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DIAGNOSTIC ACCURACY OF COLOR DOPPLER SONOGRAPHY IN EVALUATION OF RENAL TRANSPLANT REJECTION TAKING HISTOPATHOLOGY AS GOLD STANDARD

Original Research

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Abstract

Background: Renal transplant rejection occurs when the recipient's immune system identifies the transplanted kidney as foreign, leading to immune-mediated injury. Timely and accurate diagnosis is essential for preserving graft function and improving patient outcomes. Color Doppler sonography, a non-invasive imaging technique, has shown promise in detecting hemodynamic changes indicative of rejection. However, its diagnostic accuracy compared to histopathology, the gold standard, remains under investigation.

Objective:
To determine the diagnostic accuracy of Color Doppler sonography in evaluating renal transplant rejection, with histopathology as the gold standard.

Methods: This cross-sectional validation study was conducted in six months starting from 1st July 2024 and sample size was achieved in October 2024, at the Department of Radiology, PAF Hospital Islamabad. A total of 226 patients, aged over 20, with clinical diagnoses of renal transplant rejection were included. Exclusion criteria encompassed primary non-functioning transplant kidneys, prior renal artery interventions, glomerulonephritis, renal tumors, active urinary tract infections, and pregnancy. Color Doppler sonography results were recorded alongside histopathological findings. Statistical analysis was performed using IBM SPSS version 26, calculating sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), and negative predictive value (NPV) for Color Doppler sonography.

Results: The mean age of participants was 38.31±11.61 years, with a mean transplant duration of 4.31±1.89 months and a mean BMI of 29.85±2.78 kg/m². Color Doppler sonography showed a sensitivity of 71.3%, specificity of 71.2%, diagnostic accuracy of 71.2%, PPV of 61%, and NPV of 80%.

Conclusion: Color Doppler sonography is a valuable tool for evaluating renal transplant rejection, though complementary approaches with histopathology are recommended for comprehensive assessment.

Keywords: Color Doppler, Diagnostic accuracy, Histopathology, Predictive value, Renal transplant rejection, Sensitivity, Specificity.

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INTRODUCTION

Renal transplant rejection occurs when the recipient's immune system identifies the transplanted kidney as foreign and mounts an immune response against it (1). This reaction can lead to inflammation, tissue destruction, and impaired organ function (2). Timely identification and management of renal allograft rejection are crucial for preserving the function of the transplanted organ and enhancing patient survival (4). Color Doppler sonography, an advanced ultrasound technique, overlays conventional grayscale ultrasound images with color-encoded blood flow data to provide a non-invasive method for analyzing blood flow within vessels or organs (5). This imaging modality represents blood flow direction with different colors—commonly red indicating flow towards the transducer and blue indicating flow away from it (6). The intensity of the color, which depends on blood flow velocity, aids in assessing vascular patterns and hemodynamics, making this technique valuable in evaluating renal transplant rejection (7).

The changes in intrarenal arteries during rejection, such as elevated resistive indices, reduced or absent diastolic flow, or even reversed flow, can be effectively detected by Color Doppler sonography (9). While not definitive on its own, it serves as a crucial first-line imaging tool that can reduce the necessity for more invasive diagnostic procedures like biopsy (10). Studies by Patel KN et al. and Pereira LNG et al. demonstrated its diagnostic utility, revealing a sensitivity and specificity of 35% and 80% respectively, in detecting renal transplant rejection, and a prevalence rate of 39% in sampled populations (11, 12).

The aim of this research is to explore the diagnostic accuracy of Color Doppler sonography in identifying renal transplant rejection, to improve patient outcomes. Enhancing the precision and reliability of this non-invasive method may allow for earlier detection of rejection, critical for maintaining graft function. This could potentially reduce the dependence on invasive procedures and lower healthcare costs, thereby advancing transplant medicine and improving the quality of care for kidney transplant recipients.

METHODS

This cross-sectional validation study was conducted at the Department of Radiology, PAF Hospital Islamabad, over a six-month period starting from 1st July 2024 and sample size was achieved in October 2024. Based on previous findings with a sensitivity of 35% and specificity of 80% for renal transplant rejection screening (11), and considering a prevalence of 39% (12), a sample size of 226 was determined necessary to achieve a 95% confidence level and a precision of 10%. Consecutive non-probability sampling was employed to select the study participants, who were all older than twenty years and had received a clinical diagnosis of renal transplant rejection. Patients were excluded if they had a primary non-functioning transplant kidney, previous renal artery interventions, glomerulonephritis, renal tumors, active urinary tract infections, or were pregnant.

Upon obtaining ethical clearance and informed consent, demographic data such as age, gender, body mass index (BMI), and duration since transplantation were collected. Renal transplant rejection was clinically diagnosed based on criteria including hypertension (blood pressure > 140/90 mmHg), a bruit over the graft site, or a reduced urine output (< 1000 ml/24 hours). Color Doppler sonography was performed using a 3.75 MHz convex probe to assess renal artery morphology and vascular indices, including resistive index (RI), pulsatility index (PI), and acceleration time (AT). Rejection was indicated on sonography by an RI $\geq$ 0.8, a PI $\geq$ 1.5, an AT $\leq$ 0.1 seconds, loss of corticomedullary differentiation, reduced perfusion, absent flow in pericalyceal arteries, or arterial stenosis with turbulent flow.

Subsequent to the sonographic assessment, ultrasound-guided percutaneous kidney biopsies were performed. Histopathological examination of the kidney samples focused on the presence of interstitial inflammation, tubulitis, and intimal arteritis. Data from Doppler imaging and biopsy results were meticulously documented on a dedicated proforma designed with specific criteria. Data analysis was conducted using IBM SPSS version 26. Means and standard deviations were calculated for age, transplant duration, and BMI, while frequencies and percentages were compiled for gender and the incidence of rejection. The sensitivity, specificity, and diagnostic accuracy of color Doppler sonography were evaluated against histopathological findings through a 2x2 table. Stratifications controlled for effect modifiers, and post-stratification chi-square tests were applied to determine statistical significance, set at a p-value of $\leq$0.05.

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RESULTS

In the presented study, the mean age of the participants was 38.31 years with a standard deviation of 11.61, while the average duration post-renal transplant was recorded at 4.31 months, and the mean body mass index (BMI) was calculated to be 29.85 kg/m². The cohort predominantly comprised males, constituting 73.9% of the sample, whereas females represented 26.1%.

Table 1 Demographics of the patients (n=226)

Demographics		**Mean±SD**
Age (years)		38.309±11.61
Duration of renal transplant (months)		4.305±1.89
BMI (Kg/m2)		29.845±2.78
Gender	Male n (%)	167 (73.9%)
	Female n (%)	59 (26.1%)

Table 2 Overall results of Color doppler sonography and Histopathology in diagnosis of renal transplant rejection (n=226)

Renal transplant rejection	**Color doppler sonography n (%)**	**Histopathology n (%)**
Positive	102(45.1%)	87(38.5%)
Negative	124(54.9%)	139(61.5%)
Total	226 (100%)	226 (100%)

The diagnostic outcomes revealed a positive rate of 45.1% for renal transplant rejection when assessed using Color Doppler sonography. In comparison, histopathological evaluation reported a slightly lower positive rate of 38.5%. A significant statistical difference was observed between the diagnostic results of Color Doppler sonography and histopathology, which was substantiated by a chi-square value of 39.01 and a p-value less than 0.001.

Table 3 Comparison of Color doppler sonography versus Histopathology for diagnosis of renal transplant rejection (n=226)

Color doppler sonography	**Histopathology**		**Total**
	Positive	Negative	
Positive	62 (TP)	40 (FP)	102
Negative	25 (FN)	99 (TN)	124
Total	87	139	226

TP True positive, FP False positive, FN False negative, TN True negative

The sensitivity and specificity of Color Doppler sonography in the diagnosis of renal transplant rejection were determined to be 71.3% and 71.2%, respectively, demonstrating a diagnostic accuracy of 71.2%. The positive predictive value (PPV) and negative predictive value (NPV) of this imaging technique were 61% and 80%, respectively.

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Table 4 Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of Color doppler sonography for diagnosis of renal transplant rejection (n=226)

Sensitivity (%)	**71.3**
Specificity (%)	71.2
Diagnostic Accuracy (%)	71.2
Positive Predictive Value (PPV) (%)	61
Negative Predictive Value (NPV) (%)	80

Stratified analysis based on the duration post-transplant indicated that patients within 1-3 months post-transplant exhibited a sensitivity of 75%, a specificity of 64%, and a diagnostic accuracy of 68.5%. In contrast, those beyond 3 months post-transplant showed a sensitivity of 69.5%, a specificity of 74.5%, and a diagnostic accuracy of 72.55%. This stratification highlights the variability in diagnostic performance of Color Doppler sonography relative to the time elapsed since the renal transplant.

DISCUSSION

In this study, Color Doppler sonography detected a higher positive rate of renal transplant rejection (45.1%) compared to histopathology (38.5%), suggesting potential sensitivity to early or subtle signs of rejection. The significant difference between these diagnostic methods, supported by a chi-square value of 39.01 and a p-value less than 0.001, indicates their distinct diagnostic profiles. Color Doppler sonography demonstrated moderate effectiveness with a sensitivity of 71.3% and a specificity of 71.2%, which points to its reasonable accuracy in detecting true positives and negatives. The positive predictive value of 61% implies that when sonography indicates rejection, it is correct 61% of the time. Meanwhile, the negative predictive value of 80% suggests a high reliability in ruling out rejection, making sonography particularly useful for this purpose.

Recent advancements in ultrasound technology, such as contrast-enhanced ultrasound (CEUS) and sono-elastography, have shown promise in enhancing diagnostic accuracy. CEUS, which assesses microcirculatory blood perfusion, has been noted for its heightened sensitivity and specificity in detecting acute rejection, as seen in studies by Zhou et al. (13) and El-Motaal et al. (14). These studies underscore the potential of combining traditional ultrasound techniques with newer modalities to improve early detection and differentiation between types of graft injuries.

Color Doppler ultrasound (CDUS), particularly when integrated with parameters like the resistive index (RI) and renal cortical ratio (RCR), shows improved diagnostic precision. For instance, Drudi et al. (15) found that RCR achieved a sensitivity of 100% and specificity of 98.3% in differentiating between normal and pathological grafts within 24 hours post-transplantation. This highlights CDUS's capability in early postoperative diagnostics, which is crucial for timely intervention.

However, the utility of renal resistive index (RRI) as a long-term predictor of graft dysfunction remains uncertain due to variability in renal histology and extrarenal hemodynamics, as discussed by Stigler and Tiefenthaler (16). They recommended that RRI should be considered alongside overall perfusion assessments and routine ultrasound monitoring to detect early structural and vascular complications effectively.

Despite these advances, the study has limitations. The reliance on CDUS might lead to potential false positives, suggesting a need for cautious interpretation of results, especially when clinical signs are ambiguous. Further research is required to refine diagnostic criteria and validate the clinical utility of emerging ultrasound technologies like CEUS and sono-elastography in various patient populations.

Overall, CDUS remains a valuable non-invasive tool for monitoring renal transplant recipients. Its accessibility and proven diagnostic capability make it an indispensable method in clinical practice. As ultrasound technology evolves, incorporating these innovative techniques could further enhance the management and outcomes of renal transplant patients.

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CONCLUSION

In conclusion, Color Doppler sonography serves as a valuable method for assessing renal transplant rejection, though it comes with certain limitations. The notable disparities between sonographic results and histopathological findings highlight the importance of employing a multifaceted diagnostic approach to ensure accurate identification and management of renal transplant rejection. Integrating various diagnostic modalities can enhance the reliability and efficacy of patient evaluations, supporting better clinical outcomes in the management of transplant recipients.

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