# Prevalence of long-term cytopenia in kidney transplant patients: a cross-sectional study

Emad A.M. Yossef[a], Hesham M. Hefny[b]

[a]Department of Internal Medicine, Faculty of Medicine, [b]Department of Clinical Pathology, Sohag University, Sohag, Egypt

Correspondence to Emad A.M. Yossef, MD degree of Internal Medicine Sohag University, Faculty of Medicine, Sohag University Hospital, Sohag Nasr City, 82511, Egypt.
Tel: 01101779988; fax: 0934597229;
e-mail: emadabokhabar@gmail.com

**Received:** 9 February 2020
**Revised:** 17 October 2020
**Accepted:** 23 October 2020
**Published:** 2 February 2021

**Journal of The Egyptian Society of Nephrology and Transplantation** 2021, 21:25–30

**Background**
Although cytopenia is common during the first few months following transplantation owing to induction and maintenance immunosuppressant, little is known about the prevalence of cytopenia in transplant patients beyond the first 6 months after transplantations. Thus, we conducted the present study to investigate the prevalence of chronic cytopenia in renal transplant recipients.
**Patients and methods**
This was a cross-sectional descriptive study carried out on 81 kidney transplant recipients in the renal transplant clinic at Sohag University Hospital during the period from February 2018 to February 2019. A nonprobability consecutive sampling technique was employed to recruit eligible patients.
**Results**
Regarding study outcomes, we found that 44.4% of our study group had anemia, 38.3% had normocytic anemia, and 6.2% had microcytic anemia. Regarding the degree of anemia, 17.3% of the patients had severe anemia, 17.3% had mild anemia, and 9.9% had moderate anemia. In addition, 3.7% of the study groups had leukopenia and 1.2% had leukocytosis. Regarding platelets, only one (1.2%) patient had thrombocytosis.
**Conclusion**
Chronic posttransplantation cytopenia is a common complication after kidney transplantation, especially anemia. Therefore, it is recommended that physicians involved in renal transplantation consider the investigation and follow-up of transplant recipients for posttransplantation cytopenia and adopt appropriate preventive and therapeutic measures. In addition, we recommend further studies on a larger number of patients, with focus on the link between posttransplantation cytopenia and mortality.

**Keywords:**
chronic kidney disease, cytopenia, hematological abnormalities, kidney transplantation

Journal of The Egyptian Society of Nephrology and Transplantation 21:25–30

1110-9165

## Introduction

End-stage renal disease (ESRD) affects up to 20 000 cases annually and is characterized by irreversible declines in kidney function to the extent of an estimated glomerular filtration rate of less than 15 ml/min/1.73 $m^2$ or the necessity of dialysis, irrespective of estimated glomerular filtration rate [1]. In Egypt, previous epidemiolocal figures estimated that the annual incidence and prevalence of ESRD is ~74 and 264 per million, respectively [2,3]. ESRD can result from a wide range of chronic diseases, including diabetes, hypertension, glomerulonephritis, and lupus nephritis [4]. The prognosis of ESRD is devastating, with a mortality rate of 20–50%; in addition, ESRD represents a major public health burden with increased rates of hospitalization and health care cost in affected patients [4]. Dialysis, including hemodialysis and peritoneal dialysis, is the most commonly used modality for the management of ESRD; despite that technological advances improved the outcomes of dialysis, patients on maintenance dialysis still experience high rates of morbidities and mortality [5].

Renal transplantation is the best treatment modality for patients with ESRD. Since the first transplantation performed in 1954, the procedure has revolutionized the prognosis of patients with ESRD [6]. Alongside the survival benefits provided by renal transplantation, previous reports demonstrated that renal transplantation improves the quality of life and reduces the overall health-related cost compared with dialysis [7]. However, a considerable proportion of patients undergoing transplantation can experience a wide range of short-term and long-term complications. Classic complications of renal transplantation include graft rejection, infection, cardiovascular, and urological

complications [8]. Hematological abnormalities are common following renal transplantation; renal transplant recipients exhibit higher frequencies of anemia, cytopenia, erythrocytosis, and lymphoproliferative disorder than the general population [9].

Although cytopenia is common during the first few months following transplantation due to induction and maintenance immunosuppressants [10], little is known about the prevalence of cytopenia in transplant patients beyond the first 6 months after transplantations. Thus, we conducted the present study to investigate the prevalence of chronic cytopenia in renal transplant recipients.

## Patients and methods

The study's protocol gained the approval of the local ethics and research committee of Sohag University Hospital, Sohag, Egypt. Written informed consent was obtained from eligible patients before the beginning of the study.

### Study design, setting, and participants

This was a cross-sectional descriptive study that was carried out on 81 kidney transplant recipients in the renal transplant clinic at Sohag University Hospital during the period from February 2018 to February 2019. Adults (>18 years old) patients were included if they received kidney transplantation for more than 6 months before the study's enrollment. We excluded patients with multiple organ transplantation, patients on hemodialysis due to temporary or permanent failure of transplantation, patients with a history of hematological abnormalities, and/or patients with a history of recent bleeding or blood transfusion. Pregnant women were excluded as well. A nonprobability consecutive sampling technique was employed to recruit eligible patients.

### Data collection and study's visits

The following data were collected from eligible patients: demographic characteristics, history of chronic diseases, causes of ESRD, mode and duration of dialysis, donors' characteristics, history of graft rejection or dysfunction, previous medications, the presence of systemic infection, and the findings of routine laboratory findings. The laboratory investigations included complete blood count, kidney function tests, serum uric acid, serum electrolytes, urine analysis, iron profile, and parathormone hormone. Complete Blood Count (CBC): CBC was done by CELL-DYN RubyTM System Operator (Abbott Laboratories, Diagnostic Division, IL, USA).

The primary outcome in the present study was the incidence of cytopenia in kidney transplant patients. The anemia was graded into mild (defined as hemoglobin >12 and <13 g/dl for males and >11 g/dl and <12 g/dl for females), moderate (defined as hemoglobin >11 g/dl and ≤12 for males and >10 g/dl and ≤11 g/dl for females), and severe (defied as hemoglobin <11 and 10 g/dl for males and females, respectively) degrees [11]. Leukopenia was defined as white blood cell count less than 4000 cells/μl. Thrombocytopenia was defined as a platelet count less than 150 000/μl.

### Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS), version 20.0 (Chicago, IL, USA). Quantitative data were expressed as mean±SD and range. Qualitative data were expressed as frequency and percentage.

## Results

A total of 81 kidney transplant recipients were included in the present study. The mean age of the included patients was 40.4±12.41 years, and 81.5% of them were males. In addition, 64.2% of the patients were from rural areas, and 71.6% were employed. Only 13.6% of the patients were smokers. Almost 15% of the patients were obese. Regarding the cause of ESRD, we found that 35.8% of the patients had unknown causes followed by hypertension and glomerulonephritis (17.3 and 14.8%, respectively). The mean duration of remaining on dialysis was 17.91±28.94 months, and 91.4% were on hemodialysis. The mean duration after transplantation was 61.17±58.51 months, and the majority of cases (49.4%) had a duration since transplantation of 12–60 months. Moreover, 97.5% had first renal transplant, and all patients received grafts from living donors. All of our patients received steroids, 82.7% received mycophenolate mofetil, 64.2% received tacrolimus, 33.3% received cyclosporin, 17.3% received azathioprine, 14.8% received proton pump inhibitor, and 11.1% used aspirin (Table 1).

The mean age of donors was 34.31±10.01 years, and 63% of them were less than 35 years of age. Overall, 53.1% of donors were males. Moreover, 28.4% of our study group had the previous history of graft rejection approved by renal graft biopsy; only 3.7% had a history of delayed graft function. Regarding the type of rejection, 21% were cell mediated and only 7.4% antibody mediated. The mean duration of the last rejection episodes was 8.98±26.35 months. Overall,

**Table 1 Demographic and clinical data of the study group**

| Items | Patients (*N*=84) [*n* (%)] |
|---|---|
| Age (mean±SD) | 40.40±12.41 |
| Male | 66 (81.5) |
| Rural | 52 (64.2) |
| Employed | 58 (71.6) |
| Smoker | 11 (13.6) |
| Obese | 12 (14.8) |
| Hypertension | 42 (51.9) |
| DM | 10 (12.3) |
| Current infection | 3 (3.7) |
| Cause of ESRD | |
| Hypertension | 14 (17.3) |
| Glomerulonephritis | 12 (14.8) |
| Obstructive nephropathy | 4 (4.9) |
| Obstetric cause | 2 (2.5) |
| SLE | 2 (2.5) |
| Polycystic kidney | 6 (7.4) |
| Analgesic nephropathy | 1 (1.2) |
| Unknown causes | 29 (35.8) |
| Amyloidosis | 3 (3.7) |
| Pyelonephritis | 8 (9.9) |
| Duration of dialysis (mean±SD) | 17.91±28.94 |
| Hemodialysis | 74 (91.4) |
| Duration of transplantation | |
| 6–12 | 14 (17.3) |
| 12–60 | 40 (49.4) |
| >60 months | 27 (33.3) |
| First transplantation | 79 (97.5) |
| Living related type of transplantation | 36 (44.4) |
| Duration (mean±SD) | 61.17±58.51 |
| Immunosuppressant drugs | |
| Steroid | 81 (100) |
| MMF | 67 (82.7) |
| Azathioprine | 14 (17.3) |
| Tacrolimus | 52 (64.2) |
| Cyclosporin | 27 (33.3) |
| Everolimus | 0 |
| Sirolimus | 3 (3.7) |
| History of ATG | 9 (11.1) |
| History of IVIG | 4 (4.9) |
| History of rituximab | 4 (4.9) |
| History of plasmapheresis | 6 (7.4) |
| PPI | 12(14.8) |
| Aspirin | 9 (11.1) |

ATG, anti thymocyt globulin; DM, diabetes mellitus; ESRD, end-stage renal disease; IVIG, intra venous immmunoglobuline; MMF, mycophenolate mofetil; PPI, proton pump inhibitor; SLE, systemic lupus erythematosus.

19.8% of the study group had one attack of graft rejection episode and 8.6% had more than one attack of rejection episodes (Table 2). The findings of laboratory investigations are present in Table 3.

Regarding study outcomes, we found that 44.4% of our study group had anemia, 38.3% had normocytic anemia, and 6.2% had microcytic anemia. Regarding the degree of anemia, 17.3% of the patients had severe anemia, 17.3% had mild anemia, and 9.9% had moderate anemia (Figs 1 and 2). In addition, 3.7% of the study's groups had leukopenia and 1.2% had leukocytosis. Regarding platelets, only one (1.2%) patient had thrombocytosis.

**Table 2 Data of transplantation**

| Items | *n* (%) |
|---|---|
| Sex of donor | |
| Male | 43 (53.1) |
| Female | 38 (46.9) |
| Age of donor (years) | |
| <35 | 51 (63) |
| >35 | 30 (37) |
| Age of donor | |
| Mean±SD | 34.31±10.01 |
| History of delayed graft function | 3 (3.7) |
| History of rejection | 23 (28.4) |
| Type of rejection | |
| Cell mediated | 17 (21) |
| Antibody mediated | 6 (7.4) |
| No history of rejection | 58 (71.6) |
| Number of rejection episodes | |
| No history of rejection | 58 (71.6) |
| One attack | 16 (19.8) |
| More than one attack | 7 (8.6) |
| Duration of last rejection episodes | |
| Mean±SD | 8.98±26.35 |

## Discussion

Although cytopenia is common during the first few months following transplantation owing to induction and maintenance immunosuppressants [10], little is known about the prevalence of cytopenia in transplant patients beyond the first 6 months after transplantations. Thus, we conducted the present study to investigate the prevalence of long-term cytopenia in renal transplant recipients. We found that 44.4% of the patients had anemia, 3.7% had leukopenia, and none of the patients had thrombocytopenia.

Posttransplantation anemia is common in renal transplant recipients. Although the exact pathogenesis of posttransplantation anemia is not fully understood, various factors are thought to contribute to the development of anemia, such as graft dysfunction, blood group incompatibility, viral infection, and medications [12]. In the present study, we found that 44.4% of the patients had anemia, mainly normocytic anemia. Regarding the degree of anemia, 17.3% of the patients had severe anemia, 17.3% had mild anemia, and 9.9% had moderate anemia. In agreement with our findings, Wu *et al.* [13] reported that the prevalence of

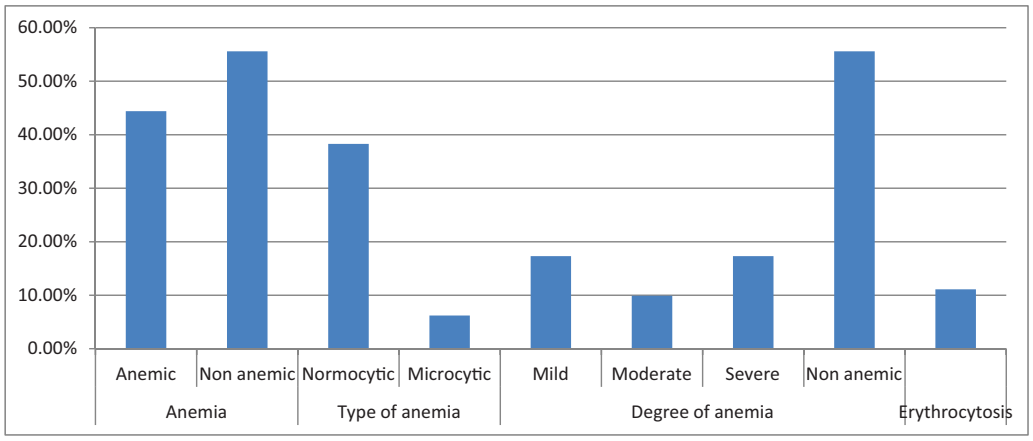
**Table 3 Results of laboratory investigations**

| Items | *n* (%) |
|---|---|
| Anemic or not | |
| Anemic | 36 (44.4) |
| Nonanemic | 45 (55.6) |
| Type of anemia | |
| Normocytic | 31 (38.3) |
| Microcytic | 5 (6.2) |
| Degree of anemia | |
| Mild | 14 (17.3) |
| Moderate | 8 (9.9) |
| Severe | 14 (17.3) |
| Nonanemic | 45 (55.6) |
| Erythrocytosis | 9 (11.1) |
| WBCs | |
| Normal | 77 (95.1) |
| Leukopenia | 3 (3.7) |
| Leukocytosis | 1 (1.2) |
| Platelets | |
| Normal | 80 (98.8) |
| Thrombocytosis | 1 (1.2) |
| HB level | |
| Mean±SD | 12.96±2.377 |
| HCT level | |
| Mean±SD | 39.43±7.736 |
| Serum iron | |
| Normal | 73 (90.1) |
| Decreased | 7 (8.6) |
| Increased | 1 (1.2) |
| Serum ferritin | |
| Normal | 53 (65.4) |
| Decreased | 1 (1.2) |
| Increased | 27 (33.3) |
| TIBC | |
| Normal | 65 (80.2) |
| Decreased | 15 (18.5) |
| Increased | 1 (1.2) |
| Transferrin | |
| Normal | 64 (79) |
| Decreased | 13 (16) |
| Increased | 4 (4.9) |
| Transferrin level | |
| Mean±SD | 34.24±15.885 |
| Ca level | |
| Mean±SD | 9.193±0.7563 |
| Ca level | |
| Normal | 67 (82.7) |
| Hypocalcemia | 9 (11.1) |
| Hypercalcemia | 5 (6.2) |
| Phosphorus level | |
| Mean±SD | 3.840±1.04 |
| Phosphorus level | |
| Normal | 62 (76.5) |
| Hypophosphatemia | 5 (6.2) |
| Hyperphosphatemia | 14 (17.3) |
| PTH level | |
| Mean±SD | 168.28±199.79 |
| PTH level | |
| Normal | 46 (56.8) |
| Hyperparathyroidism | 35 (43.2) |
| Creatinine | |
| 1 | 24 (29.6) |
| 1–2 | 36 (44.4) |
| >2 | 21 (25.9) |
| eGFR | |
| Mean±SD | 65.43±29.76 |
| Stages of eGFR | |
| Stage 1 | 20 (24.7) |
| Stage 2 | 32 (39.5) |
| Stage 3 | 16 (19.8) |
| Stage 4 | 13 (16) |
| Proteinuria | 24 (29.6) |
| Serum uric acid | |
| Normal | 68 (84) |
| Hyperuricemia | 13 (16) |
| Serum albumin | |
| Normal | 79 (97.5) |
| Hypoalbuminemia | 2 (2.5) |

Ca, calcium; eGFR, estimated glomerular filtration rate; HB, hemoglobin; HCT, hematocrit; PTH, parathyroid hormone; TIBC, total iron binding capacity; WBC, white blood cell.

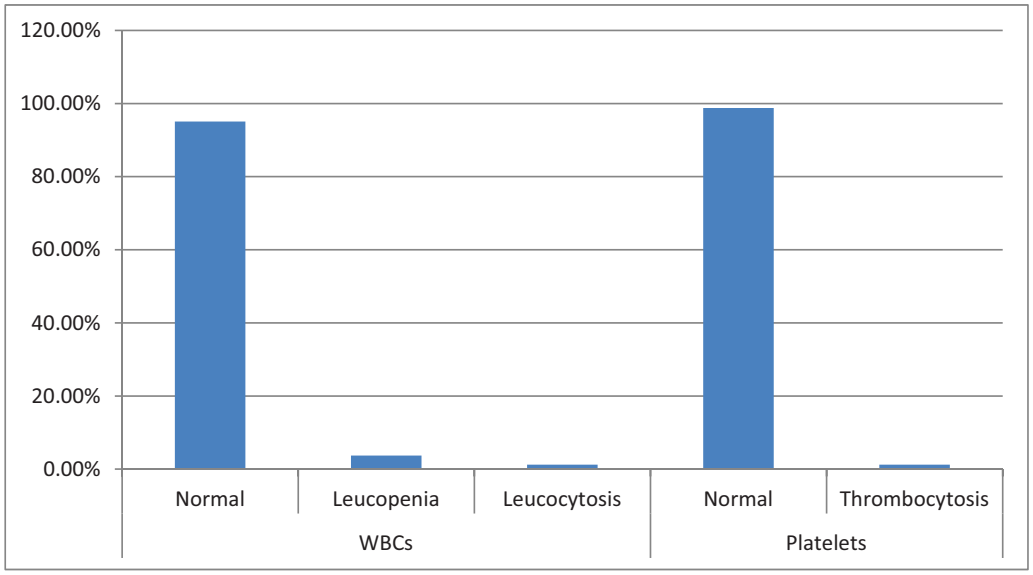
posttransplantation anemia was 45.5% immediately following transplantation and 38.3% in the overall period of follow-up. Likewise, Lim *et al.* [14] reported that the prevalence of posttransplantation moderate-to-severe anemia was 27.4%. In a large survey of more than 16 European countries, Vanrenterghem *et al.* [15] demonstrated that the prevalence of posttransplantation anemia was 38.6%. Other reports showed that the prevalence of posttransplantation anemia ranged from 20 to 40% [16–18].Posttransplantation leukopenia, mainly neutropenia, is another common hematological disorder following renal transplantation. Both immunosuppressive agents and antibiotics are thought to be the major contributors to the development of posttransplantation leukopenia [9]. Thus, previous reports indicated that posttransplantation leukopenia usually resolves within 4 weeks after transplantation [19]. In the present study, we found that 3.7% of the study groups had chronic leukopenia. To the best of our knowledge, this the first study that addressed the incidence of chronic leukopenia in renal transplant recipients. Other studies reported the prevalence of leukopenia within 6 months of transplantation. For example, Brum *et al.* [20] reported prevalence of 20.8% 3 months after the transplantation, whereas a prevalence of 40.6% was reported within 6 months of transplantation in the study by Liang *et al.* [21]. Another retrospective study reported a prevalence of 28% [22].

**Figure 1**




Characteristics of anemia.

**Figure 2**




WBC and platelet parameter of the studied population. WBC, white blood cell.

We acknowledge that the present study has a number of limitations. The study was conducted in one center only, which may affect the generalizability of our findings. Another limitation is the small sample size, which can further affect the generalizability of our findings.

## Conclusion

In conclusion, chronic posttransplantation cytopenia is a common complication after kidney transplantation, especially anemia. Therefore, it is recommended that physicians involved in renal transplantation consider the investigation and follow-up of transplant recipients for posttransplantation cytopenia and adopt appropriate preventive and therapeutic measures. In addition, we recommend further studies on a larger number of patients with focus on the link between posttransplantation cytopenia and mortality.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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