Radiology Section

Doppler Ultrasonography in Planning Arteriovenous Fistula for Haemodialysis with Follow-up for Maturity and Complications-A Cohort Study

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# ABSTRACT

**Introduction:** Patients having End Stage Renal Disease (ESRD) require kidney replacement therapy for survival. As kidney transplantation is expensive, haemodialysis using an Arteriovenous Fistula (AVF) is the preferred mode of management. Preoperative assessment of blood vessels using Doppler Ultrasonography (DUS) in the creation of an efficient AVF.

**Aim:** To use DUS for the evaluation and mapping of blood vessels, selection for AVF construction, the time taken for fistula maturation, the primary patency rate, the vascular changes in major co-morbidities and the complications on follow-up.

**Materials and Methods:** An prospective observational and cohort study of 100 patients requiring AVF for haemodialysis was undertaken between January 2015 to November 2016 at Department of Radiodiagnosis and Imaging, PES Institute of Medical sciences and Research, Kuppam, Andhra Pradesh, India. Preoperative vascular evaluation using duplex DUS was performed to know the diameter, caliber, distensibility of veins and flow velocity of arteries.

Postoperative follow-up was done in fourth and sixth week for early detection and management of complications.

**Results:** The study included total of 100 patients (64 men and 36 women, mean age of  $40\pm15.4$  years) requiring AVF aged between 16 to 65 years. Following vascular mapping, Brachio-Cephalic Fistula (BCF) was constructed in 48 and Radio-Cephalic Fistula (RCF) in 52 patients. A mean diameter of 2.1 mm for cephalic vein in forearm and 2.6 mm in arm was adequate for AVF construction. Overall maturity rate was 75% and time taken for maturation was four weeks for BCF, six weeks for RCF and one year primary patency rate was 80%. Complications were noted in 30%, included thrombosis, haematoma, stenosis, pseudoaneurysm and so on.

**Conclusion:** Preoperative DUS is an economical investigation with exceptional ability to visualise vascular features and aids in planning reliable AVF. Systematic postoperative surveillance of AVF reduces the risk of failure due to early detection and management of complications.

Keywords: Brachio-cephalic fistula, End stage renal disease, Vascular mapping

# INTRODUCTION

Human beings are blessed with two kidneys, the relentlessly working vital organs and at least one functioning kidney is required for existence. Chronic Kidney Disease (CKD) is a world-wide health problem common in the elderly and presently with the increase in diabetes mellitus, hypertension and cardiovascular diseases, there is a steep rise in younger people. Patients with renal failure require Kidney Replacement Therapy (KRT) for survival such as kidney transplantation or dialysis [1]. Escalation in the number of ESRD requiring expensive kidney transplantation with an impact on medical economics has resulted in growing focus on providing an efficient vascular access for Haemodialysis which is the less expensive option [2]. Vascular access or AVF is defined as the connection of an artery and vein constructed for the purpose of haemodialysis. The preemptive choice is the AVF of the extremity so that the complications associated with Central Venous Catheters (CVC) are avoided [3,4].

The DUS examination with B-mode gray scale and spectral doppler is the preferred modality for vessel mapping and planning of AVF with higher success rates in terms of function, patency and maturity. However, the existing literature is mostly international and it is still an upcoming modality in India. The objectives of this study were 1) to use DUS for the evaluation and mapping of vessels, 2) selecting proper ones for AVF construction, to know the time taken for maturation of AVF, 3) to find the primary patency rate, 4) to evaluate the changes associated with major co-morbidities namely diabetes mellitus, hypertension, thrombosis/thrombophlebitis and atherosclerosis and 5) to record the number and types of complications on postoperative follow-up.

# MATERIALS AND METHODS

A prospective observational cohort study of 100 patients was undertaken in the Department of Radiodiagnosis and Imaging, PES Institute of Medical Sciences and Research (PESIMSR), Kuppam, Andhra Pradesh, India, from January 2015 to November 2016. The study was done after procuring clearance from the Institutional Ethical Committee.

**Inclusion criteria:** The inclusion criteria in this study were as follows: 1) the patients with ESRD who were referred for surgical planning of vascular access placements for haemodialysis and 2) the patients having failure of previous AVF and required reconstruction at a different site.

**Exclusion criteria:** 1) having deformed or scarred upper limb; 2) upper limb arterial and veno-occlusive disorders; 3) planning for an imminent renal transplant from a living donor; 4) patients with heart valve disease or prosthesis; 5) having history of previous arm, neck, chest surgery/ trauma; and 6) extreme obesity.

Planning of the preferred site of vascular access placement was made by duplex DUS to assess vessel caliber, wall morphology, Peak Systolic Velocity (PSV) of arteries and patency of vessels. This was based on the criteria and specifications documented by the American Institute of Ultrasound in Medicine, American College of Radiology & Society of Radiologists in Ultrasound [5].

### Study Procedure

Preoperative mapping of arterial and superficial venous system was done in all patients with emphasis on radial artery, brachial artery and cephalic vein. The functional study by measuring the vessel diameter and mean flow velocity on DUS helped in the evaluation of blood flow and the capacity of the artery to dilate. Venous Diameter (VD) of cephalic vein (measured in mm), pre-operative and postoperative evaluation of PSV as cm/sec, depth of the fistula from skin surface in mm and width of anastomotic site in mm for BCF and RCF were recorded. A tourniquet was tied around the arm to get better visualisation of blood vessels. Superficial venous system namely cephalic, basilic and median cubital veins were assessed first in transverse plane and followed by longitudinal plane. Venous caliber, distensibility and diameters were noted at distal and midforearm, cubital fossa, mid-arm followed by assessment of axillary and subclavian veins. Distal non dominant limb was preferred first, followed by proximal non dominant limb and then dominant upper limb. Similar parameters were documented for radial and brachial arteries. Radial artery was assessed at the wrist upto mid forearm and brachial artery from its bifurcation superiorly upto mid-arm region. First choice for constructing AVF was the distal cephalic vein in non dominant limb and last to be considered was proximal cephalic vein in dominant limb. Distal cephalic vein was avoided in the non dominant upper limb in patients having thrombus/ thrombophlebitis or inadequate cephalic VD of <2.0 mm.

Postoperative follow-up on 28<sup>th</sup> day (fourth week) and on 42<sup>nd</sup> day (sixth week) was done mandatorily in all the cases. Equipment used in this study was HD 6 Xe PHILIPS ultrasound machine with L3-12 Probe-Linear transducer (3-12 Mhz).

## STATISTICAL ANALYSIS

The statistical analysis was performed by Statistical Software for Data Science (STATA) 11.2 (College station TX USA). Chisquare test has been used to measure the association between the patient's age, gender, diabetes mellitus, hypertension, thrombophlebitis, atherosclerosis, dominant/non dominant limb, maturity, interventions, patency and complications of AVF. They were expressed as frequency and/or percentage. The t-tests were used to find the difference between the preoperative and postoperative PSV, with respect to the type of surgery and depth of fistula. PSV in association with type of AVF and similar comparative parameter were expressed as mean with standard deviation. A p-value of <0.05 was considered as statistically significant.

## RESULTS

Out of the total 100 patients who needed haemodialysis, 64 were males and 36 were females. Their age ranged between 16 to 65 years with a mean age of 40±15.4 years. Majority of the patients (43%) were between 40 to 60 years of age. Brachio-cephalic anastomosis was made in 48 patients and 52 underwent Radio-cephalic anastomosis. All the 100 patients were able to get vascular access made for haemodialysis with preoperative clinical evaluation and mapping of the blood vessels with DUS.

Preoperative PSV of 61.57 cm/sec is the minimum for brachial artery and 45.62 cm/sec radial artery with a significant p-value of <0.001. PSV at the site of anastomosis recorded postoperatively on the sixth week observed for both types of AVF was significant with p-value of 0.016 [Table/Fig-1].

Average cephalic VD increased from 2.6 mm to 5.1 mm and 5.8 mm at fourth and six week, respectively in BCF. Average cephalic VD increased from 2.1 mm to 4.1 mm and 5.3 mm at fourth and six week respectively in RCF, which was statistically significant with p-value of <0.001 at fourth week and 0.005 at six week [Table/Fig-1].

In 29 patients, AVF were constructed in the dominant upper limb due to inadequacies or pathology found in the non dominant upper limb including 17 BCF and 12 RCF [Table/Fig-2].

Postoperatively depth of the fistula was recorded in the six week after the AVF construction. A mean depth of 6.0 mm for BCF and 5.6 mm for RCF from the skin surface was found to be associated

with good clinical outcome. Width of the anastomotic site was recorded postoperatively on the sixth week of AVF construction. Mean anastomotic site diameters were 2.9 mm for BCF and 2.5 mm for RCF (p-value of <0.001) with good clinical results.

Type of AVF	BCF Mean±SD	RCF Mean±SD	p-value
Preoperative PSV (cm/sec)	73.25±11.68	58.83±13.21	<0.001
Depth of fistula (mm)	6.08±1.93	5.65±1.88	0.263
Width of Anastomotic site (6th week, mm)	2.92±0.56	2.51±0.39	<0.001
Postoperative PSV (6th week, cm/ sec)	573.58±219.98	481.69±149.09	0.016
Preoperative arterial diameter (mm)	3.40±0.48	2.45±0.20	<0.001
Preoperative cephalic vein diameter (mm)	2.67±0.37	2.10±0.30	<0.001
Postoperative cephalic vein diameter (4 <sup>th</sup> week) (mm)	5.13±0.97	4.13±0.63	<0.001
Postoperative cephalic vein diameter (6 <sup>th</sup> week) (mm)	5.87±1.10	5.31± 0.84	<0.005

[Table/Fig-1]: Pre-operative and postoperative evaluation of Peak systolic velocity (PSV), depth of fistula from the skin surface and width of anastomotic site in Brachio-Cephalic Fistula (BCF) and Radio-Cephalic Fistula (RCF), preoperative and postoperative venous diameter of Cephalic vein. The statistical analysis performed by STATA 11.2 (College station TX USA): t-test method

Limb used for AVF	BCF	RCF	Total	p-value	
Dominant	17 (35%)	12 (23%)	29		
Non dominant	31 (65%)	40 (77%)	71	0.174	
Total	48	52	100		
(b) Matu	rity rate of the	two types of A	/F		
Maturity	BCF	RCF	Total	p-value	
Positive	34 (71%)	41 (79%)	75	0.055	
Negative	14 (29%)	11 (21%)	25	0.355	
Total	48	52	100		
(c) Interventions with respect to two types of AVF					
Intervention	BCF	RCF	Total	p-value	
Made	9 (19%)	5 (10%)	14	0.214	
Not made	39 (81%)	47 (90%)	86	0.214	
Total	48	52	100		
(d) Post interventional primary patency rate at one year					
Post intervention patency	BCF	RCF	Total	p-value	
Positive	39 (81%)	41 (79%)	80	0.054	
Negative	9 (19%)	11 (21%)	20		
Total	48	52	100		
[Table/Fig-2]: Comparison of Brachio-Cephalic Fistula (BCF) and Radio-Cephalic Fistula (RCF) with respect to (a) non dominant versus dominant limb used for creation of AVF; (b) Maturity rate; (c) postoperative interventions made; (d) Post interventional primary patency at one year. The statistical analysis performed by STATA 11.2 (College station TX USA): t-test method					

An overall maturity rate of 75% was observed and number of interventions made for the two types of AVF. Post interventions, a primary one year patency rate of 80% were recorded and the role of intervention was justified in nine BCF and five RCF type (p-value-0.054). All interventions were US guided needle aspirations and evacuation for immediate haematoma or for late infective subcutaneous collections which were causing significant stenosis [Table/Fig-2].

Increased access failure rate was observed where the preoperative mean VD was lesser than 2.6 mm and 2.1 mm for BCF and RCF, respectively. Preoperative PSV of 73.0 cm/sec and above in BCF and 58.0 cm/sec and above in RCF were associated with good outcome (p-value of <0.001). BCF with mean VD of <3.8 mm and RCF with <2.9 mm were more prone to develop thrombosis. Mean arterial diameter

of 3.4 mm and above for brachial artery and 2.4 mm and above for radial artery was observed to have good outcome (p-value <0.001).

Overall failure rate was 20% at the end of 1 year for AVF. Comparison of failure with risk factors showed association of diabetes mellitus (54 patients) with a significant 70 % vascular access failure in this study. However, association of hypertension was of borderline significance and atherosclerosis of arterial system was insignificant with respect to access failure.

An overall maturity rate of 75% was recorded, with 14% cases requiring intervention to achieve maturity. In this study, the mean time for maturation was  $4\pm1$  week for BCF and  $6\pm1$  week for RCF. There were no significant differences in patency rates among the two types of AVF. Preoperative VD of 2.3 mm and below anywhere along the cephalic vein resulted in poor outcome and maximum failure rate and VD of above 2.4 mm had minimum failure rate. Thrombophlebitis/ thrombus formation was recorded in overall 33% cases pre-operatively with18 cases in BCF and 15 in RCF.

The co-morbidities noted in this study were diabetes mellitus, hypertension and atherosclerosis. Out of the 100 patients, 54 were having diabetes, 46 had hypertension and 45 had atherosclerosis. Preoperative venous thrombus/thrombophlebitis was recorded on mapping in 33 patients. These veins were uncompressible due to echogenic/hypoechoic thrombus. Comparison of BCF and RCF constructed in these co-morbidities is shown in the [Table/Fig-3].

Comparison of BCF and RCF in patients with Hypertension					
Hypertension	BCF	RCF	Total	p-value	
Hypertensive patients	18 (38%)	28 (54%)	46	0.101	
Non hypertensive	30 (62%)	24 (46%)	54		
Total	48	52	100		
Diabetes Mellitus					
Diabetes Mellitus	BCF	RCF	Total	p-value	
Diabetics	24 (50%)	30 (58%)	54	0.441	
Non diabetics	24 (50%)	22 (42%)	46		
Total	48	52	100		
Thrombosis/ thrombophlebitis					
Thrombosis/thrombophlebitis	BCF	RCF	Total	p-value	
Present	18 (38%)	15 (29%)	33		
Absent	30 (62%)	37 (71%)	67	0.358	
Total	48	52	100		
Atherosclerosis					
Atherosclerosis	BCF	RCF	Total	p-value	
Present	23 (48%)	22 (42%)	45		
Absent	25 (52%)	30 (58%)	55	0.573	
Total	48	52	100		

[Table/Fig-3]: Comparison between Brachio-Cephalic Fistula (BCF) and Radio-Cephalic Fistula (RCF) constructed in co-morbid patients with Diabetes Mellitus, Hypertension. Atherosclerosis and Pre-operative venous thrombosis/ thrombophlebitis. The statistical analysis performed by STATA 11.2 (College station TX USA): t-test method

Significant increase in intimal thickness (>1.0 mm) and calcifications were the features of atherosclerosis.

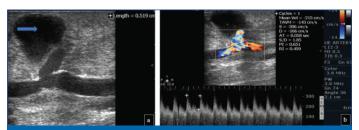
List of complications recorded postoperatively at fourth week, sixth week and on subsequent follow-up are shown in the [Table/Fig-4]. There were no complications in 70% of the cases and when found were more in RCF. In total 30% of the cases had complications following construction of AVF which included stenosis, thrombosis, haematoma, pseudoaneurysm, venous varices and subclavian steal syndrome. Intervention through ultrasound guided drainage of haematoma collection was done in 14% and an overall one-year primary patency rate of 80%. A few cases had venous wall thickening with subsequent short segment thrombus in cephalic vein and most of the times occurring at sites of previous intravenous cannulation.

Complications	BCF	RCF	Total
Nil	32 (67%)	38 (73%)	70
Haemotoma	4 (8.3%)	3 (5.8%)	7
Partial subclavian steal	0	1 (2%)	1
Pseudoaneurysm	2 (4%)	0	2
Inflow Stenosis	3 (6.2%)	2 (3.8%)	5
Thrombosis	4 (8.3%)	5 (9.6%)	9
Venous / Outflow stenosis	3 (6.2%)	2 (3.8%)	5
Venous varices	0	1 (2%)	1
Total	48	52	100
<b>[Table/Fig-4]:</b> Postoperative complications found with Brachio-Cephalic Fistula (BCF) and Radio-Cephalic Fistula (RCF). The statistical analysis performed by STATA 11.2 (College station TX USA): Chi-square test			

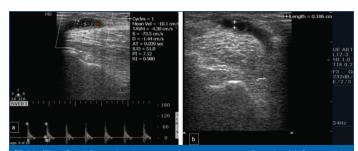
In this study, mean VD of 2.1 mm for cephalic vein in forearm and 2.5 mm for cephalic vein in arm was considered adequate for construction of AVF. [Table/Fig-5] shows the picture of RCF with a width of 2.3 mm and PSV of 657cm/sec and End Diastolic Velocity (EDV) of 406 cm/sec. Various complications of AVF observed on DUS are shown in [Table/Fig-6-10].



[Table/Fig-5]: (a) Radio-Cephalic Fistula (RCF) with width of 2.3 mm on grey scale (b) Pre-systolic Velocity (S) of 657cm/sec, End Diastolic Velocity (D) of 406 cm/sec on spectral doppler.



**[Table/Fig-6]:** Complication of AVF with haematoma. (a) Grey scale image, haematoma marked with arrow; (b) Colour and spectral doppler image.



**[Table/Fig-7]:** (a) Stenosis of anastomotic site on spectral Doppler. (b) Grey scale image showing outflow stenosis due to thrombophlebitis of cephalic vein.



**[Table/Fig-8]:** Venous varices with thrombophlebitis of cephalic vein (a) Grey scale image. (b) colour doppler image.



venous stenosis. (a) Grey scale image. (b) Spectral doppler image. (c) Colour doppler image.



[Table/Fig-10]: Complication of AVF with formation of pseudo-aneurysm. (a) Grey scale image; (b) Yin-yang sign on colour doppler; (c) Colour doppler image showing stenosis due to compression.

# DISCUSSION

The CKD is a global problem with marked economic constraints in developing countries as it causes significant morbidity than mortality and KRT is expensive. Kidney Disease Outcomes Quality Initiative (KDOQI) provides guidelines and has set the standards for high quality treatment [6]. The gold standard procedure till date for the creation of an autologous vascular access is the surgical creation of an AVF between the radial artery and the cephalic vein which is called Cimino-Brescia fistula named after the persons who described it for the first time in 1966 [7]. A lucid review by Zamboli P et al., gives all the salient features of DUS and its usefulness in planning AVF [8]. DUS is good for finding vessel diameters, anatomical variations, patency and vascular wall morphology and mapping is valuable in selecting potential sites for the creation of AVF thereby decreasing the negative surgical exploration rates [9].

The first population based study by Modi GK and Jha V from Bhopal in India found crude and age-adjusted incidence rates of ESRD as 151 and 229 per million population respectively with a mean age of 47 years, 58% of the affected were males and diabetic nephropathy was the commonest cause (44%) [10]. In this study, mean age was  $40\pm15.4$  years and 64% affected were men.

Thurlow JS et al., reported that incidence rate of CKD between 2003 to 2016 was stable in higher income countries but rose substantially and relatively more in East and Southeast Asia. The prevalence of treated CKD has been on the rise worldwide, related to better management, demographic shifts, higher prevalence of risk factors and increasing KRT mainly through vascular access in developing countries. They also reported a 5-year survival of patients on KRT as 41% in the USA, 48% in Europe, and 60% in Japan which depends on variation in Dialysis practices [11]. Present study could not have follow-up for five years.

Steep rise in the number of CKD is due to higher prevalence of diseases such as diabetes and hypertension describes Obrador GT and Levin A, who stated that increase is also due to infections and by unknown causes (CKDu) in certain areas of the world which can be called CKD hotspots [12]. In the present study, the patients were younger comparatively and did have co-morbidities.

National health and Nutrition examination survey (NHANES III) in a population-based survey in USA estimated that 11% of the adults have some stage of CKD and if these statistics are applied to India with more than 130 crore population, sheer enormity of the number of patients would overwhelm the health care system. KDOQI considers it reasonable that each patient with progressive CKD and/or with an effective Glomerular Filtration Rate (eGFR) of 15-20 mL/min/1.73 m<sup>2</sup> or already on KRT should have an individualised

ESRD life-plan, regularly reviewed and updated. Vascular access plan is required in ESRD patients for initiation of haemodialysis or in cases transitioning from other KRT such as peritoneal dialysis or failing/failed kidney transplant or in those already on haemodialysis with a failing AVF or CVC [13].

Vessels of small caliber <2 mm or having reduced distensibility are unable to create functional AVF and sufficient data does not exist with studies trying to support alteration in patency with respect to gender or raised Body Mass Index (BMI) (<35 kg/m<sup>2</sup>) [1]. An earlier study just like the present one reiterated that ultrasound mapping is good for planning vascular access as with the creation of an AVF there is 5-10 fold increase in blood flow gradually causing dilatation and arterialisation of the outflow vein [2]. Umphrey HR et al., observed that DUS can significantly improve access planning and postoperative fistula and graft evaluation in the haemodialysis patient [14]. Weber TM stated that ultrasound provides an accurate, rapid, low-cost, portable, non invasive method of screening, mapping, and surveillance of the vascular access [15]. Konner K documented that native AVF could be established in 80% and rest were candidates for AV grafts [4].

Robbin ML et al., did a retrospective analysis of 69 patients, four months after AVF placement and adequacy for dialysis was noted in 54, analysed with clinical examination, logistics with univariate and multi-variate regression. AVF adequacy doubled when the minimum VD was 0.4 cm or greater (89%) versus less than 0.4 cm (44%). Fistula adequacy was doubled for flow volume of >500 mL/min (84%) versus <500 mL/min (43%). Assessment of a combination of VD and flow volume increased fistula adequacy predictive value to 95% versus 33% when the criteria were not met [16]. These results are similar to the results of present study.

Asif A et al., stated that a good number of AVF lack maturation and do not support dialysis after which a catheter insertion may be required exposing the patient for infections. Follow-up for six months or longer to wait for the AVF to mature and support dialysis is suggested before declaring failure. Blood flow of 500 mL/min and a VD of at least 4 mm are needed for providing good access and these parameters are noted within four to six weeks with proper maturation in successful AVF. A good physical examination added with DUS helps in detecting an early access failure followed by intervention and salvage of a non maturing AVF [17]. Another study with DUS for AVF maturity documented an accuracy of 85% with the assessment of flow volume with draining VD and suggested to wait for at least a 40-day maturity period before using the access [18].

A cross sectional study of 370 patients by Yu Q et al., listed the common complications such as thrombosis (13.86%), followed by aneurysm (12.23%), anastomotic stenosis (2.17%), arterial steal syndrome (1.63%), infection (0.54%) and venous hypertension (0.27%). These results are similar to the present study. The wrist AVF was the first choice and an elbow AVF was the alternative for vascular access [19].

There is a growing body of evidence which suggests that creating an AVF in diabetic patients should not be discouraged and that diabetes is not a prognostic factor regarding outcome [20]. Stenosis is the most frequent complication of AVF, significantly affecting morbidity and mortality and the types of stenosis listed were inflow, outflow type, mid-vein and central vein stenosis [21]. In the present study, 7% inflow stenosis and 10% outflow stenosis were noted.

The KDOQI emphasises on multidisciplinary approach to haemodialysis with proper implementation of a standardised dialysis access training curriculum for all medical personnel including nephrologists, nurses, surgeons, radiologists and technicians involved in AV access care [13]. According to Schuman E et al., the gold standard for follow-up of an abnormality found during AVF surveillance is angiography which is sensitive and comparable to DUS flow measurements [22]. In a large multicentre study by Robbin ML et al., about AVF maturation including preoperative and postoperative assessment of VD and blood flow rates, it was observed that a higher proportion of upper-arm AVF placement was done in women than in men. AVFs were constructed more commonly in older patients with coronary artery disease and diabetes. There was no significant influence on fistula placement with respect to black race, BMI, or peripheral arterial disease. This study included 2800 cases, performed over six years, reported a smaller number of deaths and added good amount of data about upper arm AVF. It assisted seven institutions to standardise ultrasound protocol, training methods, quality control and radiology interpretation [23].

### Limitation(s)

Limitations of this study include short duration of follow-up of patients and the late complications that could have been missed.

# CONCLUSION(S)

Preoperative DUS assessment of morphological and functional features of blood vessels is beneficial for AVF construction due to the better selection of vessels. Postoperative surveillance of AVF with DUS is necessary for evaluating maturation, patency, ensures early detection of complications having deleterious consequences and allows measures to be taken for prevention of access failure. Hence, DUS is an economical and reliable investigation which aids in creating efficient vascular access for haemodialysis. Cohort studies having similar objectives as this study including larger number of patients with long term follow-up are needed to corroborate the findings.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

• iThenticate Software: Mar 30, 2022 (14%)

• Plagiarism X-checker: Aug 18, 2021

Manual Googling: Jan 15, 2022

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