DIAGNOSTIC ACCURACY OF COLOR DOPPLER ULTRASOUND FOR DIAGNOSIS OF ACUTE RENAL TRANSPLANT REJECTION BY TAKING HISTOPATHOLOGY AS GOLD STANDARD IN PATIENTS PRESENTING AT TERTIARY CARE HOSPITAL, KARACHI.

Kashaf Anwar[1]. Sana Shaikh[2], Sayed Muhammad Faiq[3]

ABSTRACT

OBJECTIVE: To assess how effective color Doppler ultrasound (CDUS) is in diagnosing acute renal transplant rejection (RTR) compared to using histopathology as the standard in patients showing signs of acute rejection following renal transplant at a specialized hospital in Karachi. **METHODS**: This A detailed cross-sectional research was carried out at the Radiology Department of SIUT in Karachi., from February 2019 till August 2019. All the patients of either gender aged 18 years and above who have undergone renal transplantation and are presenting with clinical suspicion of acute renal transplant rejection were included. All patients those patients underwent Color Doppler Ultrasound evaluation of the transplanted kidney followed by histopathological examination through renal transplant biopsy. Findings were cross-tabulated To evaluate the sensitivity, specificity, positive and negative predictive values, and diagnostic precision. **RESULTS:** Mean age of the patients The average age of the participants was 51.12±7.57 years. Out of the total, 18 individuals (60%) were males and 12 individuals (40%) were females. Additionally, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of CDUS in detecting acute rejection of renal transplants, with histopathology as the reference standard, were determined to be 92%, 80%, 95.8%, 66.7%, and 90%, respectively. **CONCLUSION:** CDUS observed to be an accurate, reliable, and non-invasive diagnostic tool for acute renal transplant rejection, helping to avoid unnecessary surgeries and enabling early, effective management, particularly in resource-poor settings.

KEY WORDS: Acute Rtr, Cdus, Sensitivity, Specificity

1. Assistant Professor. Radiology department SIUT.
2. Associate professor. Radiology department. SIUT.
3. Professor and HOD, Radiology department. SIUT.

Corresponding Author: **Kashaf Anwar.** Assistant Professor, Radiology department SIUT**. Email:** Kashaf.anwar81@gmail.com

INTRODUCTION

Renal transplantation, in end-stage renal dysfunction, is considered a first-line treatment for optimal management of renal failure to improve survival rates and quality of life in comparison to dialysis in long run.[1] Although postoperative care and immunosuppressive therapy have achieved significant advancements, allograft rejection still remains a clinically challenging situation in acute renal transplant cases, which is a result of recognition and response of host's immune

system to the antigens of donor by producing antibodies against the donor's antigens, termed as alloimmunization.[2]

Post-transplantation renal graft rejection is influenced by several pre-operative and post-operative factors. Pre-operative factors influencing survival of patient and graft dysfunction include several characteristics of graft donor and graft recipient such as immunologic compatibility, race, gender, and age.[3,4] On the other hand, post-operative factors include delayed graft and immunosuppressive therapy. Acute rejection is more prevalent among recipients of renal graft with history of blood transfusions or pregnancies due to elevated panel reactive antibody (PRA) in such patients.[5] The incidence of acute rejection in renal transplants has been estimated in around 50-70% of cases during the initial post-transplantation weeks, which is alarmingly high and calls for early and accurate diagnosis of acute rejection to preserve graft function through timely intervention.[6]

Biopsy is considered a gold standard in diagnosing acute rejection through histopathological analysis of renal allograft. Yet, biopsy is not only invasive procedure but also carries the risks of misinterpretation, infection, and allograft damage, limiting its feasibility in critical situations.[7] Color Doppler, a non-invasive and advanced ultrasonography procedure of blood flow analysis, is another promising imaging tool for examining renal allografts.[8] The blood flow is encoded red and/or blue, with red showing flow directing towards and blue showing flow directed away from transducer, aided by light/dark shades indicating flow speed.[9] However, not the best, but Doppler ultrasonography can be used as first-line procedure as a substitute to unnecessary, invasive processes like biopsy.[10]

This study aims to evaluate the diagnostic accuracy of color Doppler ultrasound for Histopathology is the gold standard for diagnosing acute renal transplant rejection in patients at Tertiary Care Hospital in Karachi who may have acute renal transplant rejection. The findings of the study may support the use of Doppler ultrasound as a reliable screening tool in post-renal transplant care, potentially improving patient outcomes, minimizing the need for invasive procedures, and enhancing overall clinical management.

DATA COLLECTION PROCEDURE

This study with a descriptive cross-sectional design took place at the Radiology Department of SIUT in Karachi. from February 2019 till August 2019. All the patients of either gender aged 18 years and above who have undergone renal transplantation and are presenting with clinical suspicion of acute renal transplant rejection, those patients who undergo Color Doppler Ultrasound evaluation of the transplanted kidney followed by histopathological examination through renal transplant biopsy were included. Concern to specifically on acute rejection, patients within the first year of transplantation was considered. Patients who did not provide consent, or had a known history of chronic diseases or comorbidities like hepatitis B, hepatitis C, HIV infection, type 2 diabetes mellitus, hypothyroidism, hyperthyroidism, malignancy, or renal artery stenosis, as well as those with a documented history of stroke, renal impairment, chronic obstructive pulmonary disease (COPD), congestive cardiac failure, or myocardial infarction, were excluded from the study. All patients those patients underwent Color Doppler Ultrasound evaluation of the transplanted kidney followed by histopathological examination through renal transplant biopsy. Verbal informed consent was obtained from all participants after thoroughly explaining the purpose, procedures and potential benefits of the study, and they were clearly communicated that their participation was voluntary, and refusal to participate would not affect the quality of their medical care. Additionally

the confidentiality of all personal and medical information was strictly assured. Patients were labeled as having suspected acute renal transplant rejection if they presented within two weeks and exhibited one or more of the following clinical features: blood pressure greater than 140/90 mmHg, serum creatinine more than 20% above baseline, serum urea more than 20% above baseline, bruit over the graft site on clinical examination, or urine output less than 1000 ml in 24 hours. Acute renal transplant rejection on Color Doppler Ultrasound was defined as a Resistance Index (RI) greater than 0.8 in the transplanted kidney. Acute renal transplant rejection on histopathology was diagnosed when one or more characteristic features consistent with rejection were identified. Both sets of findings were cross-tabulated to assess Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy are employed 2×2 contingency tables, and the data were analyzed with SPSS version 26.

REULTS

A minimum age of 24 years old and a maximum age of 60 years old were observed in 30 patients. In our study, the average age was 51±12 years, with a standard deviation of ±7±57. Insensitive. height, weight & duration of transplantation were 158±7.28 cm, 88.7±9.87 kg and 1.07±0.14 weeks respectively. **Table: 1.**

Out of 30 patients with suspected acute renal transplant rejection, histopathology confirmed rejection in 83.3% of cases, while Color Doppler Ultrasound indicated rejection in 80% of cases. The The accuracy of Color Doppler Ultrasound in detecting acute renal transplant rejection compared to histopathology as the gold standard was determined to be 92% for sensitivity, 80% for specificity, 95.8% for positive predictive value, 66.7% for negative predictive value, and 90% for diagnostic accuracy respectively. **Table: 2** Furthermore the stratified analysis showed that in patients aged 20–40 years, Color Doppler Ultrasound had a diagnostic accuracy of 83.3%, while in those aged 41–60 years, it was 91.6%. For males, the diagnostic accuracy was 88.8%, and for females, it was 91.6%, with higher specificity observed in females (100%) compared to males (66.6%). **Table: 2**

TABLE: 1. DESCRIPTIVE STATISTICS OF DEMOGRAPHIC CHARACTERISTICS N=30

VARIABLES	STATISTICS
Age (mean ±SD)	51.12±7.57 years
Height (mean ±SD)	158±7.28 years
Weight (mean ±SD)	88.7±9.87 years
Duration of transplantation (mean ±SD)	1.07±0.14 years
Gender Males	18(60.0%)
Females	12(40.0%)

TABLE: 2. DIAGNOSTIC ACCURACY OF CDUS OF ATR BY TAKING HISTOPATHOLOGY AS GOLD STANDARD N= 30

COLOR DOPPLER US	HISTOPATHOLOGY		TOTAL
	POSITIVE	NEGATIVE	
Positive	23(TP)	01(FP)	24
Negative	02(FN)	04(TN)	06
Total	25	05	30
	DIAGNOSTIC ACCURACY		
Sensitivity	TP/TP+FN x 100		92%
Specificity	TN/TN+FP x 100		80%
PPV	TP/TP+FP x 100		95.8%
NPV	TN/FN+TN x 100		66.7%

| **Diagnostic accuracy** | TP + TN/ total number 100 | 90% |

TABLE: 2. DIAGNOSTIC ACCURACY OF CDUS OF ATR BY TAKING HISTOPATHOLOGY AS GOLD STANDARD BASED ON AGE AND GENDER N= 30

Age	Cdus	Histopathology		Total	
		Positive	**Negative**		
20-40 years	Positive	04(tp)	00(fp)	04	Sensitivity = 80%
	Negative	01(fn)	01(tn)	02	Specificity = 100%
	Total	05	01	06	Ppv= 100%
					Npv= 50%
					Da= 83.3%
41-60 years	Positive	19(tp)	01(fp)	20	Sensitivity = 95%
	Negative	01(fn)	03(tn)	04	Specificity = 75%
	Total	20	04	24	Ppv= 95%
					Npv=75%
					Da= 91.6%
Gender					
Male	Positive	14(tp)	01(fp)	15	Sensitivity = 93.3%
	Negative	01(fn)	02(tn)	03	Specificity = 66.6%
	Total	15	03	18	Ppv = 93.3%
					Npv= 66.6%
					Da= 88.8%
Female	Positive	09(tp)	00(fp)	09	Sensitivity= 90%
	Negative	01(fn)	02(tn)	03	Specificity= 100%
	Total	10	02	12	Ppv= 100%
					Npv= 66.7%
					Da= 91.6%

DISCUSSION

Renal transplant is a treatment of choice for end-stage renal disease (ESRD) patients. Acute renal-graft rejection may occur at any point of time after kidney transplantation, possibly mediated through either antibody or T-cell. Prompt identification and management of acute rejection would improve post-renal transplant outcomes in recipients.[11] Acute rejection rates differ on the basis of characteristics of both the recipients and the donors, type of immunosuppressive therapy, and additional risk factors.[12,13] Published studies have shown that acute rejection rates have declined over time due to advancements in immunosuppressive therapy. In the present study, 30 patients suspected of acute renal transplant rejection were enrolled, with a mean age of 51.12 years; 60% were males and 40% females. These findings suggest that older age and male gender may be associated with a higher risk of acute rejection. This trend is supported by Khan et al[15] who reported a predominance of male patients (73.9%) and a mean age of 38.31 ± 11.61 years, along with an average post-transplant duration of 4.31 months and a mean BMI of 29.85 kg/m², indicating a possible link between male gender, higher BMI, and rejection risk. Similarly, Kwon et al[2] reported a majority of male patients (58%), with a higher mean age of 53.26 years, a normal BMI of 22.36 kg/m², and a mean transplant interval of 166.5 days, further supporting the association of acute rejection with older age and male

predominance. The findings align with the present study highlighting the need to monitor higher-risk groups more closely to improve post-transplant outcomes

In the present study, among 30 patients with suspected acute renal transplant rejection, 9 (30%) experienced rejection within the first week post-transplant, while 21 (70%) had rejection episodes occurring after one week, indicating a tendency toward delayed diagnosis in the majority of patients. This observation is significant, as the timing of acute rejection has been shown to impact graft outcomes. Supporting our findings, studies by Koo et al[16]

and Opelz & Döhler et al[17] have reported that late-onset acute rejection is generally more severe and less responsive to immunosuppressive therapy compared to early rejection episodes, thereby adversely affecting graft survival. Similarly, Sijpkens et al[18] found that acute rejection occurring more than three months post-transplantation was associated with significantly poorer outcomes compared to rejection occurring within the first three months. These findings underscore the importance of early detection and intervention to improve graft prognosis and long-term transplant success.

In the present study, among 30 patients with suspected acute renal transplant rejection, histopathology confirmed rejection in 83.3% of cases, while Color Doppler Ultrasound (CDUS) detected rejection in 80% of cases. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of the CDUS, using the gold standard histopathology as the reference standard,were 92%, 80%, 95.8%, 66.7%, and 90%, respectively. These findings reinforce the understanding that while CDUS is a valuable non-invasive diagnostic tool, histopathology remains the superior and definitive method for detecting acute renal transplant rejection. Supporting these results, Khan et al.[15] reported that CDUS showed a

sensitivity of 71.3%, specificity of 71.2%, and overall diagnostic accuracy of 71.2%, which are notably lower than the figures observed in our study. Their study concluded that although CDUS is beneficial as an initial screening modality, it does not match the diagnostic precision of histopathological evaluation. Similarly, Zeng et al[19] highlighted the clinical usefulness of Color Doppler Flow Imaging as a non-invasive and practical technique for the evaluation and monitoring of acute rejection episodes post-renal transplantation, facilitating early detection and timely management. Furthermore, Osman et al[20] demonstrated that the sensitivity (ranging from 4.1% to 98.6%) and specificity (ranging from 2.6% to 92.2%) of the resistive index (RI) measured by Doppler varied significantly depending on the chosen cutoff values, reflecting the variability and limitations of Doppler-based parameters. In addition, Bai et al[21] reported high diagnostic accuracy of CDUS in detecting acute rejection following allogeneic renal transplantation, particularly in evaluating the response to antirejection therapy.

In this study out of 30 patients with suspected acute renal transplant rejection, histopathology confirmed rejection in 83.3% of cases, while Color Doppler Ultrasound indicated rejection in 80% of cases. The accuracy of Color Doppler Ultrasound in diagnosing acute renal transplant rejection, with histopathology as the reference standard, was found to be 92% sensitive, 80% specific, with a positive predictive value of 95.8%, negative predictive value of 66.7%, and an overall diagnostic accuracy of 90%.respectively. These results support the view that biopsy is more effective than Color Doppler Ultrasound in detecting acute renal transplant rejection. In line with our findings, the study of Khan et al[15] reported that color Doppler ultrasonography has high sensitivity (71.3%), specificity (71.2%), and overall diagnostic accuracy (71.2%) by taking

histopathology as gold standard; however these findings are lower than ours. They further concluded that that despite being a valuable initial screening tool, color Doppler ultrasonography is not a consistent match for the diagnostic precision of histopathology. Zeng H et al[19] also reported that the Color Doppler Flow Imaging serves as a valuable and non-invasive diagnostic modality in the assessment and monitoring of acute rejection episodes following renal transplantation, aiding in early detection and timely management. In another study of Osman et al[19] the sensitivity (range 4.1% to 98.6%) and specificity (2.6% to 92.2%) of resistive index (RI) measured by Doppler significantly varied for diagnosing graft rejection depending on desired cutoff values. Additionally Bai Y et al[20] observed the high diagnostic accuracy of in CDUS detecting acute rejection following allogeneic renal transplantation, particularly in assessing the effectiveness of treatment for acute rejection. Taken together, these findings justify the integrated use of CDUS in the diagnostic process for renal transplant rejection. Hence strengths lie in being a rapid, non-invasive, and cost-effective screening tool. Though, its limitations such as operator dependence, variable RI interpretation, and occasional false negatives reinforce the indispensability of histopathology for confirmation and definitive diagnosis. However this study, while demonstrating the usefulness of CDUS in detecting acute renal transplant rejection, is limited by its small sample size, single-center design, and operator dependency, which may affect the generalizability and accuracy of results. Additionally, the lack of follow-up data limits insights into long-term outcomes. Hence, future studies are recommended with larger sample sizes, multicenter designs, integration of CDUS with other diagnostic tools or biomarkers, and standardized techniques to enhance reliability and minimize the need for invasive biopsies.

CONCLUSION

This study revealed that the CDUS is a valuable, non-invasive diagnostic modality with high sensitivity and diagnostic accuracy for detecting acute renal transplant rejection, when compared to histopathology as the gold standard. Despite its clinical usefulness in initial screening and monitoring, CDUS cannot fully replace histopathological examination, which remains the definitive diagnostic tool. Additionally findings support the role of CDUS in facilitating early detection and timely management of graft rejection, potentially reducing the reliance on invasive procedures. However, to strengthen diagnostic confidence, further research with larger multicenter cohorts and standardized protocols is recommended, and integrating CDUS with novel biomarkers and imaging parameters may enhance diagnostic accuracy and improve outcomes in renal transplant care.

AUTHORS' CONTRIBUTIONS:
All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.
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