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An Observational Study on Etiology of Proteinuria in Postrenal Transplant Recipients in a Tertiary Hospital of North India

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The presence of proteinuria from native kidneys is hard to interpret when detected after transplantation. Studies show that pre-transplant proteinuria, even within the nephrotic range, abruptly reduces during the first weeks after receiving a normal functioning kidney transplant. Immunosuppressive medications, such as calcineurin inhibitors (e.g., cyclosporine, tacrolimus), can cause nephrotoxicity and result in proteinuria. Urinary tract infections (UTIs), can cause proteinuria.

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Studies have found that proteinuria doubled the risk of graft failure in comparison with non proteinuric transplant recipients Risk for death was almost twice as high for patients with proteinuria at 1 year.

Keywords: Proteinuric transplant recipients; proteinuria; kidney transplant; kidney transplantation.

1. INTRODUCTION

"Proteinuria is common after kidney transplantation and affects between 35%-45% of patients during the same year as their transplant. Proteinuria, is an important biological marker used to identify patients and grafts with a poor prognosis. In general, the level of proteinuria is low (<500mg/day) but even those low levels significantly reduce graft and patient survival. Proteinuria may be caused by multiple factors, including glomerular disease, effects of anti-HLA class II antibodies and drugs such as mTOR inhibitors, tubulointerstitial disease of the graft" [1,2].

"The prevalence of proteinuria varies between 15% and 45% and this variation is mainly due to differences in the level of proteinuria used to define the value considered as abnormal [3-7]. It is important to diagnose proteinuria during the first few months after the transplant, to identify the patients and grafts that are at high risk. Post-transplant proteinuria is generally low-grade, and therefore in 30% of patients proteinuria varies between 150 mg/day and 500 mg/day. Albuminuria was not only related to an increase in cardiovascular risk but also to an increase in the risk of cancer-related death" [2,8-13].

2. PROTEINURIA CAUSES

Post-renal transplant proteinuria can have multiple causes, including both immunological and non-immunological factors. Patients with high-grade proteinuria (>1500mg/day) frequently have graft glomerular diseases seen in 80% of patients.

"Acute rejection episodes, especially cellular rejection, can lead to proteinuria. Proteinuria is a common feature of chronic allograft nephropathy and can be an early indicator of ongoing graft damage. Three types of glomerular disease occurs in the graft: Recurrent diseases, De novo diseases, and Post-transplant glomerular disease. Focal segmental glomerulosclerosis (FSGS) affects 30% of patients and is associated with a high risk of recurrence. Approximately 50% of patients with recurrent FSG lose their graft. Membranous nephropathy (MN) is also associated with a high risk of recurrence. IgA nephropathy frequently occurs (>50%) after the transplant, although histological changes are generally mild. Post-transplant glomerular disease (PG) is generally diagnosed several years after transplantation and that could cause high-grade proteinuria, even nephrotic range proteinuria" [2,14]. De Novo Glomerulonephritis: new-onset glomerulonephritis can develop in the transplanted kidney after transplantation. The presence of proteinuria from native kidneys is hard to interpret when detected after transplantation. Studies show that pre-transplant proteinuria, even within the nephrotic range, abruptly reduces during the first weeks after receiving a normal functioning kidney transplant [15-19]. Immunosuppressive medications, such as calcineurin inhibitors (e.g., cyclosporine, tacrolimus), can cause nephrotoxicity and result in proteinuria. Urinary tract infections (UTIs), can cause proteinuria. UTIs are relatively common in transplant recipients and can contribute to protein leakage into the urine. Proteinuria can occur in the immediate post-transplant period due to surgical trauma to the transplanted kidney [20-26]. This is usually transient and resolves over time. Vascular complications such as renal artery stenosis or thrombosis, can affect the blood supply to the transplanted kidney. Other factors include hypertension, diabetes mellitus, chronic viral infections (e.g., hepatitis C), and certain systemic diseases (e.g., systemic lupus erythematosus).

2.1 Aims and Objectives

To quantify proteinuria in renal transplant recipients, assess etiology of proteinuria in post renal transplant recipients and to assess the outcome of grafts survival and patient outcome in patients with proteinuria.

3. METHODS

3.1 Study Population

Prospective observational study done for 3 years study population includes all renal transplant recipients (live and deceased donor) with previously no documented proteinuria and renal dysfunction, who attended opd for regular follow

up during study period from January 2019 to December 2022.

3.2 Exclusion Criteria

Sepsis

Post Transplant Diabetes Mellitus (PTDM)

- Chronic viral infections
- Transplant renal artery stenosis (TRAS)
- Proteinuria detected within first month of transplant
- Non renal cause; cardiac dysfunction

3.3 Data Collection

This study analysed and quantified proteinuria in all renal transplant recipients (live and deceased donor) with previously no documented proteinuria and renal dysfunction, who attended outpatient clinic for regular follow up during study period from January 2019 to December 2022. Patients were followed up for minimum of 6 months and maximum of 3 years. Age of recipient at the time of transplant, age of donor, sex of donor and recipient, basic disease, number of human leukocyte antigen (HLA) mismatches, presence or absence of delayed graft function (DGF), urinary tract infections during posttransplant period and rejection episode recorded. Proteinuria during first month of transplant with normal renal function were excluded. But recipients with persistent proteinuria were included in study. Spot urine samples were obtained for the determination of urinary protein excretion during follow up visit. Urinary protein concentrations were measured using dipstick method. Recipients were classified into one of three groups according to their levels of post-transplant proteinuria: nil as the no proteinuria group; trace and 1+ as the minimal proteinuria group; and more than 1+ as the overt proteinuria group. Various etiologies for proteinuria were assessed after evaluating renal biopsy report, drug history, underlying urinary infections, PTDM. Patient with proteinuria and renal dysfunctionwere followed up to assess graft and patient survival.

4. RESULTS

284 patients were followed up out of which ,256 were living donor transplant recipients and 28 deceased donor transplant patients (Chart 1) Among them, 212 were males and 72 were females (Chart 2).

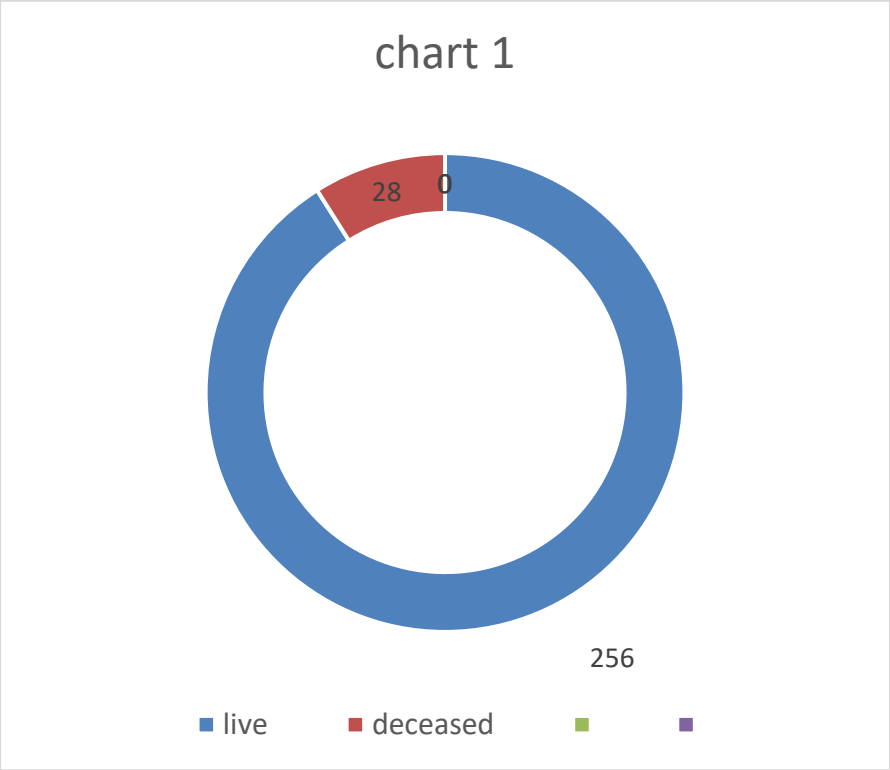


Chart 1. Pie chart showing live and deceased ratio

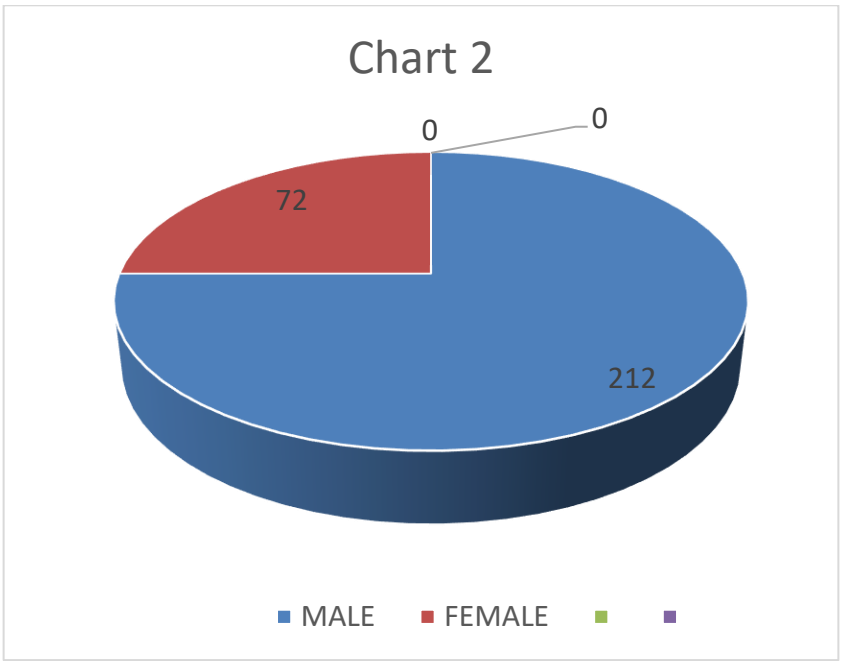


Chart 2. Pie chart showing male and female ratio

- Mean age of recipient 35.40±9.34 years. Mean age of donor was 50.73±8.14 years. Females constitute 82% of donor (233) rest were males (51) Proteinuria along with renal dysfunction were detected in 36 patients Proteinuria without renal dysfunction detected in 4 patients.

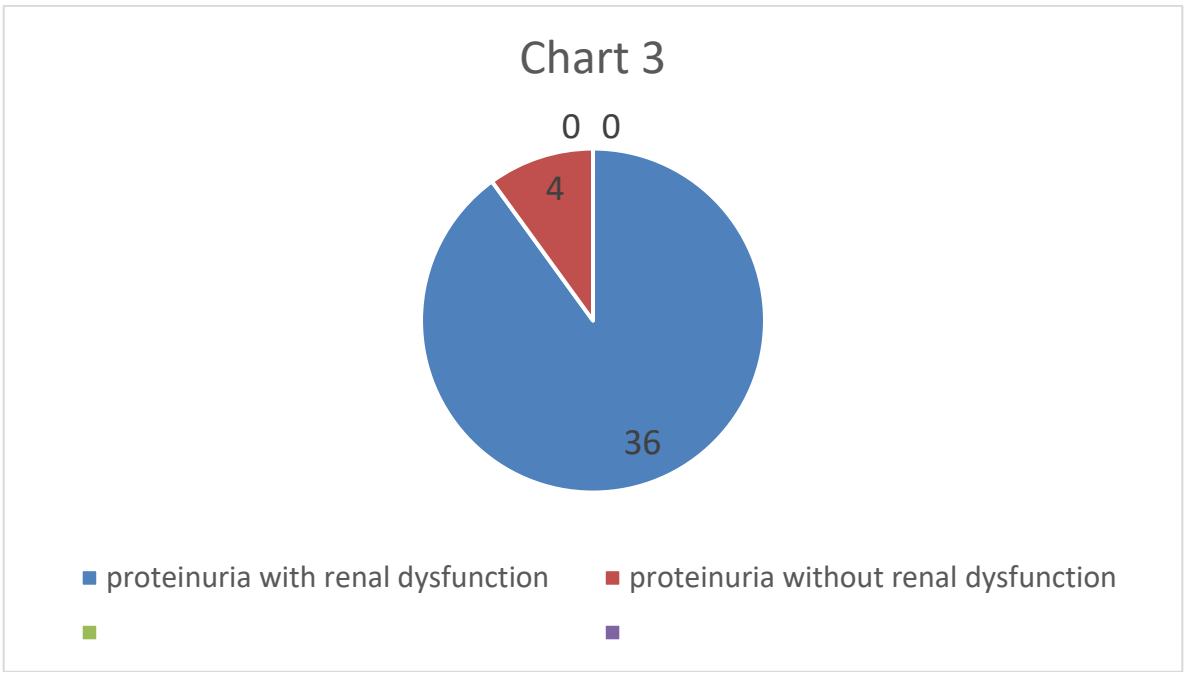
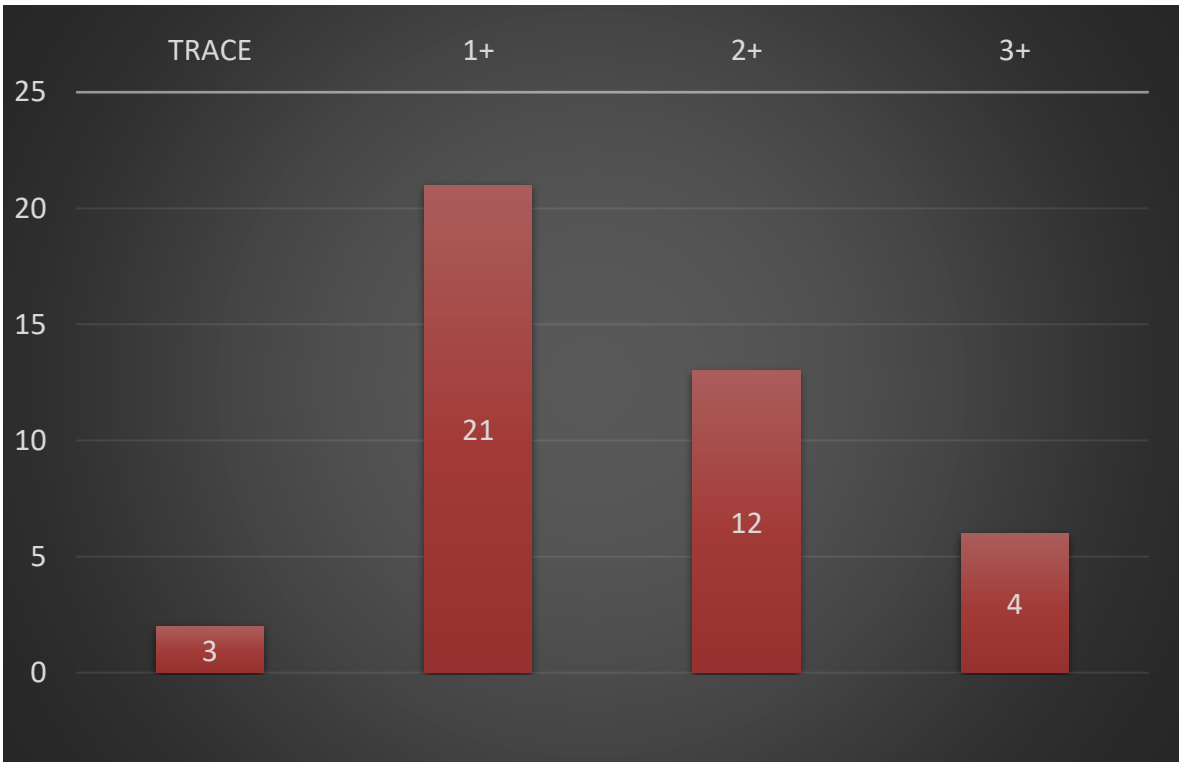


Chart 3. Pie chart showing renal dysfunction

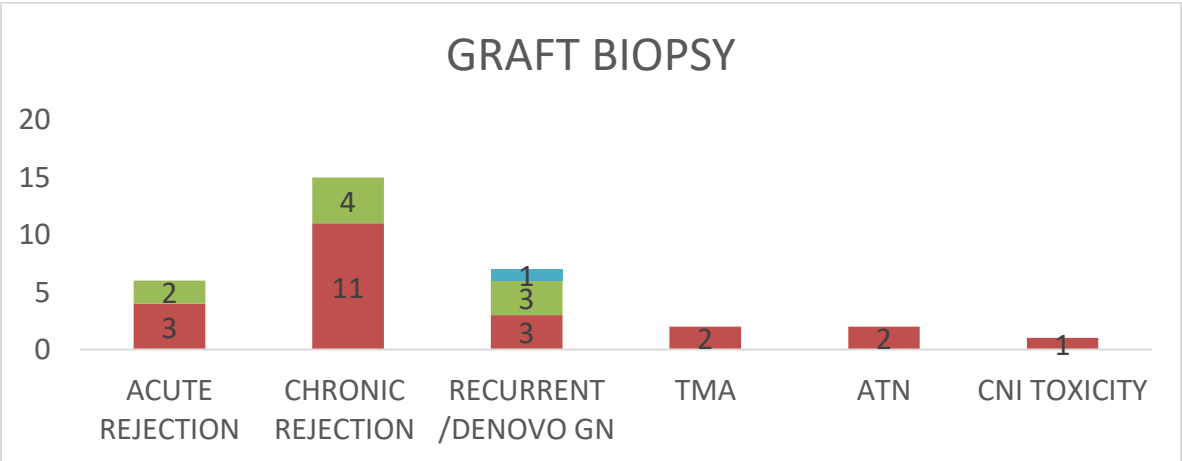
Trace proteinuria in 3 ,1+ proteinuria in 21, 2+ proteinuria in 12 and 3+ proteinuria in 4 patients.



Graph 1. Bar graph showing allograft biopsy

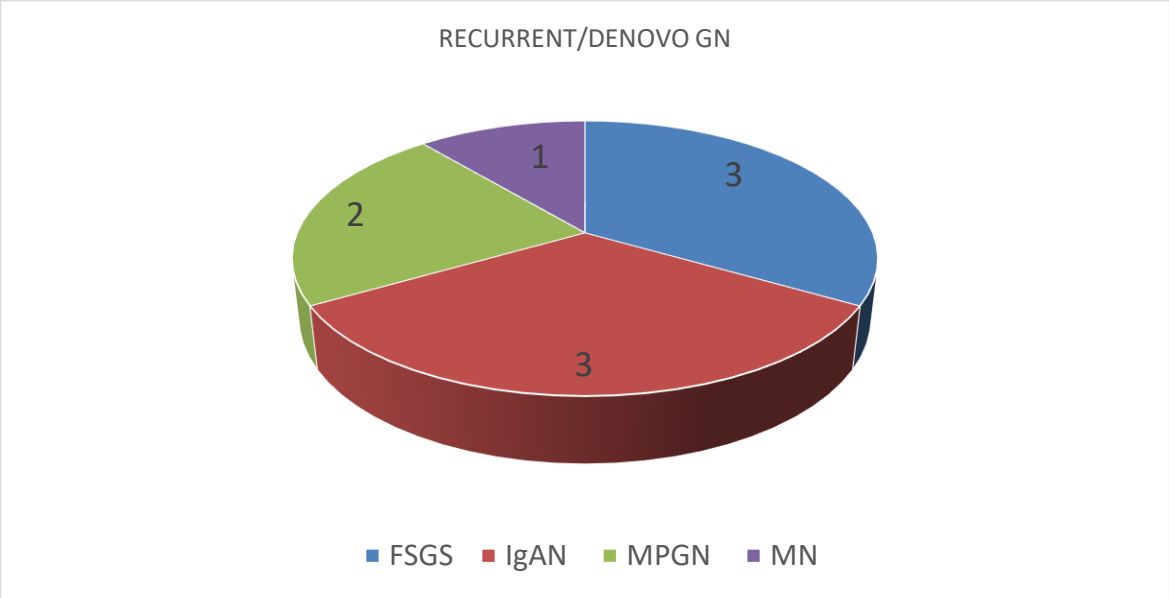
38 patients underwent allograft biopsy during study period.

Acute rejection in 9 patients with acute TCR in 3, active ABMR in 2 mixed rejection in 4 patients. Chronic rejection in 15; with chronic ABMR in 11, chronic TCR in 4, Recurrent or denovo Glomerular disease in 9 patients Others; CNI toxicity in 1, acute tubular necrosis in 2 and thrombotic microangiopathy in 2 patients.



Graph 2. Bar graph showing graft biopsy

Recurrent or denovo Glomerular disease in 9 patients, with focal segmental glomerulosclerosis in 3 patients, membranous nephropathy in 1 patient, MPGN/C3 glomerulonephritis in 2 patients, IgA nephropathy in 3 patients.



Graph 3. Pie chart showing recurrent/Denovo_GN

5. DISCUSSION AND CONCLUSION

- Proteinuria detected in 14% of study population. 1 + proteinuria detected in more than 50 % of patients. Nephrotic range proteinuria detected in 10%. Nephrotic range proteinuria after renal transplant is about 13%. In 12 patients proteinuria detected within one year of transplant. Chronic rejection accounts for major cause of proteinuria with 38% followed by acute rejection and glomerulonephritis(23%). Chronic ABMR detected in 11 patients (28%) constitute major cause of chronic rejection FSGS and IgAN were major glomerulonephritis detected followed by C3 GN. Studies have found that proteinuria doubled the risk of graft failure in comparison with non proteinuric transplant recipients Risk for death was almost twice as high for patients with proteinuria at 1 year.

5.1 Drawbacks

- lack of quantitative assessment of urinary protein like Protein/creatinine levels in spot urine or 24 hr urine protein .No data on albuminuria or proteinuria composition, which could discriminate between glomerular and tubular origin of the proteinuria .In immunologically high-risk transplants patients preformed DSA level not measured.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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