). Heart failure was present in 82% of patients without iron deficiency and 92% of those with iron deficiency, although this difference did not reach statistical significance ($P = 0.17$). Other

comorbidities, including ischemic heart disease, diabetes, and hypertension, were comparable between groups. The overall prevalence of anemia was 75% (Table 1).

Biological Characteristics of the Study Population

Prevalence of Iron Deficiency

Iron deficiency was observed in 36% of the study population (Figure 1). Among anemic patients (n = 78), 35% had iron deficiency, compared to 38% among non-anemic patients (n = 26), indicating that iron deficiency was not strictly associated with anemia status (Figure 2).

Table 1. Clinical Characteristics of the Study Population According to Iron Deficiency Statu

Parameter	No ID (N = 67)	ID (N = 37)	Total (N = 104)	*P* value
Male Sex	50 (75%)	22 (59%)	72 (69%)	0.11
Female Sex	17 (25%)	15 (41%)	32 (31%)	—
Ischemic Cardiopathy – Yes	64 (96%)	37 (100%)	101 (97%)	0.55
Ischemic Cardiopathy – No	3 (4%)	0 (0%)	3 (3%)	—
Diabetes Mellitus – Yes	22 (33%)	11 (30%)	33 (32%)	0.74
Diabetes Mellitus – No	45 (67%)	26 (70%)	71 (68%)	—
High Blood Pressure – Yes	57 (85%)	31 (84%)	88 (85%)	0.86
High Blood Pressure – No	10 (15%)	6 (16%)	16 (15%)	—
Heart Failure – Yes	55 (82%)	34 (92%)	89 (86%)	0.17
Heart Failure – No	12 (18%)	3 (8%)	15 (14%)	—
Age (years)	56.4 ± 13.9	58.5 ± 14.6	57.2 ± 14.2	0.48
Body Mass Index (kg/m²)	25.9 ± 4.37	26.7 ± 5.71	26.2 ± 5.1	0.47
Graft Duration (years)	4.58 ± 4.85	7.38 ± 5.81	5.81 ± 5.48	0.015
Pre-Graft Duration (years)	6.43 ± 5.76	8.46 ± 7.89	7.38 ± 6.65	0.17

Notes: ID = Iron Deficiency. Values are presented as N (%) for categorical variables and Mean ± SD for continuous variables

Kidney transplant recipients with iron deficiency exhibited significantly altered iron metabolism parameters compared to those without deficiency. TSAT was markedly lower in iron-deficient patients (15.8 ± 6.38%) than in non-deficient individuals (31.6 ± 8.95%, $P < 0.001$). Similarly, serum iron levels were reduced (0.746 ± 0.37 g/L vs. 1.02 ± 0.43 g/L, $P < 0.01$), and ferritin concentrations were also lower (311 ± 402 ng/mL vs. 505 ± 382 ng/mL, $P = 0.019$).

In contrast, other biological parameters such as hemoglobin, serum creatinine, C-reactive protein (CRP), vitamin B12, and folate (vitamin B9) did not differ significantly between iron-deficient and non-deficient groups ($P > 0.05$ for all comparisons), indicating that iron deficiency occurred independently of these variables (Table 2).

Therapeutic Characteristics

Table 3 presents the therapeutic characteristics of kidney

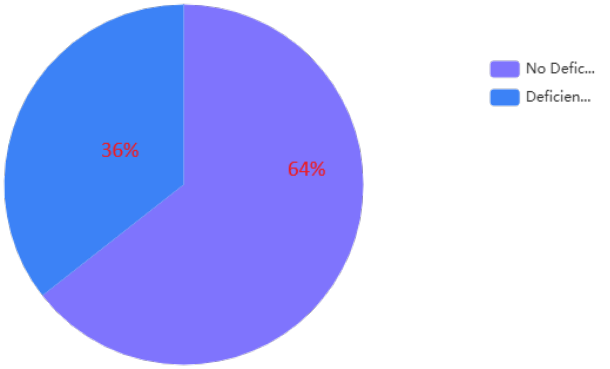

Figure 1. Distribution of Iron Deficiency Within the Study Population
Legend: Pie chart showing the proportion of kidney transplant recipients according to iron deficiency status. Among the 104 patients included, 36% (n = 37) had iron deficiency (ID1), while 64% (n = 67) did not have iron deficiency (ID0)

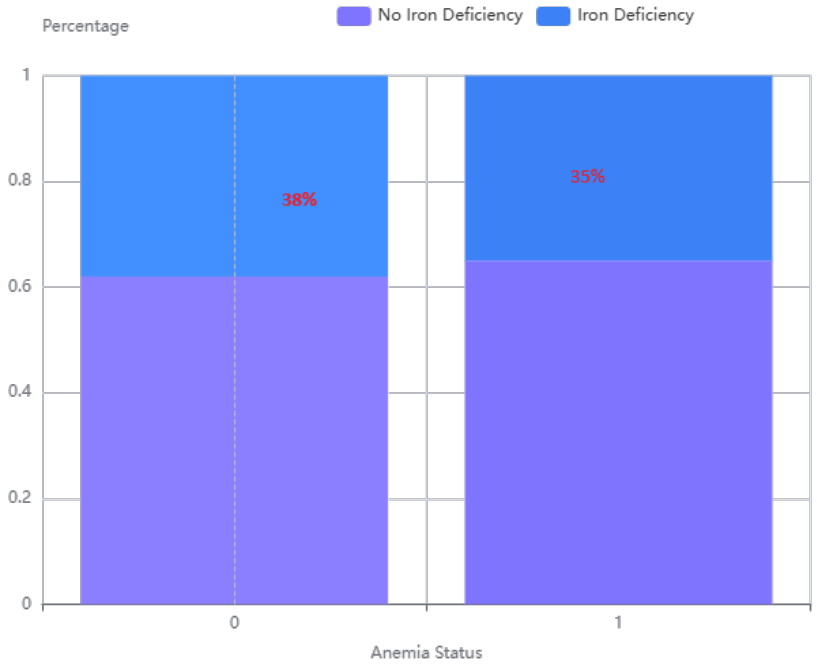

Figure 2. Distribution of Iron Deficiency by Anemia Status
This 100% stacked bar chart illustrates the proportion of patients with and without iron deficiency according to their anemia status (0 = No anemia, 1 = Anemia). Among 78 patients with anemia, 27 (35%) had iron deficiency. Among the 26 patients without anemia, 10 (38%) had iron deficiency

transplant recipients stratified by the presence or absence of iron deficiency.

- ACE inhibitors: Most patients, regardless of iron status, received angiotensin-converting enzyme inhibitors, with no significant difference between groups ($P = 0.17$).
- Induction therapy: Thymoglobulin (TG) was more frequently used in patients without iron deficiency, whereas Basiliximab (BAX) was more common among iron-deficient patients ($P = 0.018$ and $P = 0.012$, respectively).
- Maintenance therapy: The standard-of-care (SOC) protocol (calcineurin inhibitor + mycophenolate mofetil + corticosteroids) was the predominant regimen in both groups (81%; $P = 0.95$). Belatacept (BEL) use remained marginal and similar between groups (6% vs. 0%; $P = 0.29$). Other regimens were comparably distributed (13% vs. 19%; $P = 0.46$).
- Anemia management: Erythropoietin (EPO) administration was slightly higher in iron-deficient patients (27% vs. 16%; $P = 0.20$). Intravenous iron and oral iron supplementation were also slightly more frequent in the iron-deficient group (38% vs. 27%; $P = 0.25$, and 16% vs. 13%; $P = 0.70$), though these differences were not statistically significant (Table 3).

Table 2. Biological Characteristics of the Study Population According to Iron Deficiency Status

Parameter	No ID (N = 67) Mean ± SD / N (%)	ID (N = 37) Mean ± SD / N (%)	Total (N = 104)	*P* value
Vitamin B12 (pmol/L)	469 ± 376	468 ± 387	104	0.99
Folate (Vitamin B9, nmol/L)	865 ± 633	879 ± 719	104	0.92
Serum Creatinine (µmol/L)	129 ± 45.0	140 ± 38.9	104	0.19
C-Reactive Protein (CRP, mg/L)	15.9 ± 34.8	33.7 ± 62.9	104	0.12
Transferrin Saturation (TSAT, %)	31.6 ± 8.95	15.8 ± 6.38	104	< 0.001
Serum Iron (g/L)	1.02 ± 0.43	0.746 ± 0.37	104	< 0.01
Ferritin (ng/mL)	505 ± 382	311 ± 402	104	0.019
Hemoglobin (g/dL)	11.3 ± 1.82	11.4 ± 1.79	104	0.85
Anemia – Yes	51 (76%)	27 (73%)	78 (75%)	0.72
Anemia – No	16 (24%)	10 (27%)	26 (25%)	—

Legend: ID = Iron Deficiency; N (%) for categorical variables, Mean ± SD for continuous variables

Table 3. Therapeutic Characteristics of the Study Population According to Iron Deficiency Status

Parameter	No ID (N = 67) N (%)	ID (N = 37) N (%)	Total (N = 104)	*P* value
ACE inhibitors	47 (70%)	21 (57%)	68 (65%)	0.17
Thymoglobulin	29 (43%)	12 (32%)	41 (39%)	0.018
Basiliximab	12 (32%)	25 (68%)	37 (36%)	0.012
Standard of Care	54 (81%)	30 (81%)	84 (81%)	0.95
Belatacept	4 (6%)	0 (0%)	4 (4%)	0.29
Other immunosuppressive regimens	9 (13%)	7 (19%)	16 (15%)	0.46
Erythropoietin	11 (16%)	10 (27%)	21 (20%)	0.20
Intravenous iron	18 (27%)	14 (38%)	32 (31%)	0.25
Oral iron	9 (13%)	6 (16%)	15 (14%)	0.70

Notes: ID = Iron Deficiency; N (%) presented for all categorical variables. *P* value calculated using Chi-square or Fisher's exact test as appropriate

Multivariate Analysis

Several factors were significantly associated with iron deficiency (*P* values < 0.05):

- Positively associated: Graft duration and Basiliximab (BAX) administration (odds ratio > 1), suggesting an increased risk of iron deficiency.
- Serum iron (FER) and thymoglobulin (TG) are negatively associated with the outcome, indicating a protective effect, as shown by an odds ratio of less than 1.

Age and sex were not statistically associated with iron deficiency ($P > 0.05$) (Table 4).

Discussion

This retrospective study, conducted on 104 kidney transplant patients at CHU Gabriel Montpied, highlighted two major findings: a prevalence of iron deficiency of 36% and significant associations between iron deficiency, graft duration, and induction treatments, including basiliximab and thymoglobulin.

The prevalence of anemia (75%) and iron deficiency (36%) in our cohort is consistent with previously published data. Post-transplant anemia is multifactorial and may be exacerbated by iron deficiency, which is associated with frequent blood draws, depletion of iron stores due to renewed erythropoiesis, and inadequate nutritional intake. Both iron deficiency and anemia were defined according to KDIGO guidelines, with anemia thresholds aligned with WHO criteria. The relatively high prevalence observed in our series, compared with studies using lower thresholds such as Choukroun et al, may be explained by the use of these standard definitions.[17]

Our results are consistent with those reported by Yorgin et al.[10] and Zheng et al,[18] who observed a prevalence of 67% for anemia and 44% for iron deficiency. Schechter et al. reported a post-transplant prevalence of ID of 35%,[19] and Lorenz reported 20.1%.[20] However, Lorenz used a different definition (hypochromic red blood cells ≥ 2.5%), which may explain this discrepancy. Lorenz also found associations

Table 4. Multivariate logistic regression analysis of factors associated with Iron Deficiency

Variable	OR	95% CI	*P* value
Graft duration (years)	1.10	(1.02 – 1.19)	0.014
Serum iron (µg/dL)	0.18	(0.06 – 0.56)	0.003
Basiliximab (Yes vs No)	2.90	(1.25 – 6.74)	0.013
Thymoglobulin (Yes vs No)	0.37	(0.16 – 0.85)	0.019
Age (years)	1.01	(0.98 – 1.04)	0.467
Sex (Male vs Female)	2.01	(0.85 – 4.72)	0.111

Legend: OR = Odds Ratio; CI = Confidence Interval.

with erythropoietin, azathioprine, serum ferritin, and BMI. Although not statistically significant in our study, the mean BMI of patients with ID was higher (26.7 kg/m²).

Iron deficiency appears to be insufficiently treated: only 38% of deficient patients received intravenous iron, 16% received oral iron, and few received erythropoietin. This is partly explained by previous research focusing only on anemic patients, while our results show a prevalence of 27% iron deficiency in non-anemic patients.[19]

Beguin et al. demonstrated suboptimal erythropoiesis in transplant patients despite low EPO levels and low transferrin.[21] However, Zadrazil nuanced this hypothesis by finding no link between serum EPO and blood count; he reported that insufficient graft function, with a prevalence of 32.1%, was the main cause of post-transplant anemia.[22]

Our multivariate analysis identified three factors significantly associated with iron deficiency: graft duration, basiliximab induction, and thymoglobulin induction. An older graft is correlated with progressive depletion of iron stores, linked to increased erythropoiesis induced by improved renal function, especially when dietary intake is insufficient. This is consistent with Gafter-Gvili et al, who observed a correlation between late post-transplant anemia and low iron levels (HR 0.986 for each 1 mg/dL increase).[23]

Basiliximab induction is positively associated with iron deficiency. Although the known side effects are primarily hypersensitivity reactions, some cases of anemia have been reported. This potential link between basiliximab and impaired iron metabolism warrants further exploration.

Conversely, thymoglobulin induction seems to be associated with a lower frequency of iron deficiency, which is surprising. This molecule is classically associated with cytopenias, infections, and lymphoproliferative syndromes. One explanation for this paradox is inflammation, which causes iron sequestration and artificially increases ferritin levels without reflecting actual iron stores, resulting in functional iron deficiency. This hypothesis also warrants further investigation, particularly with inflammatory markers and other indices of iron metabolism.

Conclusion

Iron deficiency is common in renal transplant recipients, even without anemia, underscoring the need for routine post-transplant iron monitoring. Increased ID risk was associated with longer graft duration and basiliximab induction. Thymoglobulin induction appeared potentially protective; however, this finding remains speculative and should be interpreted with caution. Early identification and appropriate management of ID are essential to optimize long-term outcomes, quality of life, and graft function in renal transplant patients.

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Competing Interests

The authors declare no conflicts of interest.

Ethical Approval

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. It was approved by the institutional ethics committee of CHU Gabriel Montpied (Ref: CE-CCHUGM-2023-104). All included patients provided informed consent and authorization for the use of their medical data for research purposes. All data were anonymized and handled confidentially, in compliance with the General Data Protection Regulation (GDPR).
This study did not involve animal data or tissues.

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