Addis Ababa University, College of Health Sciences, Department of Radiology.

Renal Arterial Doppler Resistive Index in Differentiating Obstructive and Non-Obstructive Hydronephrosis in Children in TASH, Ethiopia, October, 2018.

A Research thesis submitted to Addis Ababa University, College of Health Sciences, Department of Radiology, Unit of Pediatric Radiology for Partial Fulfillment of The Requirement of Specialty Certificate in General Diagnostic Radiology.

By: Ayana Wasse (MD)

Advisors:

1. Dr.Daniel Zewdneh (MD, MPH ,SSPR, Associate Professor of Radiology)

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October, 2018 Addis Ababa, Ethiopia

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ABSTRACT

Background: *Most congenital anomalies of the urinary tract present with hydronephrosis due to several reasons. Some are physiological and others were pathological which persists for more than a year. Ultrasound, maturating cystourethrography, dynamic renal scintigraphy and intravenous urography , Dynamic and static MRU were used for examination. Currently renal arterial Doppler resistance index is not established as a clinically important diagnostic modality to differentiate obstructive and non obstructive hydronephrosis as observed in many conflicting research results.*

Objective*: To assess the usefulness of Doppler ultrasound measurement of resistive index (RI) in differentiating obstructive from non-obstructive hydronephrosis in children.*

Methods: *Forty two infants and children (<14 years) who were referred for the evaluation of hydronephrosis who fulfill inclusion criteria's from November 1, 2017 to July 2018 were enrolled using consecutive sampling. Ultrasonography for the assessment of the degree of hydronephrosis and a voiding cystourethrogram were used for the diagnosis of the vesicoureteral reflux and posterior urethral valve .Intravenous urogram and surgery were used to confirm causes for obstructive hydronephrosis. Then Doppler ultrasonography was done for both kidneys of each patient to determine mean resistive index for both obstructive and non-obstructive hydronephrosis as well as non-obstructive kidneys. Their medical chart was removed. Independent t test was used for analysis and p< 0.005 was used to declare significance. Results were presented with text, tables and charts.*

Results: *The study has included total of 42 children and 61 hydronephrotic kidneys. The major cause for obstructive hydronephrosis was PUJ obstruction accounting about 47.6% followed by posterior urethral valve 16.7%. For no obstructive hydronephrosis vesicoureteral reflux was main cause followed by prune belly syndrome. The mean resistive index of non -hydronephrotic kidneys was 0.6654 with SD of 0.053 non obstructive hydronephrotic kidneys 0.6825 ,SD 0.06668 and obstructive kidneys have mean RI of 0.7791 ,SD 0.11977.*

The mean resistive index difference between the obstructive and non-obstructive hydronephrosis was 0.09661 with standard error of difference 0.02443 .The statistical significance was tested with students independent t-test with P-<0.001 and 95% CI (0.0474 ,0.1457) .Using the cut-off *point of 0.7 mean RI ROC curve was constructed and showed sensitivity ,specificity and accuracy of 71.1%,81.2% ,75.4% respectively (p=0.003).*

Conclusion and Recommendation: *This study has showed mean renal arterial resistive index is significantly higher in obstructive hydronephrotic kidney than non-obstructive hydronephrotic kidney and can be potential valuable tool in resource limited countries to differentiate these conditions and as follow up tool after corrective surgeries .*

Key Words: hydronephrosis , Resistive index, Black Lion Specialized and referral hospital, children.

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Abbreviations and Acronyms

HN: Hydronephrosis

mRI: Mean Resistive Index

IVP: Intravenous Pyelogram

IVU: Intravenous Urogram

MCUG: Micturating Cystourography

VCUG: Voiding Cystourography

US: Ultrasound

ROC: receiver operating characteristic curve

DUS: Doppler ultrasound

ANH: Antenatal Hydronephrosis

PUJO: Pelviureric Junction Obstruction

SFU: Society for Fetal Urology

UTI: Urinary Tract Infection

LUTO: Lower Urinary Tract Obstruction

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CHAPTER ONE: INTRODUCTION

Background : Obstructive uropathy can be defined as an interruption of normal urine flow at some point along the urinary tract from the renal tubule to the urethra. Obstruction results in an increase in pressure within the urinary tract, causing structural and physiologic changes. However ,not all urinary tract dilatations represent urinary tract obstruction. Without intervention, obstructive nephropathy eventually leads to an irreversible loss of renal function. The various imaging techniques differ substantially in their ability to provide anatomical detail and physiological information

In patients with hydronephrosis clinicians face the biggest dilemma of differentiating a non-obstructed dilated system, where hydronephrosis will regress spontaneously over a period of time (or remain stable) from a dilated but obstructed system. This needs to be diagnosed as early as possible so that intervention can be done before renal damage occurs. The dilemma gains much significance as the clinician has to choose between conservative approach or surgical management .This differentiation needs to be done by utilizing appropriate investigations using the lowest radiation and least invasive techniques so that timely surgical intervention can be done to prevent renal function deterioration (1) .Hydronephrosis can be caused by obstructive or non-obstructive causes including transient physiologic dilatation and VUR. Differentiating the causes is very critical since management is quite different. Currently, in our routine pediatric urology practice, static anatomic investigations like IVP and VCUG with occasional static and dynamic MRU are used at our department.

Other physiological or functional methods like nuclear renograms are not available and Doppler study of renal arteries for RI to indirectly determine the nature of HN is not well established as an alternative method. This study is intended to assess clinical role of Doppler ultrasound for differentiating obstructive from non-obstructive HN depending on resistive index difference.

ETIOLOGIES OF HYDRONEPHROSIS

1. TRANSIENT HYDRONEPHROSIS

Most children with an antenatal history of renal pelvis and calyceal dilation ultimately resolve their hydronephrosis. The etiology of this finding may be related to a narrowing of the ureteropelvic junction (UPJ) or natural kinks and folds that occur early in development that resolve as the patient matures. The differentiation of transient hydronephrosis versus clinically significant UPJ obstruction remains one of the most controversial challenges in modern pediatric urology. Nevertheless, the incidence of transient hydronephrosis ranges from 41 to 88% (3).

2- PUJ OBSTRUCTION

The finding of pelvicalyceal dilatation without ureteric dilatation, commonly unilateral, is highly suggestive of UPJ obstruction. Currently, the incidence of UPJ obstruction in children with antenatal hydronephrosis (ANH) is approximately 10 -30%. Several retrospective studies reported a surgical intervention rate of 38-52% [4,5]. However, randomized trials suggested that only 19-25% of children with prenatally diagnosed UPJ obstruction require surgical intervention (6, 7). This suggests that most of them are not obstructive in nature. This might be the area where Doppler plays great role in follow up monitoring of patients to avoid unnecessary surgery.

3. VESICOURETERIC REFLUX

The finding of a variable degree of hydronephrosis or hydroureteronephrosis may suggest the possibility of VUR. Numerous studies have demonstrated that VUR occurs in 10-20% of patients with ANH .The incidence of reflux appears to increase with the degree of sonographic dilation postnatally; however, the degree of dilation does not correlate with the grade of VUR (8).In addition, a normal postnatal US does not exclude reflux. In one prospective study (9), 15% of children with mild prenatal hydronephrosis (>4 mm to <10 mm) had VUR and 43% of these children had a normal postnatal renal US scan. General pediatric population incidence of VUR is about 1-2% .VUR can be demonstrated in more 30% of the infant siblings of children with known VUR, and in up to 50% of the offspring of affected parents which signifies familial base.

4. URETEROVESICALJUNCTION (UVJ) OBSTRUCTION/ MEGAURETERS

The combination of prenatal hydronephrosis and ureteric dilation and a normal bladder suggests a megaureter. Megaureters can be refluxing, obstructed, non-refluxing/non-obstructed, and refluxing/obstructed. Prenatal ultrasonography has led more frequent postnatal diagnosis of primary megaureters. The majority (up to 72%) will spontaneously resolve during postnatal follow up (10, 11).

5. POSTERIOR URETHRAL VALVES/URETHRAL ATRESIA

Posterior urethral valves occur only in males and the incidence is 1 in4000–6000.The identification of: 1) prenatal hydronephrosis (often bilateral); 2) dilated, thick-walled bladder that fails to empty; 3) dilated posterior urethra; and 4) decreased amniotic fluid suggests the presence of lower urinary tract obstruction (LUTO). Unlike the unilateral upper tract dilation found commonly on prenatal ultrasonography, LUTO carries a worse prognosis with increased mortality and morbidity due to pulmonary hypoplasia and renal damage (12). Vesicoureteric reflux is present in 40–60% of cases at the time of initial evaluation and is unilateral in approximately two-thirds of cases.

Table 1. Summary of the common causes hydronephrosis. Source: (18)

Etiology	**Incidence (%)**
Transient hydronephrosis	41-88
UPJ obstruction	10-30
VUR	10-20
UVJ obstruction /megaureter	5-10
Ureterocele/ectopic ureter/duplex system	5-7
Others: prune belly sysndrome ,congenital ureteric strictures,megalurethra,stones and masses	Uncommon

Table 2. Grade of the hydronephrosis according to SFU. source: World J Clin Urol. Nov 24, 2014; 3(3): 283-294Postnatal management of antenatally detected hydronephrosis

Grade	Features
I	urine barely splits urinary sinus
II	Moderate renal pelvis splitting confined to renal border with dilated major calyces
III	Pelvis distended outside of renal border major and minor calyces are dilated, parenchyma is spared
IV	Parenchyma thinned out

REVIEW OF COMMON IMAGING MODALITIES OF HN

GRAY SCALE ULTRASOUND

Very sensitive in the detection of hydronephrosis with limited capability to demonstrate residual renal function, level of obstruction and to differentiate obstructive from non obstructive HN

INTRAVENOUS UROGRAPHY

As IVU is one of the most complete diagnostic tools for viewing the upper urinary tract in infants and children depicting both morphology and function, IVU persists to be basic requisite in pediatric radiology. With the addition of new methods of imaging the urinary tract, this technique is now in universal decline and the indications for an IVU (like adult radiology) have undergone some changes.

Current indication for IVP:

- hematuria and colic, or other signs or symptoms that suggest a urinary calculus, with indecisive US result
- certain congenital abnormalities, e.g. urinary dribbling in girls (ectopic ureter)
- recent urinary tract surgery, when the urinary tract will be at risk for future deterioration, or preoperative anatomic assessment
- abnormal findings on a renal US that may indicate the need for IVU like calyceal diverticula

In our setup, IVU remains one of the indispensable imaging modalities in pediatric urology despite of its high radiation dose and invasive nature with long examination time

VOIDING CYSTOUROGRAPHY

Allows for detection and evaluation as well as grading of VUR, additionally enables functional assessment.

There are some clinically important facts that illustrate the importance of VUR and its diagnosis:

- VUR and urinary tract infections (UTIs) correlate with renal scarring, and particularly bilateral reflux nephropathy or scars have a high risk for hypertension and renal insufficiency.
- UTI is much more common in patients with functional bladder disease and/or VUR, and there is a strong correlation between particularly high degree VUR and pyelonephritis.

VCUG is still considered the gold standard for VUR and urethral evaluation.

NUCLEAR RENAL SCINTIGRAPHY

Half-time drainage is considered the gold standard for the diagnosis of renal obstruction.

The calculation of half-time drainage is more objective in the diagnosis of obstruction. Those kidneys able to excrete more than half of the radioisotope in less than 10 minutes against an empty bladder are considered non-obstructed and those requiring greater than 20 minutes are considered obstructed. Although diuretic renography is non-invasive, it has the disadvantages of being expensive, ionizing radiation and having a 10 to 15% rate of false-positive and indeterminate results (Howman - Giles et al., 1987) .Differential renal function is derived by comparing isotope uptake in the two kidneys, which in turn is a reflection of renal blood flow

MAGNETIC RESONANCE UROGRAPHY

The primary indication for MR urography in pediatrics is in the evaluation of hydronephrosis. Other evolving indications for MR urography include evaluation of renal scarring and dysplasia, identification of ectopic ureters in children with urinary incontinence and, characterization of renal masses (13).

Excretory phase T1- weighted images with I.V contrast, gives morphological and functional information about the excretory system and evaluates both parenchyma and urinary tract.

MRU provides a complete morphological and functional renal study.

Renal Doppler Ultrasound as Imaging Modality in Hydronephrosis

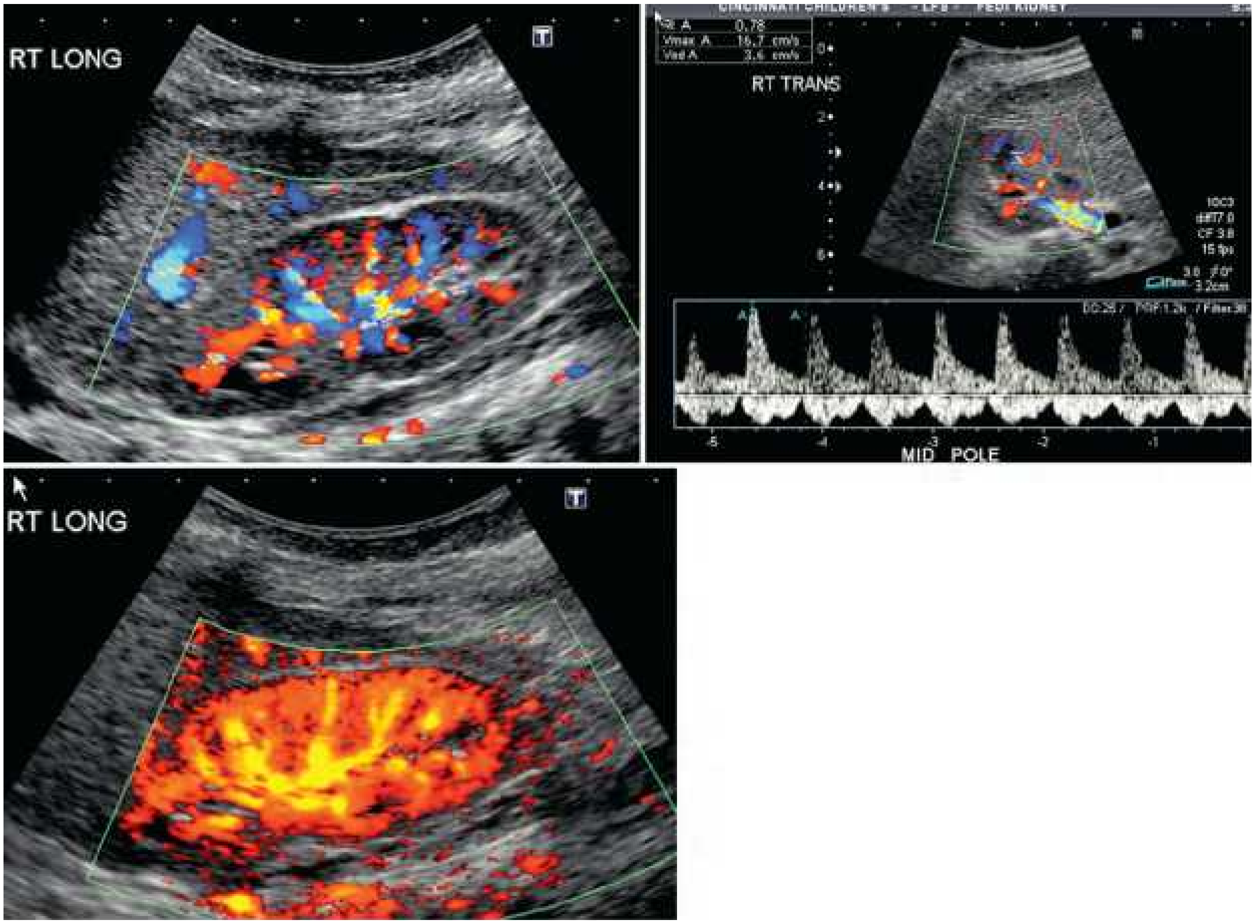
Review of Normal Vascular Anatomy and Flow Patterns *in Children*

The main renal artery divides in the renal hilum to form several pairs (anterior and posterior) of segmental arteries. These course toward the pyramids and there divide into interlobar branches, which follow the periphery of the pyramids. At the outer edge of the pyramids, interlobar arteries give rise to arcuate arteries, which follow the outer contour of the pyramids. Cortical arteries arise from the arcuate arteries and radiate into the cortex, following a direction like that of interlobar vessels. The venous circulation follows that of the arteries, and simultaneous adjacent signals are often visible both with color Doppler sonography and on spectral analysis.

The renal arterial bed normally has low resistance, and there is a constant flow into the kidney throughout the cardiac cycle (14)

The normal adult resistive index (RI) is estimated at 0.65± 0.10. In the neonatal period, probably concurrent with the physiologic low glomerular filtration rate, the resistance of the renal arterial bed is somewhat higher: RI=0.7 to 0.8. Because there is a range of normal RI values, the diagnosis of abnormal intrarenal resistance is much more reliably made by comparing waveforms from the pathologic kidney to those of the normal kidney (14).

Figure 1.



NORMAL INTRARENAL CIRCULATION.

A, Color Doppler sonogram of an infant shows the position of intrarenal vessels at the hilum (segmental) alongside the pyramids (interlobar) and at the inner edge of the cortex (arcuate). **B,** Spectral display from a normal segmented artery (parabolic, low resistance, allowing high diastolic flow) and vein (triphasic flow reflecting right atrial pulsations) **C,**Power Doppler ultrasound with increased sensitivity demonstrates flow in the renal cortex to the periphery.(source Carol M.Rumack text book of ultrasound 4th ed.)

THE ROLE OF DOPPLER ULTRASOUND IN HYDRONEPHROSIS

Platt et al (1989) described the use of renal resistive index to differentiate obstructive from non-obstructive pyelocaliectasis.In an effort to define a good discriminatory value to differentiate obstructive from non-obstructive dilatation they reported a large series of patients, including 70 with pyelocaliectasis (Platt et al., 1991). In the38 obstructed kidneys mean resistive index (0.77 ± 0.05) was elevated compared to that of 32 with non-obstructive dilatation (mean 0.63 ±0.06).

These 70 kidneys allowed Platt et al to plot a receiver operating curve that identified 0.70 as an optimal discriminatory resistive index value. This threshold value achieved 92% sensitivity, 88% specificity and 90% overall accuracy in diagnosing the presence or absence of obstruction in the adult population (15)

Mizini et al (2016) evaluated 16 children with renal Doppler and found that RI was significantly different between obstructive and non-obstructive hydronephrosis. Obstructive hydronephrosis returned higher RI values, with mean RI of 0.78. Mean RI in non-obstructive hydronephrosis was 0.70, and the difference was significant ($p < 0.05$).

FACTORS AFFECTING RENAL DOPPLER RI

Hydration status and diuretic use cause renal vasodilation and decrease vascular resistance with more effect on the diastolic phase causing reduction RI in healthy kidneys and inverse effect on obstructed kidneys. Age < 4years and renal parenchymal disease are associated with high RI because of decreased blood flow in diastolic phase (17)

STATEMENT OF THE PROBLEM

Because of universal antenatal sonographic evaluation of every pregnant woman at least once in pregnancy, most hydronephrosis cases are currently diagnosed in-utero. Dilation of the fetal renal collecting system, antenatal hydronephrosis (ANH), is one of the most common abnormalities detected on prenatal ultrasonography (US), reported in approximately 1-5% of all pregnancies (1). With the advent of routine prenatal US, children with urinary tract obstruction or reflux are being detected prior to the development of complications such as urinary tract infection (UTI), kidney stones and renal dysfunction or failure. These complications might be averted by early diagnosis. Consequently, the goals of evaluating children with ANH or post-natally diagnosed HN are to prevent these potential complications and to preserve renal function. However, not all findings on prenatal US represent pathology; many are transient and have no clinical significance. The dilemma therefore is to distinguish children who require follow up and intervention from those who do not (18). To answer this question, the first thing is to identify obstructive from non-obstructive type of urinary tract dilatation because the majority of the non-obstructive varieties resolves spontaneously on follow up. For this, different urologic imaging modalities are established like diuretic renogram which is not available in resource limited set ups and IVU which is invasive and has a significant amount of radiation. The other important clinical problem observed in our set up is, after pyeloplasty is done for PUJ obstruction, children are repeatedly referred to for IVU to see effectiveness of therapy since diuretic renography is not available. As described above, IVU has an inherent side effect and is not 100 % sensitive and specific as well. Therefore, renal Doppler study with its non-invasive nature, easy availability and good sensitivity and specificity as observed from previous studies may replace the existing imaging modality or may be used as an adjunct to increase diagnostic accuracy.

CHAPTER TWO: LITERATURE REVIEW

MAGNITUDE AND FACTORS RELATED WITH HYDRONEPHROSIS IN CHILDREN

Despite recent advances in the field of urological ultrasonography, certain disorders of the upper urinary tract such as dilatation remain elusive to conventional imaging techniques. While conventional ultrasound is a sensitive method for detecting upper urinary tract dilatation with up to 98% sensitivity reported in earlier studies (19), it lacks the ability to provide significant physiological data on renal status and, hence, cannot specifically assess the cause of observed dilatation. This lack is especially relevant in the pediatric age group, in which pyelocaliectasis is not necessarily synonymous with obstruction, and where proper management largely depends on detecting the underlying cause of dilatation. However, with the advent of Doppler ultrasound new insight into the physiology of the kidney has emerged enabling the detection of subtle renal blood flow changes associated with various pathophysiological conditions. These changes may be semi-quantified by calculating the intrarenal vascular resistive index, which is defined by the formula, resistive index = (peak systolic frequency shift − end diastolic frequency shift)/peak systolic frequency shift .Under normal homeostatic conditions the renal circulation offers low impedance to blood flow throughout the cardiac cycle with continuous antegrade flow during diastole (20).However, during conditions associated with increased renal vascular resistance the decrease in renal diastolic blood flow is more pronounced than the decrease in the systolic component (21). During extreme elevations of renal vascular resistance, diastolic flow may be non-detectable or may even show retrograde propagation. Therefore, the ability of the Doppler to characterize altered waveforms in response to elevations of renal vascular resistance may be used to calculate the resistive index and may possibly be used to discriminate among various pathophysiological conditions of the kidney (15). In addition, Doppler ultrasound obviates the need for ionizing radiation and intravenous contrast material administration in situations in which they may be undesirable, such as pregnancy, allergy and renal insufficiency.

RESISTIVE INDEX- NORMAL RANGE AND VARIABILITY

A prerequisite for the diagnostic use of resistive index measurements is the definition of a normal range, variability of measurements and an upper limit of the normal resistive index. In 1989 Platt et al (15) established a nomogram and a resistive index cutoff value that would set the basis for many of the studies in this field. In their series of 109 non-dilated non-diseased normal adult kidneys the resistive index range was 0.50 to 0.67 (mean plus or minus standard deviation 0.58 ± 0.05). The upper limit of normal was defined by analyzing a subgroup of 70 dilated kidneys, of which 38 subsequently proved to be obstructed, using conventional methods, such as percutaneous nephrostomy, retrograde pyelography, excretory urography (IVP) and contrast enhanced body computerized tomography. This analysis resulted in a resistive index of 0.70 as the optimal cutoff value of obstructed versus non-obstructed hydronephrosis, yielding 92% sensitivity, 88% specificity and 90% overall accuracy (15)

It is now generally accepted that the resistive index is an age- dependent parameter. Bude et al (22) showed that infants younger than 6 months of age had significantly higher mean resistive index values than adults and in this age group the probability of an index greater than 0.70 was as high as 57%. Values also tended to decrease with increasing age, approaching adult levels at about year 4 of life, and by age 7 years, values were similar to those in adults. Adult criteria may be applied to children from the beginning of year 4 of life with a probability of a mean resistive index of greater than 0.70 as low as 2% in healthy children (20).

THE RESISTIVE INDEX AND THE OBSTRUCTED UPPER URINARY TRACT

Obstructive uropathy is usually associated with dilatation of the upper urinary tract. However, not all dilatation is obstructive in nature. The differentiation of obstructed and non-obstructed dilatation is crucial and has important implications when contemplating treatment, particularly in children, in whom needless surgery may be avoided. Gray scale ultrasound and IVP are sensitive detectors of pyelocaliectasis but further elaboration on etiology cannot always be made based on such investigations (23). Here Doppler ultrasound may have an important role as an adjunct to conventional ultrasound.

Resistive index measurements were compared with the results of renography in the evaluation of children with hydronephrosis. The resistive index detected obstruction with 100% sensitivity and 87% specificity when considering 0.70 as the upper limit of normal. A resistive index of >0.7 and a resistive index difference of >0.10 between kidneys in children are suggestive of renal obstruction, while resistive index of <0.70 generally indicates non-obstructive dilation (15).Furthermore, there was excellent correlation of the resistive index with renography half-time drainage time (24). In another study 33 dilated kidneys with various grades of obstruction were compared with 56 normal control units, resulting in 57% sensitivity and 98% specificity (25). Further stratification of the dilated obstructed group into mild and significant obstruction subgroups based on IVP criteria improved sensitivity dramatically to 93%, leading that group to propose that mild and/or partial obstruction does not affect renal blood flow patterns and justifying observation and follow up in cases of mild obstruction with a resistive index of 0.70 or less

INTER-RENAL RESISTIVE INDEX DIFFERENCES

Under normal conditions the resistive index difference and ratio do not exceed 0.08 to 0.1 and 1.10 respectively. It has been demonstrated in a number of studies that the resistive index difference enhances the sensitivity and specificity of Doppler studies, and enables the detection of obstruction in kidneys with bilaterally elevated baseline resistive index values, as in cases of renal medical disease or when the index has not yet reached the threshold value of 0.7.A recent study of Shokeir et al (17) provided evidence of a divergent response to unilateral obstruction, that is a significant ipsilateral resistive index increase and contralateral decrease, a factor that may have a role in augmenting the resistive index difference.

DOPPLER ULTRASOUND AS A FOLLOW-UP TOOL

The relief of obstruction after reconstructive surgery, stone passage, or placement of a stent or nephrostomy tube leads to normalization of the resistive index. This finding has been documented in several clinical and experimental studies (26, 27). Doppler ultrasound has been recommended as a follow up tool by a number of groups, particularly in the pediatric age group, in which serial investigations are often needed to monitor kidney function preoperatively or postoperatively, lessening the need for studies of a more invasive nature (28).

Predicting kidney function recoverability in cases of chronic obstruction has also been suggested as a potential use of Doppler ultrasound measurement. Shokeir et al reported that the reversal of a previously elevated resistive index was a likely indicator of kidney recoverability (27). Clinically this result may be achieved by monitoring the resistive index of a chronically obstructed kidney before and after temporary release via percutaneous nephrostomy or pyeloplasty.

Doppler ultrasound sensitivity and specificity for diagnosing obstruction using various threshold values

References	No. Pts.	Cutoff Value		% Sensitivity	% Specificity	Final Diagnosis Made
		Resistive Index	Resistive Index Difference			
Platt et al[63]	23	0.70	—	87	100	IVP
		—	0.1	91	Not available	
Shokeir and Abdulmaaboud[64]	68	0.70	—	77	83	IVP
		—	0.06	88	98	
Miletic et al[65]	54	0.69	0.06	94	90	IVP
						Retrograde, antegrade pyelography, clinical course
Opdenakker et al[77]	23	0.68	0.06	83	100	IVP
Tublin et al[66]	19	0.70	—	37	84	IVP, retrograde pyelography
		—	0.1	37	100	
Deyoe et al[67]	10	0.70	0.1	30	Not available	IVP
Older et al[69]	19	0.70	0.1	42	79	IVP

Figure 2. The intrarenal resistive index as a pathophysiological marker of obstructive uropathy. Source: Rawshdeh et al. the intrarenal resistive index as a pathophysiological marker of obstructive uropathy. literatiure review. Journal of urology.May 2001Volume 165, Issue 5, Pages 1397–1404.

CHAPTER THREE: OBJECTIVES

GENERAL OBJECTIVE

- To assess renal resistive index difference as diagnostic tool to differentiate obstructive and no obstructive urinary tract dilatation among children in Tikur Anbessa specialized hospital, October, 2018.

SPECIFIC OBJECTIVES

- To assess correlation between degree of obstruction and level of RI, among children at Tikur Anbessa specialized hospital, October, 2018.
- To determine difference in RI in obstructive and non-obstructive urinary tract dilation Tikur Anbessa specialized hospital, October, 2018.
- To assess renal arterial RI diferrence between surgicaly corrected and uncorrected urinary tract dilataltion at Tikur Anbessa specialized hospital, October, 2018.
- To determine specificity, sensitivity, and overall accuracy of Doppler RI in differentiating obstructive and non –obstructive hydronephrosis among children at Tikur Anbessa specialized hospital, October, 2018.

CHAPTER FOUR: METHODOLOGY

4.1. Study Area and Period

The study was conducted at Tikur Anbessa Specialized Hospital department of Radiology. The study was conducted from Hidar 1/2010-Hamle 30/2010 for a period of 8 months

4.2. Study design: Institution based cross sectional study.

4.3, Source population

All children who were referred to ultrasound department of Tikur Anbessa Specialized hospital from November, 2017 to July, 2018.

4.4 Study population

All children who are diagnosed with hydronephrosis referred to Tikur Anbessa Specialized hospital from November, 2017 to July, 2018.

4.5. Inclusion and exclusion criteria

Inclusion Criteria's

All children who were diagnosed with hydronephrosis ranging from new born to 14 years of age.

Exclusion Criteria's

Children who had additional diagnosis of medical renal disease or vascular renal disease were excluded from the study.

4.6. Sample size determination and sampling technique

4.6.1. Sample size determination

In this study the main purpose is determining mRI difference between obstructive and non-obstructive hydronephrosis. Therefore, sample was calculated using comparison between two groups when endpoint is quantitative data.

The formula for this type of sample size determination is as follows

$n = (s_1^2 + s_2^2)\ f(\alpha,\beta) / (m_1 - m_2)^2$

n is sample size in each group and total sample size N=2n assumed that equal number of subjects will be involved in each group

m1 and $s1^2$ are mean and variance of group 1 respectively.

m2 and $s2^2$ are mean and variance of group 2 respectively

$f(\alpha,\beta)=(1.96+1.282)^2{}_{=10.5}$

α=0.05(two sided),Z=1.96 and power of study is assumed 90% value of β=1.282

The results from similar study done in Malaysia in renal Doppler assessments of the intra-renal renal arteries were performed on 16 children (19 kidneys) with congenital hydronephrosis. Their result showed RI ranging from 0.73 to 0.85 in obstructive hydronephrosis with a mean of 0.78 and standard deviation (SD) of 0.04. The RI in non-obstructive hydronephrosis ranged from 0.62 to 0.81 with a mean of 0.70 and SD of 0.07 . There was significant difference in the mean RI between obstructive and non-obstructive hydronephrosis .Convenience sampling method was used in this study and all children with diagnosis of hydronephrosis and who fulfill inclusion criteria were included with a p-value of 0.04 ($p<0.05$). Substituting these numbers in the appropriate place the final sample size was 42 patients . Adding 10% contingency the total sample size will be 46

4.6.2. Sampling methods: Consecutive convenient sampling was used .

4.7. Data collection method and tools

3.5-6 MHz frequency transducer sector was used for older and heavy children and linear high frequency 6.9-11MHz transducer was used for neonates and small children. Renal arteries at the hilum were approached trans-abdominally anteriorly or trans-lumbar posteriorly depending on technical choice.

Renal arterial Doppler study was done on both hydronephrotic and non-hydronephrotic kidney by senior radiology resident who is practicing in pediatric unit as per assignment and data was filled in structured data format sheet.

Grade of hydronephrosis was documented according SFU. The patient’s medical file was reviewd at scanning site concerning confirmation nature of hydronephrosis and operative treatments for obstructive hydronephrosis.

To maintain data quality main investigator has discussed and resolved difficulties during Doppler data collection.

4.8. Study Variables

A. Independent Variables

- Sociodemographic factors: age of the child and gender
- Obstructive hydronephrosis
- Non-obstructive hydronephrosis
- Surgically treated obstructive hydronephrosis
- Grade of hydronephrosis

B. **Dependent Variable**

- Renal arterial Doppler resistive index of hydronephrotic kidneys
- Mean RI deference between obstructive and non-obstructive hydronephrosis
- The relationship between degree of hydronephrosis and mean RI
- The mean RI difference between treated and non-treated obstructive HN

4.9. Operational Definitions and Definition of Terms

Doppler: is measurement of frequency shift in moving physical entities like bled cells in the blood vessel and measuring of flow velocity and determination of flow direction.

Doppler ultrasound: is technique to measure flow velocity and direction based on the Doppler principle as described above.

Hydronephrosis: dilatation of upper urinary tract including renal pelvis, calyces and ureters

Obstructive: any lesion or pathology which impedes flow of urine from kidneys to bladder.

Non-obstructive: dilatation of upper urinary tract without apparent obstructive lesion or cause

Resistive index: is defined as ratio of (peak systolic velocity-diastolic velocity)/ peak systolic velocity as measured by Doppler ultrasound.

Renal cortical thickness: it represents average of renal cortical-thickness measured by centimeters at upper pole, midpole and lower pole.

IVP/IVU: study of function and anatomy of kidneys, ureters and bladder after intravenous injection of iodinated contrast media and series of x-ray films are taken according to predetermined time sequence like immediate, 5minutes, and 15 minutes

VCUG/MCUG: study of lower urinary tract while contrast is being injected through the urethra and during active voiding to see urethral pathology and refluxing of contrast in to the ureters during voiding as intravesical pressure increases.

4.10. Ethical considerations

Written ethical approval was obtained from Ethical Review committee of the department of radiology before the actual data collection commenced as this research is conducted on human subjects

4.11. Data analysis

Data was manually entered in to the SPSS25.0 and appropriate descriptive and analytic statistics was done**.** During the analyses P-value < 0.05 with 95% confidence interval (CI) for t-test was used in judging the significance of the difference . Finally results were displayed using text, frequency tables, charts , statistical analysis was done using independent t-test for mean difference of RI between obstructive and non-obstructive hydronephrosis . Receiver operative characteristic curves was constructed to demonstrate sensitivity ,specificity and diagnostic accuracy of Doppler mean RI in differentiating obstructive HN from non-obstructive HN.

3.12. Plan of Dissemination

The finding will be presented in Addis Ababa University, Department of Radiology with invited guests from pediatric urologic surgery. Finally, efforts will be made to publish it in a scientific journal.

CHAPTER FIVE: RESULTS

Sociodemographic character of Participants

The study has included total of 42 children who were scanned for gross grading of hydronephrosis and Doppler assessment of RI. Among these three forth 31 (73.8%) were males and 11 were females (26.2%). The age of participants ranged from 0-14years and mean age was 4.43 years with SD of 4.11, median 4.75years .About six in ten (62%) participants had unilateral and (38%) participants had bilateral hydronephrosis .Total hydronephrotic kidneys were 61 where obstructive one accounts 45(73.8%).

Cause and diagnosis of Hydronephrosis and Doppler results

Two third of the hydronephrosis was detected postnatally 66.7 % and prenatal was 33%. Hydronehrosis which was detected antenataly was caused by PUJ obstruction and PUV .The most common cause for obstructive hydronephrosis was PUJ obstruction accounting about 47.6% followed by posterior urethral valve 16.7%. For non- obstructive hydronephrosis VUR was the main cause followed by prune belly syndrome and rarely bladder exstrophy. Two patients had mass one neuroblastoma and the other was ovarian tumor, and one patient had retroperitoneal fibrosis

Almost all of the hydronephrosis was detected initially by ultrasound and confirmation was done with IVP for PUJ obstruction 10 (23.8%),VCUG for posterior urethral valve and VUR 16 (35.7%) surgery alone 14.3% and IVP+ surgery 9.5 % and the rest was by CT scan. Contrast enhanced CT has confirmed diagnosis of neuroblastoma , ovarian mass and retroperitoneal fibrosis as cause of obstructive hydronephrosis

Concerning severity of hydronephrosis more than half have moderate hydronephrosis which accounts about 54.8% and mild and severe accounted 14.3&31 % respectively according to the grading system of fetal urology

The mean resistive index of non -hydronephrotic kidneys was 0.6654 with SD of 0.053 non obstructive hydronephrotic kidneys 0.6825 ,SD 0.06668 and obstructive kidneys had mean RI of 0.7791 ,SD 0.11977.

The mean RI difference between the obstructive and non-obstructive hydronephrosis was 0.09661 with standard error of difference 0.02443 .The statistical significance was tested with students independent t-test with P-value of< 0.0001 and CI (0.04749 ,0.1457) where critical t-value of 2.01 and calculated t-value 0f 3.955.

The test had confirmed significant difference between mean RI of obstructive and non obstructive hydronephrosis but Levine's test of equality of variance disproved the equality of the variances between the groups. No statistically significant difference was found between the degree of hydronephrosis and mean RI.

The mean RI untreated obstructive hydronephrosis is 0.8347, SD.08626 that of surgically corrected hydronephrosis 0.7100 SD 0.129 which was statistically significant (p=0.04)

Table 3. Mean RI of hydronephrotic kidneys among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

Group Statistics

	nature of hydronephrosis	N	Mean	Std. Deviation	Std. Error Mean
average RI of hydronephrotic kidney	Obstructive	45	.7791	.11977	.01785
	non-obstructive	16	.6825	.06668	.01667

Table 4. Participants age distribution among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

Age	Frequency	Percentage
<1yr	13	31
1-4 yr	11	27.1
>4yr	18	41.9

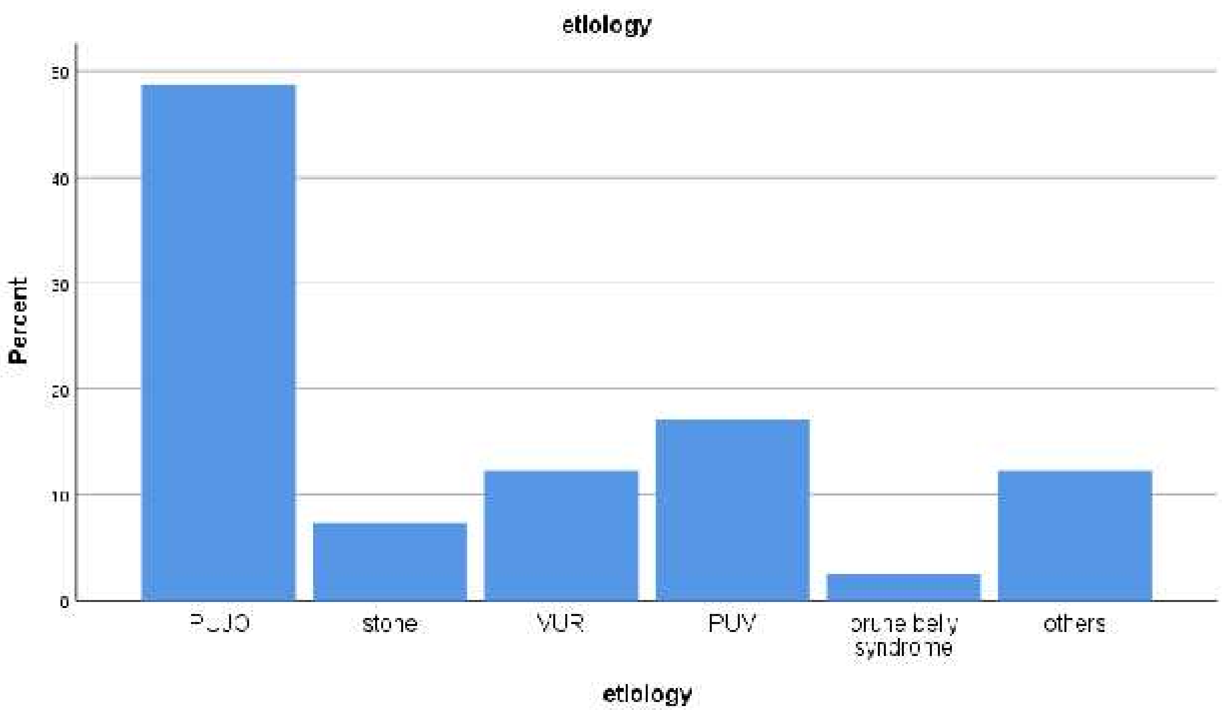


Figure 3. Etiology of hydronephrosis among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

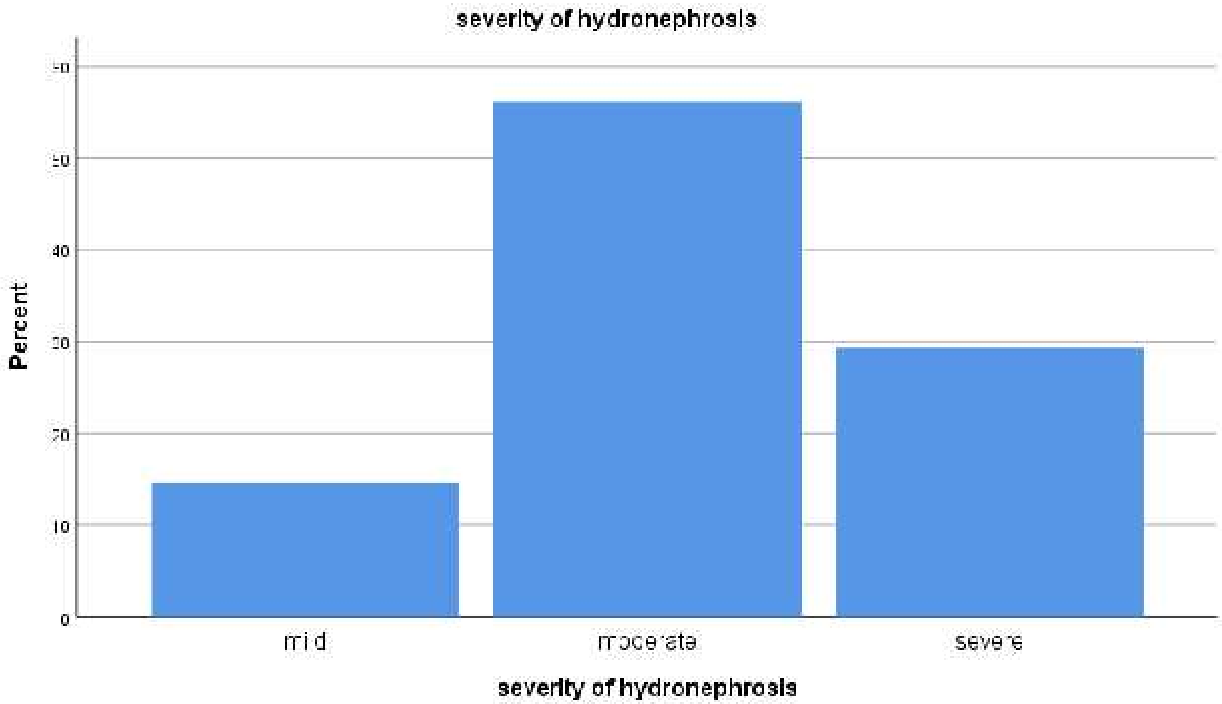
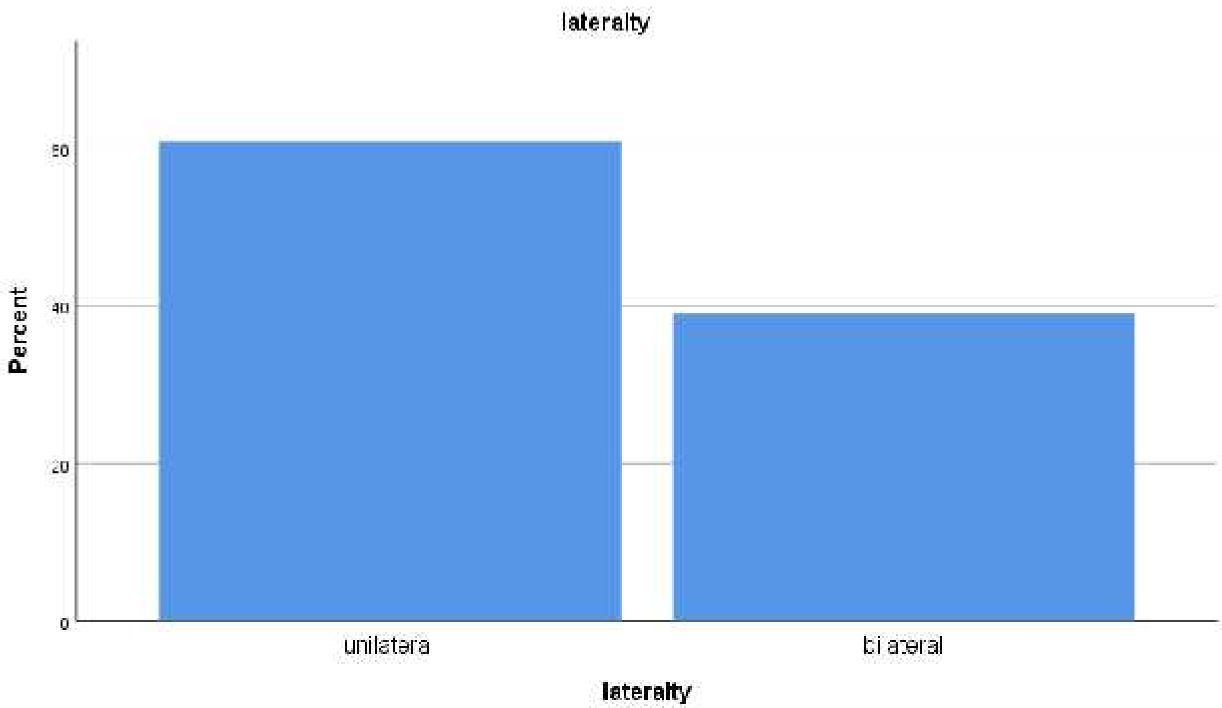


Figure4. Severity of hydronephrosis among children in Tikur Anbessa specialized hospital (n=42), October, 2018.



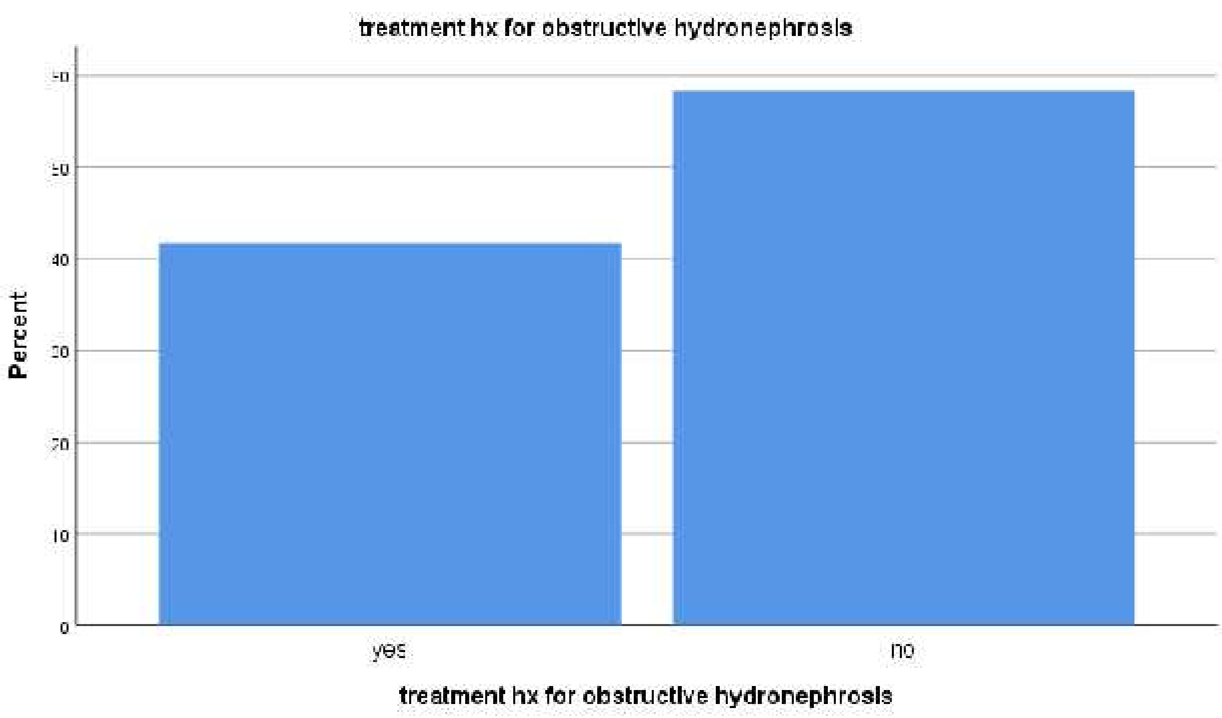


Figure5. Treatment history for obstructive hydronephrosis among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

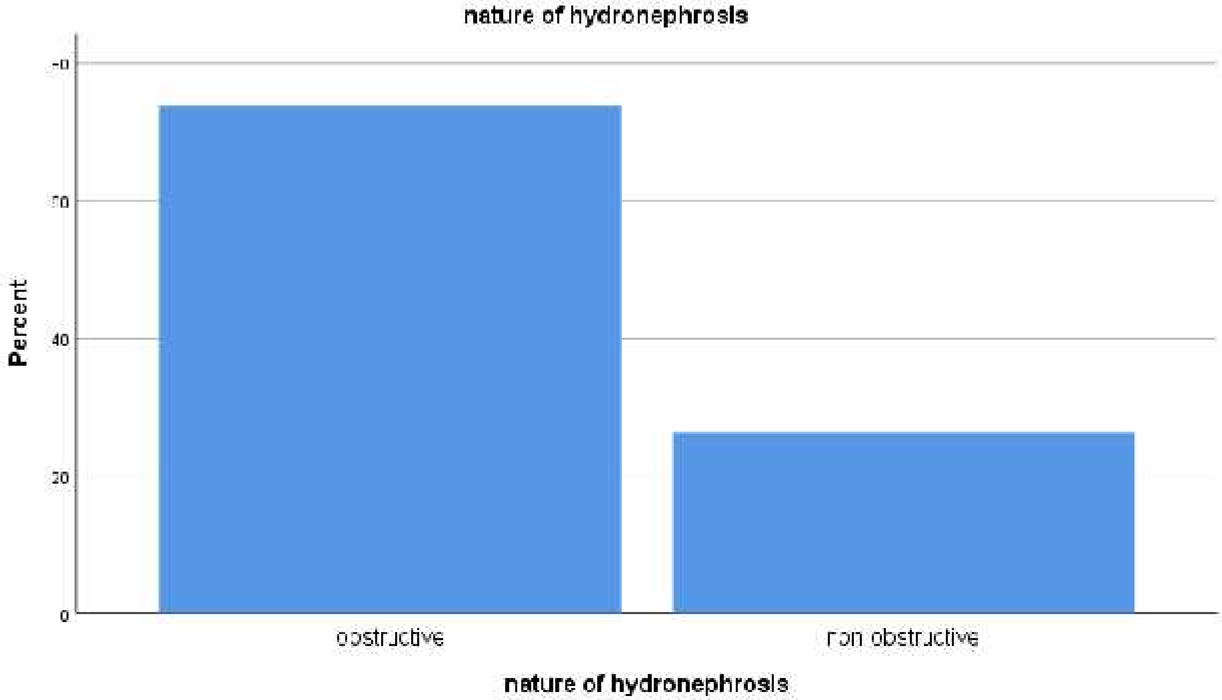


Figure6. Nature of hydronephrosis among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

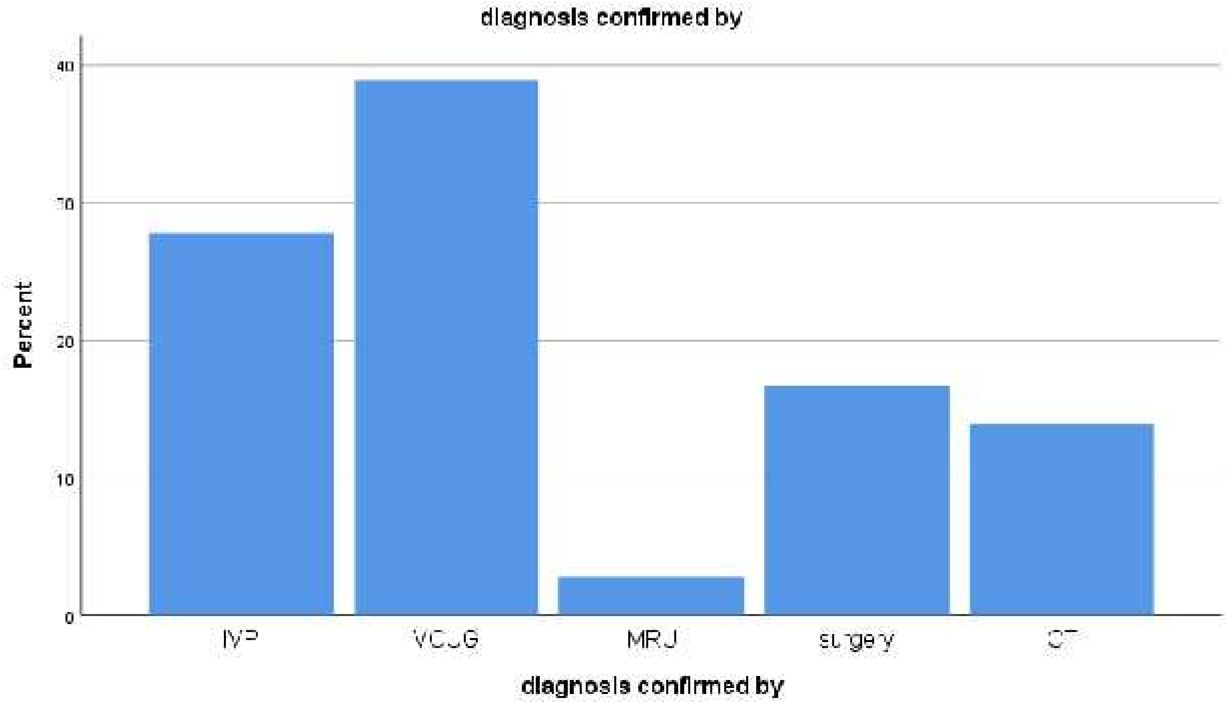


Figure7. Hydronephrosis confirmation diagnosis among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

CHAPTER SIX: DISCUSSION

The majority (73.8%) of the participants in this study were male children likely due to posterior urethral valve which is common and exclusively occurs in males. PUJ obstruction was also common in males than females particularly infant males were affected five times more than their counterpart. That is why hydronephrptic male children were significantly higher than female children in this study which is consistent with previous studies from other researchers.

In this study the most common cause of the obstructive hydronephrosis was PUJ obstruction which is consistent with other studies (Palmer LS et.al1998, Okada et.al 2001) followed by PUV. In other studies PUV is discovered rarely and has accounted only about 1-2%.

In this study, hydronephrosis was mainly detected by ultrasound and natures & etiology was confirmed by IV& surgery for PUJ obstruction and VCUG was main diagnostic modality and confirmatory for PUV and VUR. This consistent with other studies (Hashim H,et.al.2012). But other studies use nuclear scintigraphy as gold standard to confirm obstructive versus no obstructive hydronephrosis depending on the calculation of half time drainage. The kidneys which are able to excrete more than half of the radioisotope in less than 10 minutes against an empty bladder are considered non-obstructed and those requiring greater than 20 minutes were considered obstructed (Howman - Giles et al., 1987).

MRU was not widely used as diagnostic test in this study most probably because relatively new imaging modality and sedation and length scan time. Most referring physicians are also stacked worth old modalities like IVP and CUG

Different investigators had tried a number of researches to use mean resistive index of renal artery to differentiate obstructive and non obstructive hydronephrosis.

Duplex Doppler ultrasound is a tool which can provide useful information about hemodynamics of kidneys while it is non-ionizing modality. It has been demonstrated that obstruction causes a decrease in vascular flow due to increasing in vascular resistance. This might be of particular importance in our set up since we do not practice nuclear renogram and duplex Doppler may substitute it.

This study has shown significant RI difference between the obstructive and non obstructive hydronephrosis with mean RI difference between the obstructive and non-obstructive hydronephrosis is 0.09661 with standard error of difference 0.02443 , P-value of <0.001and confidence interval CI (0.04749-0.1457)

The result is consistent with many studies as shown below in the table

Table 5 : Comparison of the Doppler results with pervious published data, October, 2018.

Study	**Total no-of kidneys**	**Obstructed**		**Non-obstructed**	
		RI ± SD	**N**	**RI ± SD**	**N**
Okada et.al (2001)	22	.84	**7**	.65	15
Svitac et al	19	.77	11	.69	8
Kessler etal (1993)	36	.77±0.05	20	.63±.06	16
Mallek et al	20	0.77±0.03	8	.63±.0.08	12
Platt et a l(1989)	21	0.77±0.04	14	.64±..04	7
Our Study (2018)	61	.7791±.119	45	.6825±..066	16

The above comparative table shows that our result is consistent with previous studies even has better sample size than those mentioned which increases statistical power

Using 0.7 as cut point area under the ROC curve of RI is 0.754 with CI 0.626-0.882, P-value of 0.003 which is equivalent to accuracy of the test and sensitivity and specificity of 71.1%, 81.2% respectively

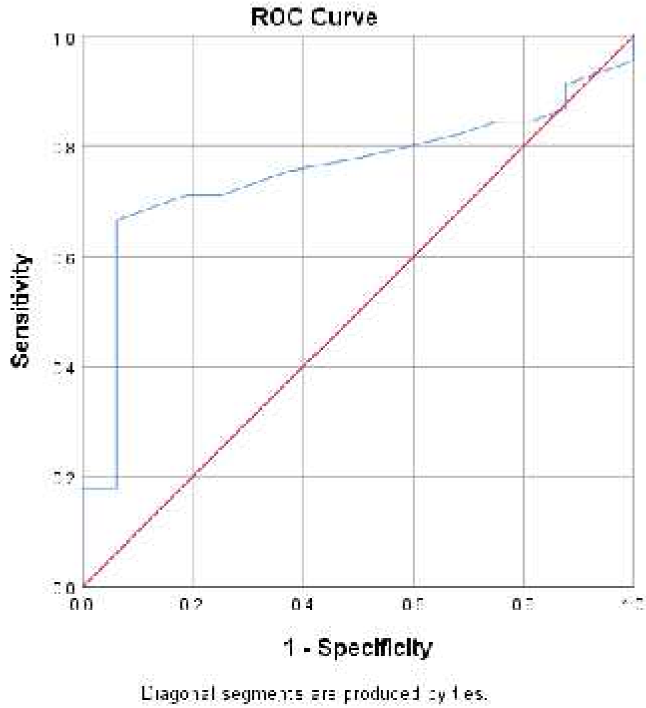


Figure 8. ROC curve among children in Tikur Anbessa specialized hospital (n=42), October, 2018.

Investigator	Sample size(units of kidneys)	Sensitivity	Specificity	accuracy
Kessler et.al (1993)	36 (20 obstructed)	100%	94%	-
Platt et.al (1993)	21 (14 obstructed)	92%	88%	-
Brkljacic *et al (2002)*	29 (17 obstructed)	70%	92%	-
Misni et,al(2015)	19 (6 obstructed)	93 %	53%	-
This study (2018)	61(45 obstructed)	71.1%	81.2%	75.4%

30

Table 6: coparison of sensitivity specificity and accuracy of Doppler in different studies from literature review

Most of the studies used 0.7 RI as discriminator and have found good diagnostic accuracy. This has also shown almost similar result with those previous studies.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

CONCLUSION

This study has showed mean renal arterial resistive index was significantly higher in obstructive hydronephrotic kidney than non-obstructive hydronephrotic kidney and can be potential valuable tool in resource limited countries to differentiate these conditions and as follow up tool after corrective surgeries.

LIMITATION

Hydration status and hear rate affect mean arterial resistance which are no considered in this study. Small sample makes statistical power poor Difficulty in measurement of mean Doppler resistive index in irritable children may have affected actual measurement results. Very small difference between the obstructive and non-obstructive resistive index makes the measurement imprecise Confirmatory studies used in differentiating the obstructive from non-obstructive hydronephrosis are static anatomic imaging modalities unlike nuclear renogram used in other studies.

RECOMMENDATION

Further investigation and validation is recommended with larger sample size and by experienced radiologist in Doppler scanning

Population based age dependent normal RI nomogram should be developed and stratified RI should be used in clinical decision making

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Annex

Annex I

DATA COLLECTION SHEET

I. Dempgraphic data

Patiet medical record no.______________Age______________gender____--

II. Diagnostic data

1. 1.Hydronephrosis diagnosed at: a. antenatal _________b .postnatal_________
2. 2.Hydronrphrosis detected by:A/ultrasound B/ IVP C / voiding CUG
3. Nature of hydronephrosis :A/ obstructive B/non obstructive
4. 3. Etiology: A/PUJ obstruction B/Stone C/VUR D/ posterior urethral valve E/ureterocele F/other (specify
5. Diagnosis confirmed by :A/ IVP B / voiding CUG C/ MRU D/ surgery
6. Laterality :A/ single kidney B/ both kidneys
7. 4.Degree of hydronephrosis according to SFA grading : A mild B/ moderate C/ severe
8. Treatment history of hydronephrosis (only for obstructive type) A/ treated B/ not treated

III DOPPLER DATA

1. Interrogated artery :A/main renal artery B/interlobar artery C/arcuate artery
2. Average RI of :A/non-hydronephrotic kidney _________B/hydronephrotic kidney_______
3. RI difference between non-hydronephrotic and hydronephrotic kidney_________
4. RI ratio of hydronephrotic-to-non-hydronephrotic kidney___________
5. For bilateral hydronephrosis RI of kidney__________RI of left kidney_____________